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Basis for skin notation. Part 1.

Dermal penetration data for substances on the Swedish OEL list

Gunnar Johanson, Matias Rauma

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Preface

Skin notations are used by many organizations and in many countries including Sweden. Thus, substances that may easily be absorbed percutaneously are marked with an “H” in the Swedish provisions on occupational exposure limits (OELs) (AFS 2005). This procedure started already with the first list of OELs introduced in 1974. OELs are given for 368 substances or substance groups in the present provisions (AFS 2005). Out of these, 101 substances/groups (27%) have a skin notation.

No formal or quantitative criteria have been developed in Sweden. The intent was originally that the skin notation would give a qualitative indication of possible dermal absorption of the chemical at work. In other words, the attempt was mainly to evaluate the ability of penetration through intact “healthy” skin, i.e. the intrinsic properties of the chemical relative to skin.

In an international perspective the criteria for assigning a skin notation vary widely but are generally qualitative rather than quantitative in nature. During the last few years, however, focus has shifted towards more quantitative assessments, either by expressing the intrinsic properties of the chemical in numerical terms, such as dermal absorption rate (flux) at defined conditions or by expressing the systemic exposure (absorbed dose), i.e. a combination of the intrinsic properties and the exposure conditions (exposed skin area, exposure duration etc).

In view of the large and increasing numbers of H-labeled substances, there is a need for more formal criteria. There is also a risk that the warning effect of the label is diminished if too many substances are labeled.

In view of these concerns, the Swedish Work Environment Authority (SWEA) has initiated a project with the aim to develop new criteria and procedures for skin notation. As input for the project, SWEA requested the Division of Work Environment Toxicology at the Institute for Environmental Medicine, Karolinska Institutet to produce two reports on dermal absorption in relation to skin notations and OELs.

The aim of the first report, presented herein, is to describe methods used to measure dermal absorption and to compile and evaluate published quantitative data on dermal absorption focusing on substances listed in the ordinance on Swedish OELs (AFS 2005). The second report will address different approaches to skin notation.

Literature searches, compilations and writing of the report were carried out by MSc Matias Rauma and professor Gunnar Johanson at the Division of Work Environment Toxicology. The final literature search was performed in January 2007. The cited papers were to a large extent supplied by the library at the Swedish National Institute for Working Life.

The major sources used were:

- Medline,
- the EDETOX database on the web (www.ncl.ac.uk/edetox/),
- consensus reports and criteria documents (and publications cited therein) published by the Swedish Criteria Group for Occupational Standards at the National Institute for Working Life,
- criteria documents (and publications cited therein) published by the Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals (NEG),
- the documentation (and publications cited therein) published by the Chemical Substance - Threshold Limit Values (CS-TLV) Committee of the American Conference of Industrial Governmental Hygienists (ACGIH), and
- secondary sources, i.e. references given in the above sources.

We wish to express our gratitude to associate professor Anders Boman (Occupational and Environmental Dermatology, Karolinska Institutet, Stockholm), professor Magnus Lindberg (Dermatology Unit, Örebro University Hospital), associate professor Pierre-Olivier Droz (Institute of Occupational Health, Lausanne), Dr. Karin Sørig Hougaard (National Research Centre for the Working Environment, Copenhagen) and associate professor Margareta Warholm (SWEA, Solna) for valuable comments on the manuscript. We are also grateful to MSc Tina Isaksson for compilation of some of the data.

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Stockholm July 2007

Gunnar Johanson Matias Rauma

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1. Introduction

The aim of this report is to review the published data on dermal penetration of workplace chemicals, as a basis for assignment of skin notations.

Dermal exposure is a major route of systemic exposure at work. Along with reductions in OELs and occupational exposure via air, the dermal route has become even more important.

Data on dermal absorption are input for so called skin notations. Skin notations are used as warning signals for chemicals that may easily be taken up via the skin, thereby causing - or increasing the risk of - systemic toxicity (see e.g. AFS 2005, SCOEL 1999). The decision to assign a skin notation is largely based on the ability of the chemical to penetrate skin. Sometimes experience from work practice is also considered, so that chemicals for which health effects have been seen at work after (presumed) dermal exposure are also assigned with a skin notation. Direct effects on the skin, such as irritation, corrosion and sensitization, are usually not considered.

The criteria for skin notations and their practical application are beyond the scope of the present report but will be described and discussed in a second report. Nevertheless, it should be mentioned that the relations between the presence of a chemical in the work environment and dermal dose, as well as that between dermal dose and systemic dose is very complex and highly variable. Thus, the first relationship is affected by a number of factors, such as the volatility and other properties of the chemical, how the chemical is used, the work process, the individual’s behavior and work practices, type of clothing and protective equipment, and so on. The influence of some of these factors may be highly variable and is often difficult to predict. The second relationship (and the focus of this report) depends on the properties of the chemical and the skin and is, at least in principle, more easily described and measured.

2. Anatomy of the skin

The skin provides a barrier between the human body and its environment. The major function is to prevent loss of water and heat to the environment. It also protects the body from mechanical, biological and chemical hazards.

The skin is the largest organ of the human body (15% of total adult body weight). The skin consists of three layers (from inside to outside): *hypodermis, dermis, epidermis* (figure 1). The hypodermis (subcutis) is the deepest part of the skin and contains mainly adipose tissue. The subcutaneous layer is important for protection from mechanical injuries, energy provision, thermoregulation and insulation.

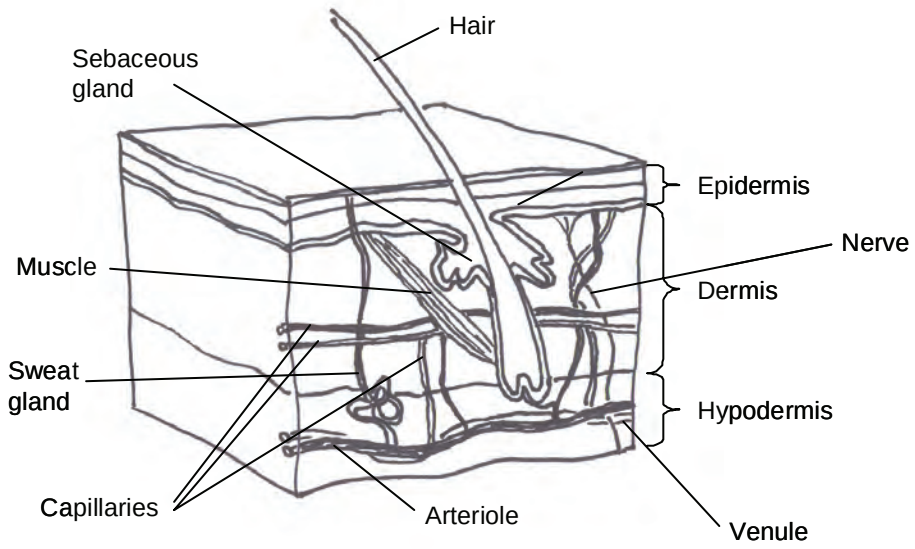

Figure 1. Drawing of the skin (adapted from http://www.nku.edu/~dempseyd/SKIN.htm).

The *dermis* contains connective tissue and provides elasticity, flexibility, strength and stability to the skin. The main cells are fibroblasts (synthesizing the collagen fibres), dermal dendrocytes and mast cells (belonging to the immune system). The dermis is in close contact with the abundant ridges and grooves of the epidermis. The ridges are enlarging the surface area between dermis and epidermis, allowing for a better adhesion and a more efficient exchange of nutrients and waste.

Both the dermis and hypodermis are richly innervated and vascularized. The skin appendages (hair, nails, sweat glands, sebaceous glands) originate in these parts of the skin, mostly in the dermis.

The *epidermal* layer consists mainly of keratinocytes (90-95%), Langerhan's cells (skin immune response), melanocytes (skin color and UV protection) and Merkel cells (slow-adapting mechanoreceptors for touch). The keratinocytes are constantly being replaced. The shape of the cells changes during their migration from the innermost part of the epidermis towards the surface of the skin (figure 2).

Based on the appearance in the microscope, the epidermis is subdivided in five different layers (from inside to outside): *stratum basale, stratum spinosum, stratum granulosum, stratum lucidum* and *stratum corneum* (figure 3).

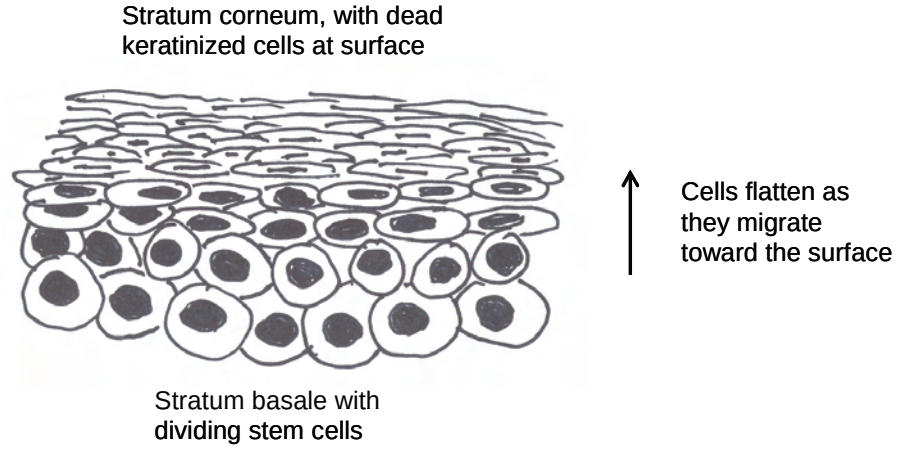

Figure 2. The maintenance of the epidermis (adapted from http://www.mhhe.com/biosci/ap /histology_mh/stratepi.html).

The *stratum corneum* consists of several layers of completely keratinized dead cells without a nucleus (corneocytes). The cells are stacked, leaving little space between them. Keratin is a tough, insoluble protein that is also the chief structural constituent of hair, nails, and hooves. Thus, the stratum corneum mainly consists of keratin and highly resistant to diffusion of water and other molecules (figure 3).

Thick skin has many layers of corneocytes cemented together. Thin skin has fewer layers of living and dead cells but the same overall structure.

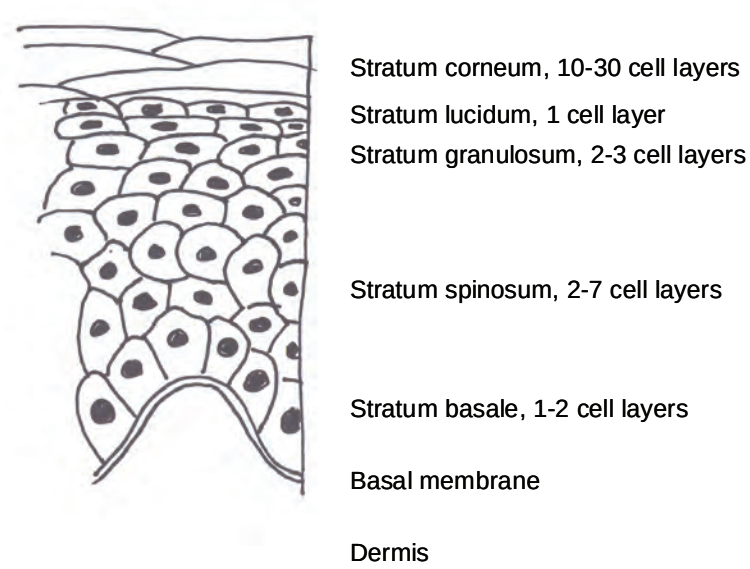

Figure 3. The five layers of the epidermis (adapted from Forslind & Lindberg 2004).

3. Skin as a diffusion barrier

A major function of the skin is to prevent loss of water to the environment. The humidity in the ambient air is often low and without an effective barrier the organism would rapidly loose large amounts of water. This would preclude life on land.

The major diffusion barrier is the stratum corneum. However, this skin layer is not entirely impermeable. Water as well as other small molecules diffuse more or less slowly through the skin. Water is very important to maintain the flexibility of the skin. Dry skin becomes rough and flaky and completely dried stratum corneum is reduced to a very brittle, thin sheet. Water is also important for thermoregulation, as the heat used to evaporate the water excreted via sweat glands lowers the temperature of the skin.

In principle, there are three possible diffusion pathways through the skin. The major route, especially for fat soluble, nonpolar molecules, is likely to be the intercellular lipid pathway. Due to the brick and mortar structure (figure 4), the "true" diffusion path is very much longer than the thickness of the stratum corneum. The diffusional pathlength has been estimated to be as long as 500 µm for stratum corneum of 20 µm thickness (Hadgraft 2004). Further, since impermeable corneocytes make up most of the skin and intercellular lipids constitute only a small part, the area accessible for diffusion is very small compared to the total skin area. Another factor that complicates diffusion is that the intercellular spaces contain structured lipids and a diffusing molecule has to cross a variety of lipophilic and hydrophilic domains.

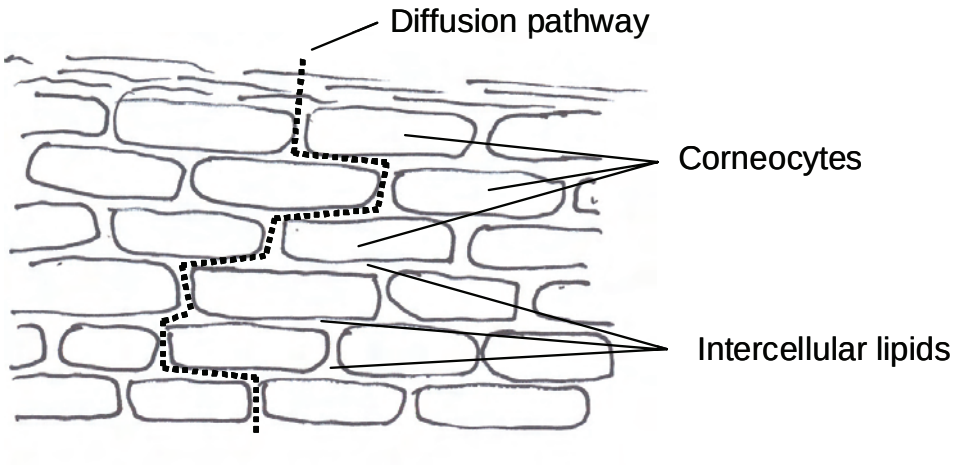

Figure 4. Brick and mortar structure of the stratum corneum showing dense, keratinized corneocytes, intercellular lipid layers and one of the diffusion pathways.

The second possibility is that of transcellular permeation, i.e. that the molecules diffuse through the corneocytes.

A third route of absorption is through the appendages (hair follicles). In most cases, this route is insignificant as the area of appendages is very small compared to the total skin area. However, in the initial phase of the absorption and for very slowly permeating chemicals, this route may be of importance.

The structure of the skin and the stratum corneum contrasts that of the lungs and the respiratory airways. Thus, whereas the skin is designed to resist diffusion (and loss of water) the lungs are built to facilitate diffusion (uptake of oxygen and release of carbon dioxide). In the skin, this is manifested by:

- a relatively small surface area (approximately 2 m^2 in a human adult), and
- a stratum corneum consisting of several densely packed layers of cells filled with highly resistant protein (keratin), resulting in high resistance long diffusion pathways (figures 2-4).

In contrast, the alveolae in the lungs have:

- a relatively large surface area (approximately 80 m^2 in a human adult), and
- only two thin cell layers (alveolar epithelium and capillary endothelium), resulting in a low resistance, short diffusion distance from ambient air to blood (figure 5).

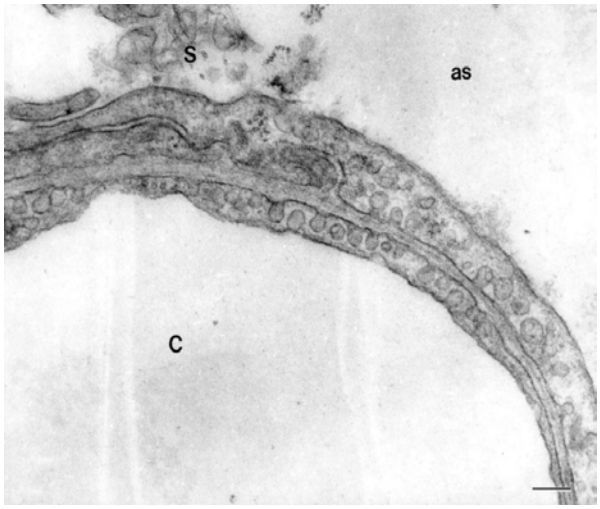

Figure 5. Transmission electron micrograph of the lung showing as: the alveolar airspace and c: the capillary lumen, separated by two thin cell layers with a total thickness of about 1 µm (taken from http://www.cf.ac.uk/phrmy/PCB/PageLungAlveolarepithelium.htm).

4. Fick's law of diffusion

The driving force for dermal absorption of practically all chemicals is diffusion, i.e. the spontaneous movement of molecules. The flux of molecules from the outer side to the inner side of a barrier (for example the skin) is proportional to the number of molecules at the outer side and the resistance of the barrier. Likewise, the flux from the inner to the outer side is proportional to the number of molecules at the inner side and the resistance of the barrier. The net flux is the difference between the two fluxes and can be described mathematically as:

$$P = K_p \, x \, (A_1 - A_2) \qquad (1)$$

Equation 1 is known as Fick's first law of diffusion. The parameter P is the net flux (number of molecules per time unit) and K_p is the permeability coefficient (resistance to diffusion). A_1 and A_2 the number of freely moving molecules outside and inside the barrier, respectively. Chemical activity is a measure of how different molecules in a non-ideal gas or solution interact with each other. For very dilute gases and solutions, molecular interactions are negligible and activity is also proportional to concentration. For gases, activity is proportional to partial pressure. A can thus be substituted by thermodynamic activity, partial pressure or, for dilute solutions, concentration. Such substitution will only alter the value of K_p, as these parameters are directly proportional to the number of molecules.

In most cases with dermal exposure to chemicals, the concentration at the inner side (in the body) is negligible compared to the outer side (skin surface) and may be approximated to zero. In this case, the flux depends only on the K_p and the concentration at the outer skin surface.

Obviously, the value of, K_p depends on the properties of both the skin and the chemical. Further, the numerical value and units of K_p depend on the units chosen for P and A. It is common to express K_p in cm/h, from which follows that suitable units for P are µmol/h/cm^2 or mg/h/cm^2. A is then expressed as µmol/cm^3 (mM) or mg/cm^3.

5. Factors affecting dermal penetration

In this report the term *dermal penetration* is used for the amount of chemical that passes through the skin and reaches the systemic circulation. A synonymous term is *percutaneous absorption*. These two terms are different from *dermal absorption* which denotes the amount of chemical that has entered the skin from the outer environment. The dermally absorbed chemical may stay in the skin, diffuse back to the outer environment, be metabolized or pass on to the inner environment (penetration). If excess chemical is applied on the skin for a sufficiently long time (so that a steady-state is reached) and if metabolism in the skin is negligible, penetration equals absorption.

From equation 1 in Chapter 4 follows that the unit penetration rate (flux) across the skin is directly proportional to:

- the concentration (activity, partial pressure) of the chemical at the skin surface (provided that the inner concentration is negligible) of the chemical, and
- the permeability of the skin (expressed by K_p).

The permeability depends on the properties of the chemical as well as the properties of the skin. The total penetration is proportional to (in addition to concentration and permeability):

- the exposed area (since K_p is expressed per area unit), and
- the duration of exposure.

5.1 Concentration

Other factors held constant, the flux is always proportional to chemical activity (figure 6, left), the slope is determined by the permeability coefficient (K_p). At high concentrations, e.g. when the skin is exposed to neat chemical, the molecules begin to interact so that the concentration is no longer proportional to the number of freely moving “particles”. Hence, the relation between flux and concentration becomes sublinear at high concentrations (figure 6, right). In conclusion, dermal absorption rates cannot easily be translated from one concentration to the other and experimentally determined values for K_p are concentration-dependent.

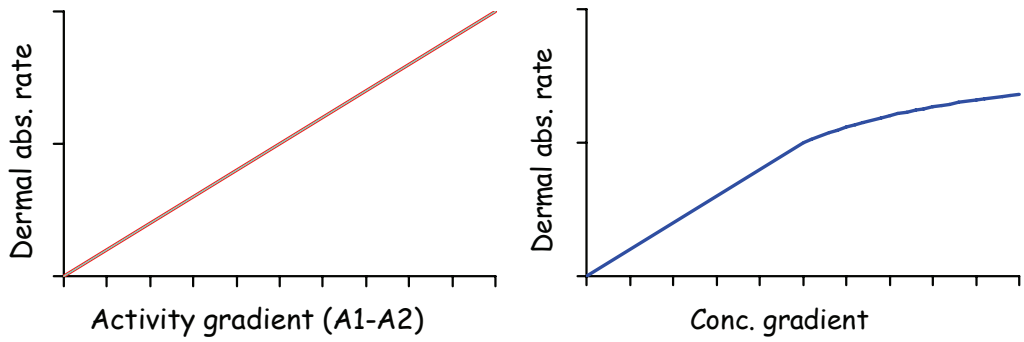

Figure 6. According to Fick's first law of diffusion (see also Chapter 4), the dermal absorption rate is proportional to the activity gradient (A1-A2) over the skin. The rate is further proportional to the concentration gradient for diluted, but not concentrated, chemicals.

5.2 Properties of the chemical

Molecular size and solubility are the major physical properties that determine the diffusion coefficient. Small molecules diffuse more easily through the skin than big molecules. Further, substances such as many organic solvents that easily dissolve in nonpolar (lipids) as well as polar (water) media, diffuse more easily through the skin. Conversely, substances that are either ionized, highly lipophobic or highly hydrophobic exhibit low skin permeability.

5.3 Properties of the skin

A thicker keratin layer of the stratum corneum will make the diffusion path length longer and, hence, the permeability lower (=higher resistance). Roughly, the K_p is inversely proportional to the thickness of the stratum corneum. The number of cell layers as well as the thickness varies widely between different parts of the body. At the extreme ends are the genitals with as little as 6 and the heels with as much as 86 cell layers (table 1).

Table 1. Number of stratum corneum cell layers at different locations (from Ya-Xian, Suetake et al. 1999).

Location	Number of cell layers (mean±sd)
Genital	6±2
Ear	7±2
Eyelid	8±2
Face	9±2
Lip	10
Scalp	12±2
Trunk	13±4
Extremities	15±4
Dorsum of hand	25±11
Dorsum of foot	30±6
Palm	50±10
Sole	55±14
Heel	86±36

The palms and soles, and especially the heels, have the thickest stratum corneum of as much as 1.5 mm, whereas that of the eyelids is as little as 0.05 mm. Densely furred species such as rats and mice have a much thinner skin than hairless species, such as humans and pigs. This difference includes the stratum corneum, as well as the epidermis (figure 7).

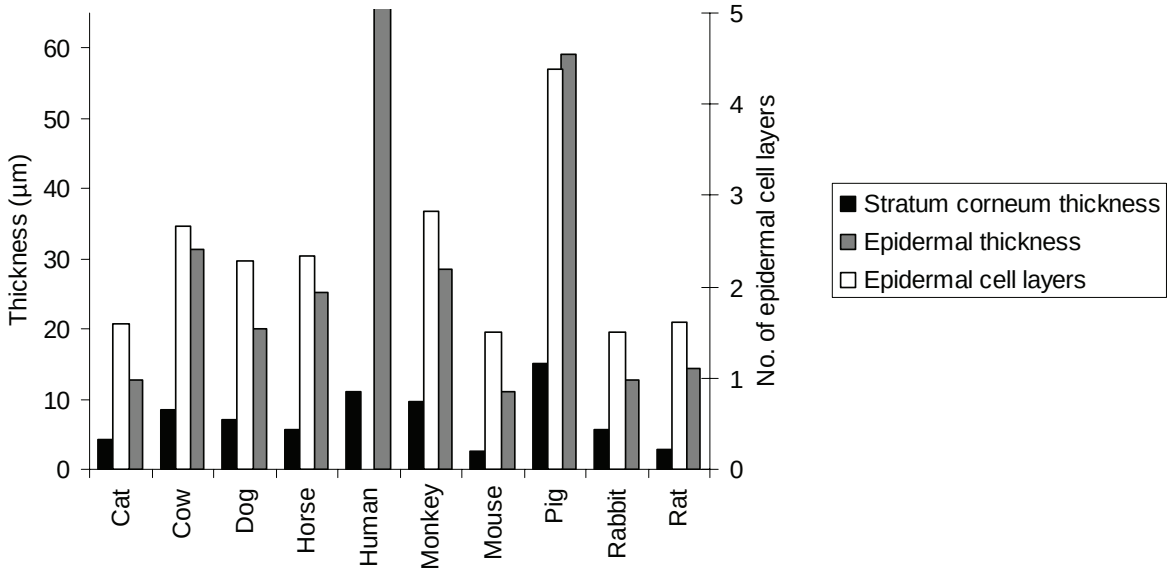

Figure 7. Thickness of stratum corneum and epidermis. The figure is based on measurements of the skin over the shoulder (animal data from Monteiro-Riviere, Bristol et al. 1990, human data from Sandby-Möller, Poulsen et al. 2003).

The stratum corneum is optimized to provide minimum permeability (maximum resistance) at “normal” conditions. Various conditions and factors may affect the structure of the stratum corneum, thereby increasing permeability. These conditions include skin damage caused, e.g. by disease, detergents or ultraviolet radiation, as well as temperature and humidity.

There is little data on the influence of skin lesions on dermal penetration in exposed human populations. A recent case report on four workers with different skin status (healthy, erythematous and burned skin and dishydrotic eczema) envolved in exposed to ortho-toluidine during rubber vulcanisation suggests that the absorption of o-toluidine is 1.5- to 2-fold higher through damaged than through healthy skin (Korinth, Weiss et al. 2006). In a follow-up study with 51 workers occupationally exposed to aniline and o-toluidine, the hemoglobin-aromatic amine-adduct levels in workers with erythema were on average 73% higher than in workers with healthy skin (Korinth, Weiss et al. 2007).

Similar results have been obtained in animal experiments. The permeation of hydrocortisone was studied *in vitro* using skin from a monkey diagnosed as having eczematous dermatitis. The permeation was approximately twice as high in eczematous skin, as compared to unaffected skin from the same individual. The absorption of another anti-inflammatory steroid, triamcinolone acetonide, was also enhanced through the eczematous skin (Bronaugh, Weingarten et al. 1986).

Soap washing and dermal exposure to solvents causes extraction of stratum corneum lipids, and increased permeability. Thus, for example, experimental 3-h treatment of human skin *in vitro* with 0.1% or 0.3% sodium lauryl sulphate caused an impaired barrier function as indicated by up to three-fold increases in the penetration of tritiated water and various pesticides (Nielsen 2005). In hairless mice topically treated with acetone, the permeation of hydrophilic substances (sucrose, caffeine, hydrocortisone) increased through stratum corneum as well as whole skin *in vitro*. In contrast, the permeation of lipophilic substances (propegesterone, estradiol) increased through stratum corneum but not whole skin (Tsai, Sheu et al. 2001).

Considering ultraviolet radiation, the permeation methanol and ethanol nearly tripled through UVA-treated as compared to untreated human human epidermis. In contrast, the permeation of higher, more lipophilic primary alcohols (propanol, butanol, hexanol, and heptanol) was not significantly altered (McAuliffe & Blank 1991).

Increased skin temperature increases the kinetic energy, .i.e. the movements, of the molecules, thereby affecting the lipid structure in the stratum corneum. Also, skin humidity increases as a result of sweating. All these factors may increase the dermal penetration. Johanson and Boman (1991) demonstrated that the percutaneous absorption of 2-butoxyethanol vapour was slightly increased at 33ºC ambient air temperature and 71% relative humidity, as compared to 23ºC and 29% relative humidity. *In vitro* experiments with freshly prepared human skin showed that the permeability coefficient of benzene in water nearly doubled at 50ºC and decreased slightly at 15ºC, as compared to 26ºC (Nakai, Chu et al. 1997).

5.4 Summary

The permeability of a given piece of skin for a specific substance is reflected by the permeability coefficient. The permeability coefficient is mainly determined by the:

- properties of the chemical,
- properties of the vehicles (if present),
- thickness of the keratin layer in stratum corneum,
- condition of the skin, e.g. skin damage.

The thickness of stratum corneum varies widely between species and between different parts of the body. The condition of the skin varies with, e.g. the temperature and the degree of hydration of the skin.

6. Assessment of dermal penetration

In principle, studies of dermal absorption measures the diffusion of the test substance from a test preparation placed on the skin through the stratum corneum and into the skin. The methods can be divided into two categories: *in vivo* and *in vitro*.

6.1 *In vivo* tests

The rat is the most commonly used species for *in vivo* testing. However, a wide variety of other species and strains are being used, including (hairless) rats, humans, monkeys, dogs, pigs, mini pigs, (hairless) guinea pigs, and (hairless) mice.

In vivo studies in laboratory animals are preferably conducted as described by OECD (2004). In brief, the exposed area, ideally about 10 cm^2 in rats, should be defined by a device that is attached to the skin surface. The test sample is applied to the surface of skin and allowed to remain for a specified period of time, relevant to human exposure. At the end of the exposure period excess sample is removed. During the study, animals are housed individually in metabolism cages from which excreta are collected. If measurable volatile metabolites (such as radiolabelled carbon dioxide) are expected, exhaled breath is also collected. At the end of the study, the removable remains of the dose are washed from the skin surface. The animals are then killed and the amount of parent chemical and metabolites in skin, carcass and excreta is determined. These data allow for an estimate of the total recovery of the test substance.

Test chemical remaining in the skin after wash-off will disappear over time by four pathways, by diffusion into the environment, by desquamation (shedding of the outer layers of the skin), by ingestion when the animal grooms itself, and by diffusion into the systemic circulation. To avoid overestimation of the systemically absorbed dose, measures have to be taken to prevent grooming of the site of application, and to prevent desquamated skin from falling into the urine and fecal collection systems.

The skin absorption of the test substance can be expressed as the percentage of dose absorbed per unit time or, preferably, as an average absorption rate per unit area of skin, e.g. $\mu g/cm^2/h$.

By necessity, *in vivo* studies in humans must use a different experimental protocol, as the total recovery cannot be directly determined. The dermal dose is thus determined indirectly, by comparison to a known dose, for instance the net uptake by inhalation exposure ($D_{inhaled}$), where the bioavailability is known to be 100%. The dermal uptake, or rather, the systemic dose via the dermal route (D_{dermal}), may then be calculated for example by comparing the urinary recoveries of the chemical or its metabolite(s) (R). Alternatively, since the area under of the

concentration-time curve (*AUC*) in e.g. plasma or blood is proportional to dose, dermal uptake may be obtained by comparing the two AUCs. Thus:

$$\frac{D_{dermal}}{R_{dermal}} = \frac{D_{inhaled}}{R_{inhaled}} \qquad \Rightarrow \quad D_{dermal} = \frac{D_{inhaled} \cdot R_{dermal}}{R_{inhaled}} \tag{2}$$

or

$$\frac{D_{dermal}}{AUC_{dermal}} = \frac{D_{inhaled}}{AUC_{inhaled}} \qquad \Rightarrow \quad D_{dermal} = \frac{D_{inhaled} \cdot AUC_{dermal}}{AUC_{inhaled}} \tag{3}$$

For examples of this approach, see e.g. studies by Johanson and colleagues (Johanson & Boman 1991, Johanson, Boman et al. 1988, Johanson & Fernström 1986, 1988).

A different approach to measure dermal absorption is that of microdialysis. A small probe equipped with a semi permeable hollow fiber is inserted superficially into the dermis, parallel to the skin surface. A physiological solution is slowly pumped through the fiber, allowing the solutes of interest to equilibrate with the surrounding extracellular space. For overviews, see e.g. Anderson (2006), Schnetz & Fartasch (2001) or Stahl, Bouwet et al. (2002).

Human pharmacokinetic microdialysis has only been carried out for two decades and there is limited data, mainly on pharmaceutical drugs, on dermal absorption using this technique. There are several difficulties in obtaining quantitative measures, maybe the major one being that concentration and not flux is measured. The concentration will depend not only on influx via stratum corneum but also on outflux via the blood stream. Other related difficulties reside in determining the position of the probe (since the concentration decreases with distance from the skin surface) and in defining the exposed skin area.

6.2 *In vitro* tests

Skin from many mammalian species, including humans, as well as non-mammalian species, e.g. snakes, can be used. The receptor compartment of a so-called static diffusion cell or Franz cell (figure 8) is filled with a suitable fluid. An excised skin sample is mounted on top of the cell so that the inner side is in close contact with the receptor medium. The test sample is applied in the donor compartment so that it covers the skin surface. For more detailed descriptions, see e.g. the OECD guideline (2004).

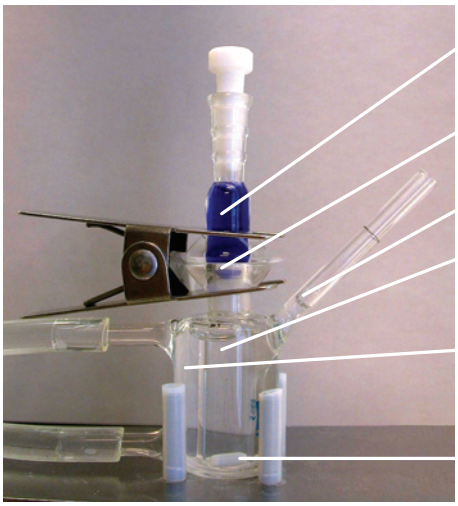

Figure 8. Static diffusion cell for dermal absorption studies *in vitro*.

As in the *in vivo* studies, the exposure duration should be relevant for human situations. At the end of exposure, excess sample is removed from the skin by appropriate cleansing.

The receptor fluid is sampled at defined time points throughout the experiment and the concentration of the parent chemical as well as any significant metabolite(s) is determined by a suitable method, e.g. gas chromatography, to ascertain the mass of the test substance (including any significant metabolite) that has passed through the skin. At the end of the study, the dislodgeable dose, the amount contained in the skin and the amount in the receptor fluid are determined. These data are necessary to calculate the total skin absorption, and allow for an estimate of the total recovery of the test substance.

When calculating the dermal penetration rate, the concentration in the receptor fluid translated to absolute mass by multiplying with the volume. The absolute mass rate, i.e. the increase in mass with time during steady-state condition, is obtained as the slope of the linear part of the mass versus time curve (figure 9). Finally, the unit penetration rate or flux is obtained by dividing the mass rate by the exposed skin area.

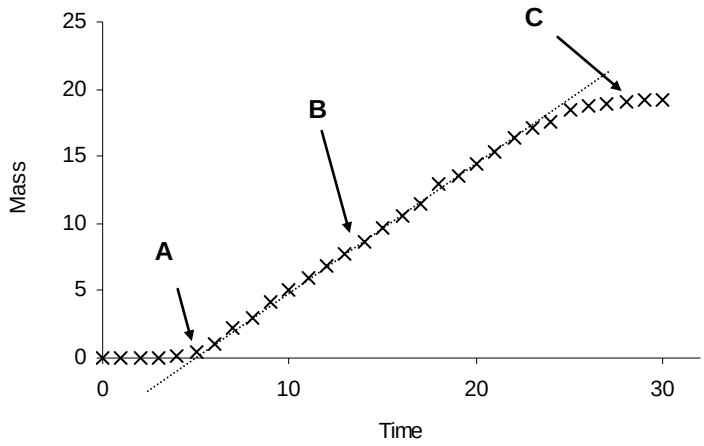

Figure 9. Mass of chemical versus time in the receptor medium static diffusion cell. A: Lag time of skin penetration, B: Steady-state, slope of increase equals penetration rate, C: Penetration rate decreases (curve levels off), either due to back diffusion (limited solubility in receptor medium) or depletion at donor site.

It has to be assured that the test chemical is sufficiently soluble in the receptor medium. For highly water soluble chemicals this is no problem and physiological saline or isotonic buffer are sufficient as solvents. However, if this kind of receptor medium is used with non-polar, poorly soluble chemicals such as hexane, an equilibrium will soon be established between the donor and the receptor compartment (phase C in figure 9). Thus, the net movement of chemical approaches zero and the flux and permeability coefficient may be seriously underestimated.

The static diffusion cells may be replaced by a flow-through, so-called Bronaugh cell. Advantages of the latter type of cell are that saturation of the receptor medium can be avoided and that the system can easily be automated by connecting to an autosampler.

6.3 Structure-activity based methods

Several regression equations have been developed that relates permeability coefficients to easily obtained chemical properties, such as the octanol:water partition coefficient (K_{ow}) and molecular weight (MW). The K_{ow} is thought to represent the solubility and MW the size and hence diffusivity of the molecule in the skin. The equations are often of the form (McCarley & Bunge 2001):

$$\log K_p = a + b \cdot \log K_{ow} + c \cdot MW \qquad (4)$$

The constants *a*, *b*, and *c* are determined by fitting the equation to specific experimental data sets. One of the most commonly referred equations was developed by Potts and Guy (1992):

$$\log K_p = -2.72 + 0.71 \cdot \log K_{ow} - 0.0061 \cdot MW \qquad (5)$$

where K_p is expressed in cm/h. More complicated models have also been developed, e.g. the modified Guy (Wilschut, ten Berge et al. 1995), the Cleek and Bunge (1993), the McKone and Howd (1992), the modified Robinson (Wilschut, ten Berge, Robinson & McKone 1995) and the Frasch model (2002). The US National Institute of Occupational Safety and Health (NIOSH) has developed an on-line skin permeation calculator that makes use of the Potts and Guy, the modified Robinson and the Frasch models (figure 10).

These equations generally work well within homologous series and structurally related chemicals, but are often unreliable outside that range. The error may be up to one or two orders of magnitude, compared to experimental data.

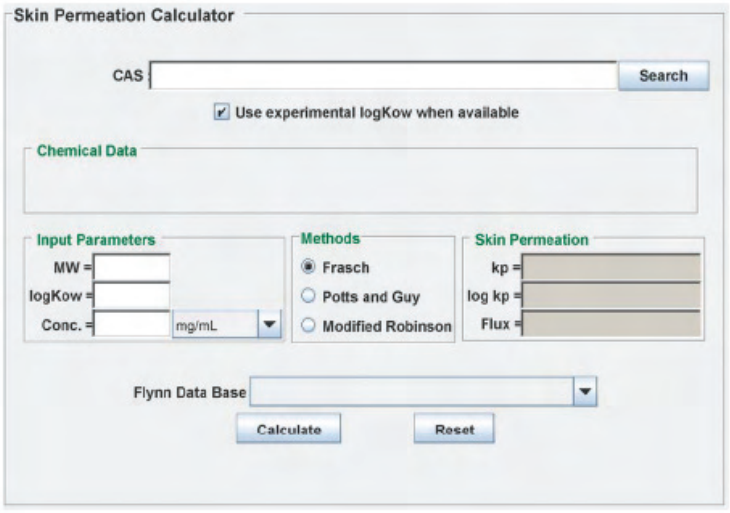

Figure 10. Screen dump of the US NIOSH skin permeation calculator available at http://www.cdc.gov/niosh/topics/skin/skinPermCalc.html.

7. Dermal penetration data for substances on the Swedish OEL list

7.1 Approach

Published percutaneous absorption data were searched for 165 substances. The compilation includes all 117 substances denoted with “H”, i.e. a skin notation in the ordinance on Swedish OELs (AFS 2005). In addition, 50 listed substances without skin notation but with published quantitative data on dermal absorption were included. Detailed information on each substance is given in the Appendix.

All substances in the Appendix except nicotine correspond to a defined entry with its own value in the Swedish ordinance. For nicotine the indicative OEL value of the European Commission should be used as a recommendation pending the introduction of a Swedish OEL. A few closely related substances, e.g. the PCB congeners, the mercury salts and the dinitrotoluene, butyl amine and cresol isomers, are given a single OEL in the Swedish list. Thus, the 165 substances correspond to 150 OEL entries.

All published dermal uptake data were listed for each substance. The compilations include information on species, type of experiment (*in vitro/in vivo*), type of diffusion cell, skin location, thickness and area, vehicle, concentration, number of experiments, exposure duration, observation time, lag time of penetration and percent absorbed chemical. Abbreviations and terms are given in table 2. Flux and permeability (K_p) are either listed as stated by the authors or calculated by us (numbers in italic).

In addition, physico-chemical properties are provided for each substance. This includes molecular weight, density at 25ºC, melting and boiling points, vapor pressure at 25ºC and evaporation rate relative to n-butyl acetate. These properties were obtained from Chemfinder (http://chemfinder.cambridgesoft.com), Swedish consensus reports published in Arbete och Hälsa, the NIOSH Pocket Guide to Chemical Hazards, and data on the internet supplied by various companies and organizations (see Appendix for references). Octanol:water partition coefficients were obtained using the KowWin software from Syracuse Research Corporation (http://www.syrres.com/esc/kowwin.htm).

In cases with multiple data, a preferred data set (marked by dots in figure 12) was selected according to the following criteria:

1. Human skin preferred over animal skin
2. *In vivo* studies preferred over *in vitro* studies
3. Neat liquid preferred over vapor or diluted liquid
4. Water preferred over other vehicles
5. Infinite or large dose preferred over low dose

Infinite or large doses, although perhaps unrealistic considering workplace conditions, were preferred over low doses as they allow for assessment of steady-state fluxes.

Although experimental exposure to neat (pure) chemical may affect the skin barrier and may reflect reality less well than exposures to vapors and dilutions, the former type of studies was preferred for two reasons; (a) they are more common facilitating comparisons between and ranking of chemicals and (b) they are less dependent on exposure conditions and thus more closely reflect the intrinsic properties of the chemical. The motives for selecting the preferred study for each individual chemical are given in the Assessment section of each substance in Appendix A.

Based on the preferred K_p value, substances were grouped in seven categories, from "Extremely low" to "Extremely high" permeability, according to a logarithmic scheme (figure 11) slightly modified from Marzulli et al. (1965) and Barber et al. (1995).

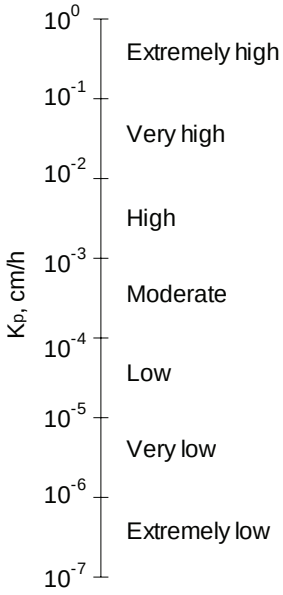

Figure 11. Grouping scheme according to skin permeability (Kp). The grouping does not take toxic potency into account.

For chemicals lacking quantitative data, indirect data such as comparisons between oral and dermal LD_{50} values and other statements on dermal penetration ability were identified in the documentation published by the Swedish Criteria Group and by the Threshold Limit Value Committee of the American Conference for Governmental Industrial Hygienists. These statements, if any, are also provided in the Assessment section.

7.2 Conclusions

Quantitative dermal penetration data were missing for 53 of the 165 substances, i.e. about one third of the substances. Figure 12 summarizes the permeability coefficients for the 108 substances where a permeability coefficient could be obtained (see appendix for details). As can be seen in the figure, there is a trillionfold (10^{12}) range in permeability. Moreover, multiple K_p values are reported for many substances (represented by vertical lines in figure 12) and these within-substance deviations are sometimes several orders of magnitude.

The wide within-substance range of permeability indicates that experimental design is critical. Thus, the K_p depends on the type of skin (species, location etc.) as well as the exposure conditions (solid, liquid or vapor, neat or diluted, vehicle, exposure duration etc.).

One major issue is that of using concentrated versus diluted chemicals. Two concerns already mentioned above is that exposure to neat chemical may affect the skin barrier and may also be unrealistic from the occupational viewpoint. An additional concern is that, at least for some chemicals, the permeability is heavily influenced by dilution with water. Thus, the flux of 2-butoxyethanol reaches its maximum at about 50% dilution and the permeability coefficient increases approximately 100-fold moving from neat to very dilute aqueous solutions (Johanson & Fernström 1988, Korinth, Schaller et al. 2005).

Another aspect not covered by our preferred studies approach is that of evaporation. Thus, following exposures of short duration, such as when spills occur at a workplace, some chemical will evaporate back to the atmosphere. This reduces the amount available for dermal penetration. The extent of evaporation depends on the volatility and skin permeability of the chemical, the exposure duration, and the lag time of penetration (Kasting & Miller 2006, N'Dri-Stempfer & Bunge 2005). Theoretical calculations suggest that the fraction lost by evaporation may be significant for volatile chemicals. For example, it has been estimated that following a 1-h exposure to chloroform, 73% of the chemical in the skin evaporates (N'Dri-Stempfer & Bunge 2005). To date, no systematic evaluation of the impact of evaporation has been performed for industrial chemicals.

About two thirds of the chemicals with dermal permeability data have a skin notation (table 3 and figure 13). One might expect that skin notations would occur more frequently among chemicals with higher permeability. However, no clear relation between permeability and frequency of skin notation was seen (figure 13).

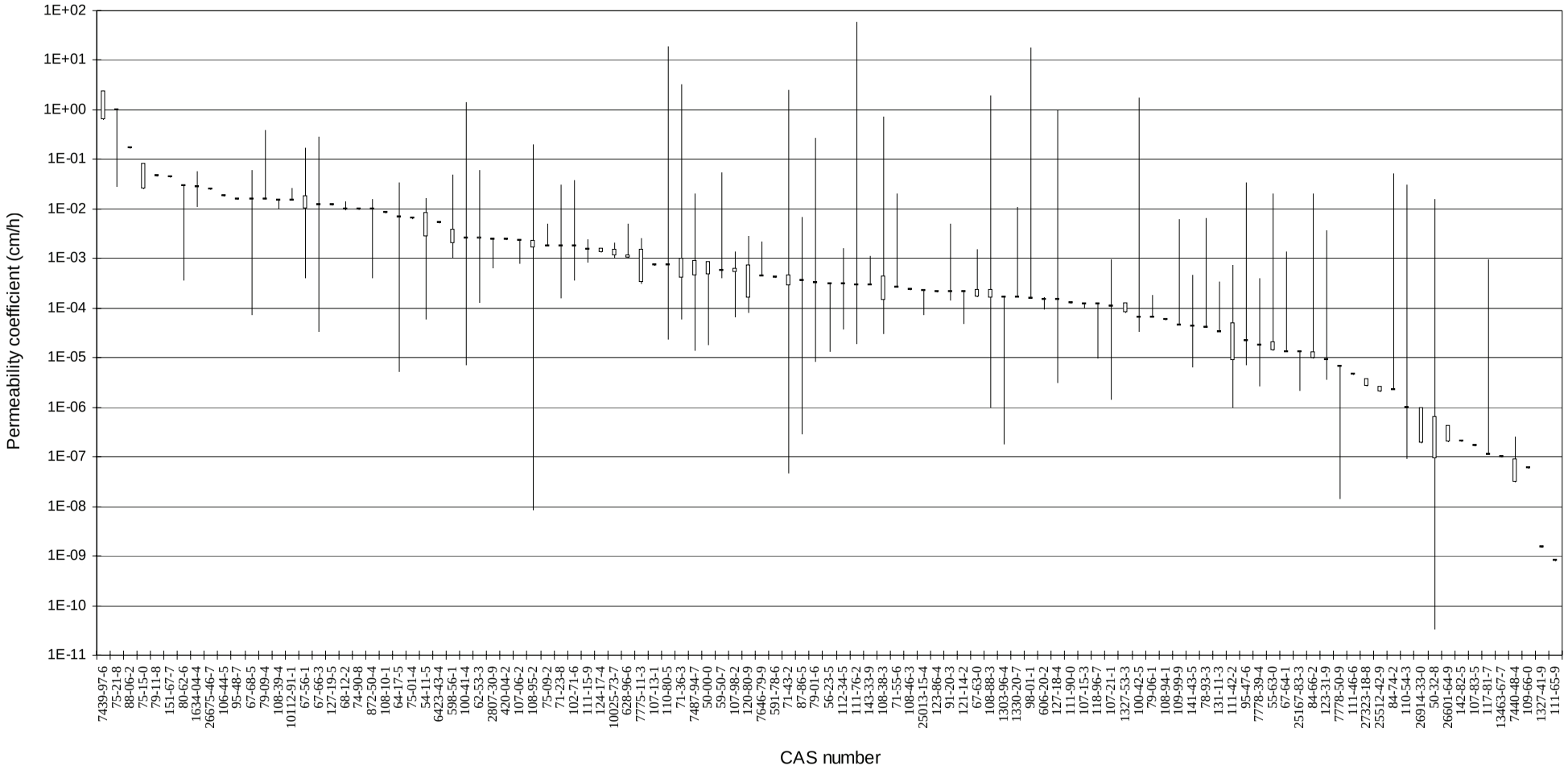

Figure 12. Summary of experimentally determined permeability coefficients (K_p, cm/h) for the investigated chemical. The chemicals are sorted in decreasing order with respect to the preferred value (dots). Ranges of values are given as vertical lines. Note the logarithmic scale of the y axis.

It should be pointed out that this grouping solely according to permeability (such as in figure 13) does not take toxic potency into account. The European Centre for Ecotoxicology & Toxicology of Chemicals has suggested a skin notation should be assigned when the amount of chemical absorbed upon exposure of both hands and lower arms (2000 cm^2) for one hour is expected to contribute more than 10% to the systemic dose, compared to the amount absorbed via inhalation exposure at the OEL during a full work day (assuming that 10 m^3 air is inhaled during an 8-h workday and that 50% is absorbed). This applies only for chemicals for which the OEL is based on systemic toxicity (ECETOC 1993).

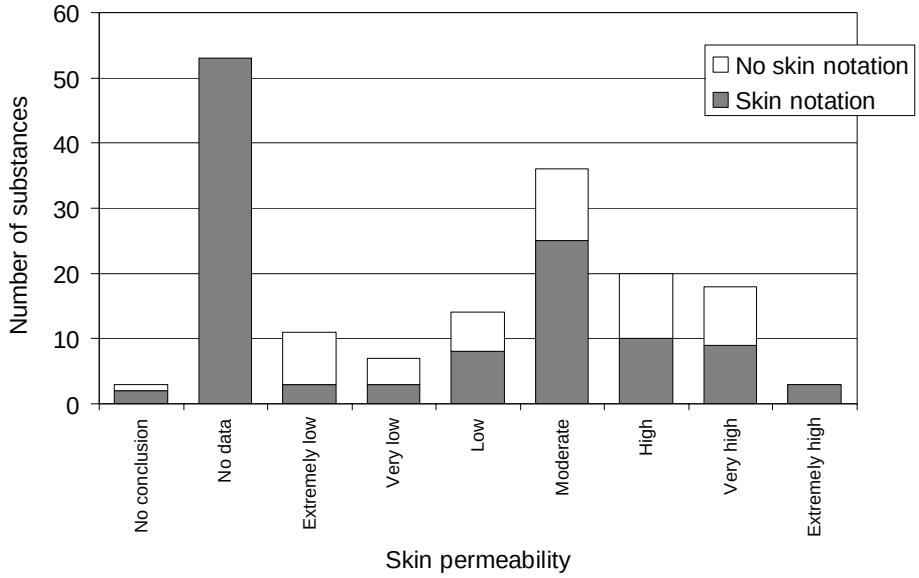

Figure 13. Number of substances with and without a skin notation in the Swedish OEL list, grouped by experimentally determined skin permeability. This grouping does not take the toxic potency into account.

A comparison between the ECETOC criteria and the Swedish skin notations produces some interesting results (table 3 and figure 14). Thus, two (*o*-xylene and diethylene glycol) of 12 substances with a dermal/inhalation ratio of less than 0.1 (i.e. should not have a notation according to ECETOC) do have a skin notation in the Swedish list. For *o*-xylene this is maybe not so controversial, as another study with mixed xylenes in solution yields a ratio above 0.1. On the other hand, 6 out of 14 substances with a ratio between 0.1 and 1 lack a skin notation. Even more remarkable is that 30 out of 82 with a ratio above 1 lack the notation. For the latter chemicals the dermal route contributes to more than 90% of the total dose, according to the ECETOC calculation. For some substances (such as formaldehyde) it may be argued that the systemic dose, and hence the dermal/inhalation ratio, is irrelevant since the OEL is based on a non-systemic effect (such as irritation). Nevertheless these comparisons suggest that a revision of the Swedish skin notations would be appropriate.

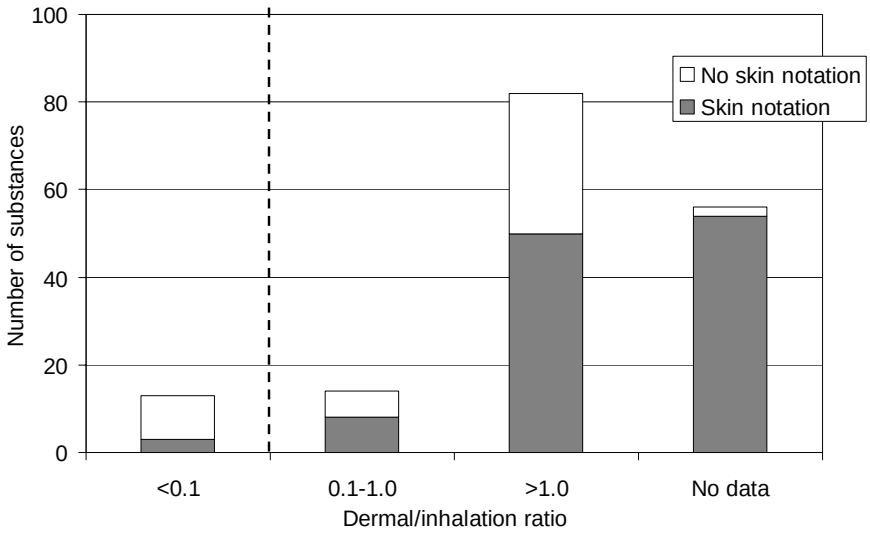

Figure 14. Number of substances with and without a skin notation in the Swedish OEL list, categorized by the ratio between dermal and inhalation uptake rate. As inhalation is calculated at the OEL, this ratio does take toxic potency into account. The ECETOC criterion for skin notation (>0.1) is marked by a dotted line.

Table 2. Abbreviations and terms as used in tables and appendix.

A	Area of exposed skin	Me	Methanol
Ab	Abdomen	Mon	Monkey
Abs	Per cent absorbed chemical	Mou	Mouse
Ac	Acetone	MP	Minipig
AoH	Arbete och Hälsa	n	Number of experiments
Ax	Axilla	NaCl	Physiological saline (0.9% NaCl)
Ba	Back	n-Bu	n-Butanol
Br	Breast	NC	Nitrocellulose
Bw	Body weight	Ne	Neck
C	Concentration of chemical in vehicle	Neat	Undiluted chemical
CAS	Chemical Abstracts Service Registry No.	DMF	Dimethylformamide
Chf	Chloroform	Oct	Octane
Der	Dermis	OiW	Oil in water emulsion
EB	Elbow	PB	Phosfate buffer
Epi	Epidermis	PCP	Pentachlorophenol
Et	Ethanol	PG	Propyleneglycol
FH	Forehead	Ph	Phenol
Fi	Finger	Ph/NaCl	Phenol and saline
Fk	Flank	PHD	Permanent Hair Dye
Fl	Flow-through diffusion cell	Pit	Armpit
FS	Fore skin	Pol fab	Polyester fabric
FS/TM	Fore skin, cultured	Rab	Rabbit
Full	Full thickness skin	Sat Vap	Saturated vapour
Gas	Gasoline	Sc	Scalp
GP	Guinea pig	SC	Stratum corneum
H:M	Hexane:Methylene chloride	Sn	Snake
Ha	Hand	Solv	Solvent
Ham	Hamster	Sp	Examined species
Has	Hands	SpSt	Explosive (Sprengstoff in German)
HD	Hexadecane	St	Static diffusion cell
HDP	Hair Dye Precursors	TCP	Tetrachlorophenol
Hep	n-Heptane	Texp	Duration of exposure
Hex	n-Hexane	Th	Thigh
HGP	Hairless guinea pig	Ti	Tinker soil
HM	Hairless mouse	T_{lag}	Time lag for penetration
HR	Hairless rat	T_{obs}	Duration of observation
Hum	Human	Tol	Toluene
JP-8	Jet fuel, type JP-8	V	Applied volume
K_p	Permeability coefficient	Vap	Vapor
L	Thickness of exposed skin	VIC	Vaseline Intensive Care
Loc	Body location of the skin	WB	Whole body
Log K_{ow}	Log octanol:water partition coefficient	Yo	Yolo soil
Ma	Marmoset		

Table 3. Summary descriptors on dermal absorption for the investigated chemicals.

Substance	Year of listing	CAS number	Quantitative data available on		Physical state	ECETOC dermal /inhalation ratio			Skin notation[a]	
			Vapor pressure	Dermal absorption		<0.1	0.1-1	>1	by ECETOC	in Sweden
Acetone	1993	67-64-1	Yes	Yes	Neat liquid	X			No	No
Acetonitrile; methyl cyanide	1993	75-05-8	Yes	No						No
Acrylamide	1993	79-06-1	Yes	Yes	Aq. sol.			X	Yes	Yes
Acrylonitrile	1993	107-13-1	Yes	Yes	Neat liquid			X	Yes	Yes
Allyl alcohol; 2-propen-1-ol	1993	107-18-6	Yes	No						Yes
Allylamine; 3-aminopropene	1984	107-11-9	Yes	No						Yes
Allylchloride; 3-chloroprene	1993	107-05-1	Yes	No						Yes
Aluminium chlorohydrate	1996	1327-41-9	No	Yes	Aq. sol.	X			No	No
Aniline	1993	62-53-3	Yes	Yes	Aq. sol.			X	Yes	Yes
Arsenic acid	2004	7778-39-4	No	Yes	Aq. sol.			X	**Yes**	**No**
Arsenic trioxide	2004	1327-53-3	No	Yes	Aq. sol.			X	**Yes**	**No**
Benzene	1990	71-43-2	Yes	Yes	Neat liquid			X	Yes	Yes
Benzoapyrene	1993	50-32-8	No	Yes	Neat solid			X	Yes	Yes
Borax	1978	1303-96-4	No	Yes	Aq. sol.			X	Yes	Yes
Butanol, iso-	1987	78-83-1	Yes	No						Yes
Butanol, n-	1989	71-36-3	Yes	Yes	Neat liquid			X	Yes	Yes
Butanol, sek-	1987	78-92-2	Yes	No						Yes
Butanol, tert-	1987	75-65-0	Yes	No						Yes
Butyl acetate, n-	2000	123-86-4	Yes	Yes	Neat liquid		X		**Yes**	**No**
Butylamine, iso-	1984	78-81-9	Yes	No						Yes
Butylamine, n-	1984	109-73-9	Yes	No						Yes
Butylamine, sec-	1984	13952-84-6	Yes	No						Yes
Butylamine, tert-	1984	75-64-9	Yes	No						Yes
Carbon disulfide	1978	75-15-0	Yes	Yes	Aq. sol.			X	Yes	Yes

[a] Bold text is used to highlight discordancies between the Swedish ordinance and the ECETOC proposal

Substance	Year of listing	CAS number	Quantitative data available on		Physical state	ECETOC dermal /inhalation ratio			Skin notation	
			Vapor pressure	Dermal absorption		<0.1	0.1-1	>1	by ECETOC	in Sweden
Carbon tetrachloride	1978	56-23-5	Yes	Yes	Neat liquid			X	Yes	Yes
Catechol	1993	120-80-9	Yes	Yes	Solution			X	Yes	Yes
Chlorinated biphenyls, poly- (PCB)	1978	1336-36-3	No	No						Yes
Chloro-1,3-butadiene, 2-; chloroprene	1990	126-99-8	Yes	No						Yes
Chlorobiphenyl, di- (DCB)	1978[b]	25512-42-9	No	Yes	Neat solid			X	Yes	Yes[b]
Chlorobiphenyl, hexa- (HCB)	1978[b]	26601-64-9	No	Yes	Neat solid			X	Yes	Yes[b]
Chlorobiphenyl, mono- (MCB)	1978[b]	27323-18-8	No	Yes	Neat liquid			X	Yes	Yes[b]
Chlorobiphenyl, tetra- (TCB)	1978[b]	26914-33-0	No	Yes	Neat solid			X	Yes	Yes[b]
Chlorocresol; 4-chloro-3-methylphenol	1993	59-50-7	Yes	Yes	Aq. sol.			X	**Yes**	**No**
Chloroethanol, 2-	1981	107-07-3	Yes	No						Yes
Chloroform; trichloromethane	1978	67-66-3	Yes	Yes	Neat liquid			X	**Yes**	**No**
Chromate, potassium di-	2004	7778-50-9	Yes	Yes	Aq. sol.			X	**Yes**	**No**
Chromate, sodium di-	2004	7775-11-3	No	Yes	Aq. sol.			X	**Yes**	**No**
Chromic chloride	2004	10025-73-7	No	Yes	Aq. sol.			X	**Yes**	**No**
Cobalt	1978	7440-48-4	No	Yes	Solution			X	**Yes**	**No**
Cobalt dichloride	1978	7646-79-9	Yes	Yes	Aq. sol.			X	**Yes**	**No**
Cresol, m-	2000	108-39-4	Yes	Yes	Aq. sol.			X	**Yes**	**No**
Cresol, o-	2000	95-48-7	Yes	Yes	Aq. sol.			X	**Yes**	**No**
Cresol, p-	2000	106-44-5	Yes	Yes	Aq. sol.			X	**Yes**	**No**
Cyanamide, hydrogen	2000	420-04-2	No	Yes	Aq. sol.			X	**Yes**	**No**
Cyclohexanone	2004	108-94-1	Yes	Yes	Neat liquid		X		Yes	Yes
Di-(2-ethylhexyl)phthalate (DEHP)	1987	117-81-7	Yes	Yes	Neat liquid	X			No	No
Dibutyl phthalate (DBP)	1987	84-74-2	Yes	Yes	Neat liquid		X		**Yes**	**No**
Dichloroethane, 1,2-	1981	107-06-2	Yes	Yes	Neat liquid			X	Yes	Yes
Diethanolamine	1993	111-42-2	Yes	Yes	Aq. sol.		X		Yes	Yes
Diethyl phthalate (DEP)	1987	84-66-2	Yes	Yes	Neat liquid			X	**Yes**	**No**

[b] Refers to PCB, CAS no. 1336-36-3

Substance	Year of listing	CAS number	Quantitative data available on		Physical state	ECETOC dermal /inhalation ratio			Skin notation	
			Vapor pressure	Dermal absorption		<0.1	0.1-1	>1	by ECETOC	in Sweden
Diethylamine	1984	109-89-7	Yes	No						Yes
Diethylaminoethanol, 2-	1996	100-37-8	Yes	No						Yes
Diethylene glycol	1993	111-46-6	Yes	Yes	Neat liquid	X			**No**	**Yes**
Diethylene glycol monobutyl ether (DEGBE)	1996	112-34-5	Yes	Yes	Neat liquid			X	**Yes**	**No**
Diethylene glycol monobutyl ether acetate (DEGBEA)	1996	124-17-4	Yes	Yes	Neat liquid			X	**Yes**	**No**
Diethylene glycol monoethyl ether (DEGEE)	2000	111-90-0	Yes	Yes	Neat liquid		X		Yes	Yes
Diethylene glycol monoethyl ether acetate (DEGEEA)	2000	112-15-2	Yes	No						Yes
Diethylentriamine	1996	111-40-0	Yes	No						Yes
Diisopropylamine	1993	108-18-9	Yes	No						Yes
Dimethyl phthalate	1987	131-11-3	Yes	Yes	Neat liquid			X	**Yes**	**No**
Dimethylacetamide, N-	1996	127-19-5	Yes	Yes	Neat liquid			X	Yes	Yes
Dimethylanilline, N,N-	1993	121-69-7	Yes	No						Yes
Dimethylethylamine	1993	598-56-1	Yes	Yes	Solution			X	**Yes**	**No**
Dimethylformamide	1987	68-12-2	Yes	Yes	Neat liquid			X	Yes	Yes
Dimethylsulfoxide	1993	67-68-5	Yes	Yes	Neat liquid			X	Yes	Yes
Dinitrobenzene	1978	25154-54-5	Yes	No						Yes
Dinitrotoluene	1993	25321-14-6	Yes	No						Yes
Dinitrotoluene, 2,4-	1993	121-14-2	Yes	Yes	Solution			X	Yes	Yes
Dinitrotoluene, 2,6-	1993	606-20-2	Yes	Yes	Solution			X	Yes	Yes
Dioxane	1996	123-91-1	Yes	No						Yes
Dipropylene glycol monomethyl ether (DPGME)	1993	34590-94-8	Yes	No						Yes
Epichlorohydrin	1978	106-89-8	Yes	No						Yes
Ethanol	1993	64-17-5	Yes	Yes	Neat liquid			X	**Yes**	**No**
Ethanolamine	1993	141-43-5	Yes	Yes	Aq. sol.			X	Yes	Yes

Substance	Year of listing	CAS number	Quantitative data available on		Physical state	ECETOC dermal /inhalation ratio			Skin notation	
			Vapor pressure	Dermal absorption		<0.1	0.1-1	>1	by ECETOC	in Sweden
Ethyl 2-cyanoacrylate	2000	7085-85-0	Yes	No						Yes
Ethyl acrylate	1987	140-88-5	Yes	No						Yes
Ethyl benzene	1987	100-41-4	Yes	Yes	Neat liquid			X	**Yes**	**No**
Ethyl ether	1996	60-29-7	Yes	No						No
Ethylamine	1984	75-04-7	Yes	No						Yes
Ethylene glycol	1993	107-21-1	Yes	Yes	Neat liquid			X	Yes	Yes
Ethylene glycol dinitrate	1990	628-96-6	Yes	Yes	Solution			X	Yes	Yes
Ethylene oxide	1989	75-21-8	Yes	Yes	Solution			X	Yes	Yes
Ethylenediamine	1978	107-15-3	Yes	Yes	Aq. sol.			X	Yes	Yes
Ethylene glycol monobutyl ether (EGBE)	1993	111-76-2	Yes	Yes	Neat liquid			X	Yes	Yes
Ethylene glycol monobutyl ether acetate (EGBEA)	1993	112-07-2	Yes	No						Yes
Ethylene glycol monoethyl ether (EGEE)	2000	110-80-5	Yes	Yes	Neat liquid			X	Yes	Yes
Ethylene glycol monoethyl ether acetate (EGEEA)	2000	111-15-9	Yes	Yes	Neat liquid			X	Yes	Yes
Ethylene glycol monoisopropyl ether (EGiPE)	1996	109-59-1	Yes	No						Yes
Ethylene glycol monoisopropyl ether acetate (EGiPEA)	1996	19234-20-9	No	No						Yes
Ethylene glycol monopropyl ether (EGPE)	1996	2807-30-9	Yes	Yes	Neat liquid			X	Yes	Yes
Ethyl morpholine, N-	1984	100-74-3	Yes	No						Yes
Formaldehyde	1987	50-00-0	No	Yes	Aq. sol.			X	**Yes**	**No**
Formamide	1993	75-12-7	Yes	No						Yes
Furfural	1990	98-01-1	Yes	Yes	Neat liquid			X	Yes	Yes
Furfuryl alcohol	1990	98-00-0	Yes	No						Yes
Halothane	1990	151-67-7	Yes	Yes	Vapour			X	**Yes**	**No**
Heptane, n-	1989	142-82-5	Yes	Yes	Neat liquid	X			No	No
Hexane, n-	1989	110-54-3	Yes	Yes	Neat liquid	X			No	No
Hexanone, 2-; methyl n-butyl ketone	1993	591-78-6	Yes	Yes	Neat liquid			X	Yes	Yes

Substance	Year of listing	CAS number	Quantitative data available on		Physical state	ECETOC dermal /inhalation ratio			Skin notation	
			Vapor pressure	Dermal absorption		<0.1	0.1-1	>1	by ECETOC	in Sweden
Hydrogen cyanide	1974	74-90-8	Yes	Yes	Vapour			X	Yes	Yes
Hydroquinone	1993	123-31-9	Yes	Yes	Aq. sol.			X	**Yes**	**No**
Hydroxyethylacrylate, 2-; propenoic acid, 2-	1981	818-61-1	Yes	No						Yes
Isoflurane	1990	26675-46-7	Yes	Yes	Vapour		X		**Yes**	**No**
Isopropanol	1989	67-63-0	Yes	Yes	Aq. sol.		X		**Yes**	**No**
Isopropylbenzene; cumene	1984	98-82-8	Yes	No						Yes
Mercury bichloride; dichloromercury	1993	7487-94-7	No	Yes	Aq. sol.			X	Yes	Yes
Mercury chloride; dimercury dichloride	1993	10112-91-1	No	Yes	Aq. sol.			X	Yes	Yes
Mercury, dimethyl	1993	593-74-8	Yes	No						Yes
Mercury, metal	1993	7439-97-6	Yes	Yes	Vapour		X		Yes	Yes
Methanol	1990	67-56-1	Yes	Yes	Neat liquid			X	Yes	Yes
Methyl ethyl ketone (MEK); 2-butanone	1987	78-93-3	Yes	Yes	Neat liquid	X			No	No
Methyl iodide	1981	74-88-4	Yes	No						Yes
Methyl isobutyl ketone (MiBK)	1989	108-10-1	Yes	Yes	Neat liquid			X	**Yes**	**No**
Methyl tert-butyl ether (MTBE)	2000	1634-04-4	Yes	Yes	Aq. sol.			X	**Yes**	**No**
Methyl-2-pentanol, 4-	1996	108-11-2	Yes	No						Yes
Methyl-2-pyrrolidone, n- (NMP)	1990	872-50-4	Yes	Yes	Neat liquid			X	**Yes**	**No**
Methyl acrylate	1987	96-33-3	Yes	No						Yes
Methylamine	1984	74-89-5	Yes	No						Yes
Methyl bromide	1990	74-83-9	Yes	No						Yes
Methylene chloride; dichloromethane	1989	75-09-2	Yes	Yes	Neat liquid			X	Yes	Yes
Methyl metacrylate	1987	80-62-6	Yes	Yes	Neat liquid			X	Yes	Yes
Methyl morpholine, N-	1984	109-02-4	Yes	No						Yes
Methylpentane, 2-	1989	107-83-5	Yes	Yes	Neat liquid	X			No	No
Monochloroacetic acid	1993	79-11-8	Yes	Yes	Solution			X	Yes	Yes
Morpholine	2000	110-91-8	Yes	No						Yes
Naphtalenes, chlorinated	1978	1321-65-9	Yes	No						Yes
Naphthalene	2000	91-20-3	Yes	Yes	Solution			X	**Yes**	**No**

Substance	Year of listing	CAS number	Quantitative data available on		Physical state	ECETOC dermal /inhalation ratio			Skin notation	
			Vapor pressure	Dermal absorption		<0.1	0.1-1	>1	by ECETOC	in Sweden
Nicotine		54-11-5	Yes	Yes	Aq. sol.			X	Yes	Yes
Nitrobenzene	1974	98-95-3	Yes	No						Yes
Nitroglycerin	1990	55-63-0	Yes	Yes	Neat liquid			X	Yes	Yes
Nitrotoluene	1993	1321-12-6	Yes	No						Yes
Octanes	1989	111-65-9	Yes	Yes	Neat liquid	X			No	No
Pentachlorophenol	1974	87-86-5	Yes	Yes	Aq. sol.			X	Yes	Yes
Pentane	1978	109-66-0	Yes	Yes	Neat liquid	X			No	No
Phenol	1987	108-95-2	Yes	Yes	Aq. sol.			X	Yes	Yes
Propanol, n-	1989	71-23-8	Yes	Yes	Neat liquid			X	**Yes**	**No**
Propionic acid	1990	79-09-4	Yes	Yes	Neat liquid			X	**Yes**	**No**
Propylene glycol dinitrate	1987	6423-43-4	Yes	Yes	Solution			X	Yes	Yes
Propylene glycol monomethyl ether (PGME); 1-methoxy-2-propanol	1990	107-98-2	Yes	Yes	Neat liquid			X	Yes	Yes
-“- acetate (PGMEA)	1990	108-65-6	Yes	No						Yes
Resorcinol	1993	108-46-3	Yes	Yes	Aq. sol.			X	Yes	Yes
Sodium cyanide	1974	143-33-9	No	Yes	Aq. sol.			X	Yes	Yes
Styrene	1990	100-42-5	Yes	Yes	Neat liquid		X		Yes	Yes
Tetrachloroethylene	1989	127-18-4	Yes	Yes	Neat liquid			X	**Yes**	**No**
Tetrachlorophenol	1990	25167-83-3	No	Yes	Aq. sol.			X	Yes	Yes
Tetraethyl lead	1981	78-00-2	Yes	No						Yes
Tetrahydrofuran	1993	109-99-9	Yes	Yes	Neat liquid		X		**Yes**	**No**
Tetramethyl lead	1981	75-74-1	Yes	No						Yes
Thioglycolic acid	1996	68-11-1	Yes	No						Yes
Titanium dioxide	1990	13463-67-7	No	Yes	Aq. sol.	X			No	No
Toluene	1987	108-88-3	Yes	Yes	Neat liquid		X		Yes	Yes
Tributyltin	1978	56573-85-4	Yes	No						Yes
Trichlorethane, 1,1,1-	1989	71-55-6	Yes	Yes	Neat liquid		X		**Yes**	**No**
Trichloroethylene, 1,1,2-	1989	79-01-6	Yes	Yes	Neat liquid			X	**Yes**	**No**

Substance	Year of listing	CAS number	Quantitative data available on		Physical state	ECETOC dermal /inhalation ratio			Skin notation	
			Vapor pressure	Dermal absorption		<0.1	0.1-1	>1	by ECETOC	in Sweden
Trichlorophenol	1990	25167-82-2	No	No						Yes
Trichlorophenol, 2,4,6-	1990	88-06-2	Yes	Yes	Solution			X	Yes	Yes
Triethanolamine	1984	102-71-6	Yes	Yes	Neat solid			X	**Yes**	**No**
Trinitrotoluene, 2,4,6-	1993	118-96-7	Yes	Yes	Solution			X	Yes	Yes
Turpentine	1990	8006-64-2	Yes	No						Yes
Vinyl chloride	1974	75-01-4	Yes	Yes	Gas			X	Yes	Yes
Vinyl toluene; methyl styrene	1993	25013-15-4	Yes	Yes	Neat liquid			X	Yes	Yes
Xylene, m-	1987	108-38-3	Yes	Yes	Neat liquid		X		Yes	Yes
Xylene, o-	1987	95-47-6	Yes	Yes	Neat liquid	X			**No**	**Yes**
Xylene, p-	1987	106-42-3	Yes	No						Yes
Xylenes	1987	1330-20-7	Yes	Yes	Solution		X		Yes	Yes

8. Summary

Johanson G & Rauma M. *Basis for skin notation. Part 1. Dermal penetration data for substances on the Swedish OEL list.* Arbete och Hälsa 2008;42:2.

The aim of this report is to review the published data on dermal penetration of workplace chemicals, as a basis for assignment of skin notations. Short chapters describe the anatomy of the skin, the skin as a diffusion barrier, Fick's law of diffusion, factors affecting dermal penetration and methods to assess dermal penetration.

The major part of the report is devoted to compilation of data assessment of dermal penetration (fluxes and permeability coefficients) for 165 substances corresponding to 150 entries listed in the Swedish ordinance (AFS 2005) on Occupational Expsoure Limits (OELs). The compilation covers all 117 substances marked with an "H" in the ordinance and, in addition, 50 substances that have not been given a skin notation. The compiled data can be used in future revision of skin notations.

An analysis of the data shows that quantitative information on dermal penetration is lacking for 53 or about one third of the 165 substances. For those who have quantitative data, a variety of species and experimental techniques have been used. There is a trillion-fold (10^{12}) span in permeability coefficients between the substances. Moreover, for many chemicals with several experimental data sets on permeability, there is a huge intra-chemical span, sometimes several orders of magnitude. In these cases, a preferred study was selected, mainly based on the following criteria: human skin, *in vivo* studies, neat liquid, water as vehicle and infinite or large dose were preferred over animal skin, *in vitro* studies, vapor or diluted liquid, other vehicles and low dose, respectively.

Notably, more than one third of the chemicals with high skin permeability and with a dermal/inhalation ratio higher than 0.1 according to the ECETOC criteria (1993) lacks a skin notation. This suggests a need for revision of all substances, including those without a skin notation, in the Swedish list.

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Substance: Acetone
CAS: 67-64-1
Scientific basis: AoH 1988:32

Skin notation: No
Skin permeability: Low

Molecular weight: 58.1
Density: 0.786 g/cm³
Melting point: -94.3°C
Boiling point: 56.2°C
Vapour pressure: 24 kPa (at 25°C)
Evaporation rate: 10
Log Kow: -0.24

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Br	Fl	280	0.64	0.2		Neat	5	24	24	0.31	0.05	0.13	10	Wilkinson et al. (2001)
Hum	Br	Fl	280	0.64	0.2	H2O	3	5	24	24	0.38	0.41	14	4.2	Wilkinson et al. (2001)
In vivo															
Hum	Fi				Inf	H2O	1%	12	15s	0.3			*0.28*	0.22	Naitoh et al. (2002)
Hum	Fi				Inf	H2O	1%	12	15s	0.3			*12*	9.5	Naitoh et al. (2002)

Asessment

The only available in vivo study is that of Naitoh et al. (2002). An unconventional technique was used in that one thumb was dipped once or several times (15 sec/occasion) in an aqueous solution. The flux was calculated from the evaporation from the thumb. The evaporation profile was biphasic, thus two different fluxes were reported. The reported fluxes reflects absorption into (and out of) rather than through skin. Thus the calculated Kp may represent an serious overestimate of the "true" value.

The permeability for neat acetone ($1 \cdot 10^{-5}$) may be considered as "low", whereas the permeability in water ($1 \cdot 10^{-3}$) is about 100-fold higher and may be considered as "high". Thus, there is a strong vehicle effect of water.

Based on neat solvent, the permeability is considered "low".

Substance: Acetonitrile; methyl cyanide
CAS: 75-05-8
Scientific basis: AoH 1991:8

Skin notation: No
Skin permeability: No data

Molecular weight: 41.1
Density: 0.7857 g/cm³
Melting point: -45°C
Boiling point: 81.6°C
Vapour pressure: 9.7 kPa (at 20°C)
Evaporation rate: 5.79
Log Kow: -0.34

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The Swedish consensus report (AoH 1991:8) does not mention dermal uptake of acetonitrile.

According to ACGIH (2001), the oral LD50 value varies much between species, i.e. rat 6500-24000 mg/kg bw and mouse 180 mg/kg bw. The basis for skin notation is a case report where a two-year-old child was dermally exposed to 30 ml of acetonitrile nail polish remover (conc. 98-100%). Eight hours later, vomiting and pain appeared. The intoxication was resolved with oxygen and dextrose support therapy.

Substance: Acrylamide
CAS: 79-06-1
Scientific basis: AoH 1992:6

Skin notation: Yes
Skin permeability: Low

Molecular weight: 71.1
Density: 1.13 g/cm³
Melting point: 84.5°C
Boiling point: 192.6°C
Vapour pressure: 0.9 Pa (at 25°C)
Evaporation rate: Not available
Log Kow: -0.67

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
Hum	Arm			24		H2O	50% (2.5 mg/kg bw)	5	72	72		32	*0.64*	*32*	Fennell et al. (2005)
Rat	Ba			2.5			Neat (160 mg/kg bw)	4	24	24		14-30	*0.85-1.8*	*95-200*	Sumner et al. (2003)

Asessment
Only %absorbed dose has been reported.
The rat and human studies are in agreement.

The permeability of acrylamide may be considered as "low".

Substance: Acrylonitrile
CAS: 107-13-1
Scientific basis: AoH 1987:39

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 53.1
Density: 0.808 g/cm³
Melting point: -83.6°C
Boiling point: 77.3°C
Vapour pressure: 13 kPa (at 22.8°C)
Evaporation rate: 5.8
Log Kow: 0.25

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
Hum	Arm						Neat	4					*7.5*	600	Rogaczewska et al. (1968)

Asessment

No quantitative experimental data on dermal uptake was found in the literature, except for Rogaczewska et al. (1968) cited in WHO (1983).

The permeability of acrylonitrile may be considered as "moderate".

Substance: Allyl alcohol; 2-propen-1-ol
CAS: 107-18-6
Scientific basis: AoH 1987:39

Skin notation: Yes
Skin permeability: No data

Molecular weight: 58.1
Density: 0.854 g/cm³
Melting point: -129°C
Boiling point: 97°C
Vapour pressure: 3.2 kPa (at 25°C)
Evaporation rate: 1
Log Kow: 0.7

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

According to the Swedish consensus report (AoH 1987:39) the LD50 value in animal studies show that allyl alcohol is absorbed via the skin. No further details are given.

Smyth et al. (1948) report similar oral and dermal LD50 values (oral LD50 in rat 64 mg/kg bw, dermal LD50 in rabbits 45 mg/kg bw), suggesting efficient dermal penetration.

Theoretical calculations by Fiserova-Bergerova et al. (1990) suggest that the potential for dermal absorption and resulting toxicity is significant.

Substance: Allylamine; 3-aminopropene
CAS: 107-11-9
Scientific basis: AoH 1983:36

Skin notation: Yes
Skin permeability: No data

Molecular weight: 57.1
Density: 0.761 g/cm³
Melting point: -88°C
Boiling point: 53°C
Vapour pressure: 26 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 0.03

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

According to the Swedish consensus document (AoH 1983:36) skin uptake may occur with massive exposure. No further details are given.

Clayton et al. (1981) (page 3146) refers to a dermal LD50 of 27 mg/kg bw in rabbits. This very low LD50 is even lower than the oral LD50 in rats of 81 mg/kg bw.

Substance: Allylchloride; 3-chloroprene
CAS: 107-05-1
Scientific basis: AoH 1989:32

Skin notation: Yes
Skin permeability: No data

Molecular weight: 76.5
Density: 0.938 g/cm³
Melting point: -134.5°C
Boiling point: 44 to 46°C
Vapour pressure: 39 kPa (at 20°C)
Evaporation rate: 7
Log Kow: 1.93 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux ($\mu g/cm^2/h$)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

No information regarding dermal toxicity is given in the scientific basis (AoH 1989).

The proposal of a skin notation by ACGIH (2001) is based upon an unpublished industrial report.

Substance: Aluminium chlorohydrate
CAS: 1327-41-9
Scientific basis: Not available

Skin notation: No
Skin permeability: Extremely low

Molecular weight: Not available
Density: 1.15 g/cm³
Melting point: Not available
Boiling point: Not available
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: Not available

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
Hum	Pit			77	0.4	H2O	21% (13mg Al)	2	144	1272	~6	3.6 µg	*0.000015*	*0.00032*	Flarend et al. (2001)

Asessment
The study of Flarend et al. (2001) is performed on humans subjects by exposing them to deodorants containing aluminium.

The permeability corresponds to "extremely low".

Substance: Aniline
CAS: 62-53-3
Scientific basis: AoH 1989:32

Skin notation: Yes
Skin permeability: High

Molecular weight: 93.1
Density: 1.022 g/cm³
Melting point: -6.2°C
Boiling point: 184°C
Vapour pressure: 40 Pa (at 20°C)
Evaporation rate: 0.048
Log Kow: 0.90

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Ab		320				Neat	4-6	9	9			27	1900	Barry et al. (1985)
Hum	Ab		320			Vap	Saturated	4-6	9	9			24	260	Barry et al. (1985)
In vivo															
HM	Ba			0.8	0.01		Neat	10	2	4		220 µg	*1.3*	140	Susten et al. (1990)
Hum	Arm			26	0.25		Neat	5	0.5	24		39 mg	27	3000	Baranowska-Dutkiewicz (1982b)
Hum	Arm			26	0.25	H2O	97%	6	0.5	24		33 mg	24	2500	Baranowska-Dutkiewicz (1982b)
Hum	Ha			350-460	Inf	H2O	2%	4	0.5	24		230 mg	600	1220	Baranowska-Dutkiewicz (1982b)
Hum	Ha			350-370	Inf	H2O	2%	2	1	24		300 mg	390	820	Baranowska-Dutkiewicz (1982b)
Hum	Ha			350-420	Inf	H2O	1%	4	0.5	24		58 mg	32	320	Baranowska-Dutkiewicz (1982b)
Hum	Ha			350-440	Inf	H2O	1%	4	1	24		80 mg	200	200	Baranowska-Dutkiewicz (1982b)

Asessment

The studies with minute volumes applied (≤ 0.25 ml) are excluded since depletion may have occurred, resulting in underestimates of flux and Kp.
A number of quantitative studies are available, therefore the human in vivo studies are preferred.

The Kp values of neat aniline range from $2 \cdot 10^{-3}$ to $3 \cdot 10^{-3}$ cm/h, corresponding to "high" permeability.

Substance: Arsenic acid
CAS: 7778-39-4
Scientific basis: AoH 1984:44

Skin notation: No
Skin permeability: Low

Molecular weight: 141.9
Density: 2 g/cm³
Melting point: 35°C
Boiling point: 160°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: -3.14 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum		Fl	500	1		Soil	0.6 µg/cm²	9	24	24		0.4		*0.00011*	Wester et al. (1993a)
Hum		Fl	500	1	0.01	H2O	*0.42*	9	24	24		0.9	*0.038*	*0.0016*	Wester et al. (1993a)
Hum	Br	Fl		0.32	400	H2O	0.01	1	>6	5-6		2.5	0.31	0.00031	Bernstam et al. (2002)
Hum	Br	Fl		0.32	400	H2O	0.1	1	>6	5-6		1.3	0.16	0.0016	Bernstam et al. (2002)
Hum	Br	Fl		0.32	400	H2O	0.25	1	>6	5-6		4.7	0.59	0.015	Bernstam et al. (2002)
Hum	Br	Fl		0.32	400	H2O	0.5	1	>6	5-6		5.4	0.68	0.034	Bernstam et al. (2002)
Hum	Br	Fl		0.32	400	H2O	1	1	>6	5-6		7.5	3.9	0.39	Bernstam et al. (2002)
Pig	Ab	Fl	200	0.64	0.01	Et	2.5 µg	14	16	16		0.4	*0.039*	*0.00098*	Turkall et al. (2003)
In vivo															
Mon	Ab			12		Soil		4	24	168		3.2			Wester et al. (1993a)
Mon	Ab			12	0.06	H2O	*0.42*	3	24	168		2	*0.042*	*0.0018*	Wester et al. (1993a)
Mon				100	0.5	H2O	2.7 (1430 µg)	3	8	96		2.8	*0.18*	*0.05*	Lowney et al. (2005)
Mon				100		Soil	1.4 mg/g (560 µg)	3	8	96		0.1	*0.6*	*0.00084*	Lowney et al. (2005)
Rat	Tail					H2O	0.01-0.2M		1	1			*0.027*	1.1-33	Dutkiewicz (1977)

Asessment

The Kp of Dutkiewicz (1977) was calculated by Bernstam et al. (2002).
Bernstam et al. (2002) used artificial human skin (cultured keratinocytes), therefore the validity of the results is questionable.
The same problem applies to the studies by Wester et al. (1993a) that used soil as "vehicle" or used a very small applied volume of 0.01 ml.
The preferred study is that of Lowney et al. (2005) who applied an aqueous solution of arsenic acid on the skin of Rhesus monkeys for 8h. The 96-h excretion in urine and faeces was compared to that of a known i.v. dose of arsenic.

The permeability of arsenic in monkeys corresponds to "low".

Substance: Arsenic trioxide
CAS: 1327-53-3
Scientific basis: AoH 1984:44

Skin notation: No
Skin permeability: Moderate

Molecular weight: 395.7
Density: 3.74 g/cm³
Melting point: 193°C
Boiling point: 465°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: -0.13 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Hum	Br	Fl		0.32	400	H2O	0.1	1	>6	5-6			0.94	0.0094	Bernstam et al. (2002)
Hum	Br	Fl		0.32	400	H2O	0.25	1	>6	5-6			0.96	0.024	Bernstam et al. (2002)
Hum	Br	Fl		0.32	400	H2O	0.5	1	>6	5-6			0.79	0.04	Bernstam et al. (2002)
Hum	Br	Fl		0.32	400	H2O	1	1	>6	5-6			1.3	0.13	Bernstam et al. (2002)
In vivo															
No data available															

Asessment
The only found study on arsenic trioxide was the one by Bernstam et al. (2002).
In the study, artificial human skin (cultured keratinocytes) was used, therefore the validity of the results are questionable.

The reported Kp values correspond to "moderate" permeability.

Substance: Benzene
CAS: 71-43-2
Scientific basis: AoH 1988:32

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 78.1
Density: 0.879 g/cm³
Melting point: 5.5°C
Boiling point: 80.1°C
Vapour pressure: 7.3 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 2.13

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Ab	St	Epi		Inf	H2O	1.8	13	4	4			1100	0.19	Blank et al. (1985)
Hum	Ab	St	Epi		Inf	HD	44	14		0			9.4	0.044	Blank et al. (1985)
Hum	Ab	St	Epi		Inf	Oct	44	11		0			37	0.17	Blank et al. (1985)
Hum	Ab	St	Epi		Inf	Hex	44			0			24	0.11	Blank et al. (1985)
Hum	Ab	St	Epi		Inf	Gas	44	9		0			14	0.061	Blank et al. (1985)
Hum	Ab	St	40				Neat		4	4			*21*	1800	Blank et al. (1985)
Hum	Ab	St	40			Vap	*0.36* (Saturated)		4	4			*25000*	910	Blank et al. (1985)
Hum	Ab	St	40			H2O	*1.8* (2 µl/ml)	13	4	4			*1100*	190	Blank et al. (1985)
Hum	Br		Full	0.35	0.035		Neat	10	0.5	0.5		0.25 mg/cm²	*5.7*	*500*	Loden (1986a)
Hum	Br	Fl	Full				Neat	7	13.5	13.5	*~3.7*		*1.1*	99	Loden (1986b)
Hum	Ab/Br	Fl	200-400	0.2	400	H2O	15-50 µg/l	210	8	8	0.8		600-3300		Nakai et al. (1997)
Hum					5 µl/cm²	Tol	*0.44 µg/cm²* (0.01%)	4	*1-12*			0.12	*0.005-0.06*	*0.000044-0.00053*	Wester et al. (2000)
Hum					5 µl/cm²	Tol	*4.4 µg/cm²* (0.1%)	4	*1-12*			0.11	*0.00046-0.055*	*0.0004-0.0048*	Wester et al. (2000)
Hum					5 µl/cm²	Tol	*6.6 µg/cm²* (0.15%)	4	*1-12*			0.1	*0.0042-0.05*	*0.00055-0.0066*	Wester et al. (2000)
Hum					5 µl/cm²	Tol	*22 µg/cm²* (0.5%)	4	*1-12*			0.08	*0.0034-0.04*	*0.0015-0.0176*	Wester et al. (2000)
Hum					5 µl/cm²	H2O	*4.4 µg/cm²* (0.1%)	4	*1-12*			5	*0.2-2.5*	*0.018-0.22*	Wester et al. (2000)
Hum					5 µl/cm²	H2O	*22 µg/cm²* (0.5%)	4	*1-12*			3.9	*0.16-2*	*0.072-0.86*	Wester et al. (2000)
Mon							Neat		2.5	2.5			*1.8*	160	Franz (1984)
MP		Fl	900	3.1			Neat	6	18	18			*2.4*	210	Jacobs et al. (1993)
MP		Fl	900	3.1		Vap	0.36 (Saturated)	6	18	18			*3800*	140	Jacobs et al. (1993)
Rat	Ab	St	Full	2.6	1		Neat	46	0.5-2.5	0.5-2.5	0.67	41-920 µg	*2.2*	190	Tsuruta (1982)

Sp	Loc	Cell	L (µm)	A (cm²)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_p (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vivo															
HM	Ba			0.8	0.0045		Neat	7	52 s	4		39 µg	*38*	3400	Susten et al. (1985)
HM	WB					Vap	*0.0097* (3000ppm)	6	2-6	2-6			*6200*	5.9	Tsuruta (1989)
HM	WB					Vap	*0.0032* (1000ppm)	6	2-6	2-6			*6200*	1.9	Tsuruta (1989)
HM	WB					Vap	*0.00064* (200ppm)	6	2-6	2-6			*6200*	0.32	Tsuruta (1989)
Hum	Arm			35-45			Neat	5	2	24		10 mg	*2.8-4.7*	240-400	Hanke et al. (2000)
Mon	Arm			13	0.05		Neat (3.4 mg/cm²)	3	4	120		0.17	*0.016*	*1.4*	Maibach et al. (1981)
Mon	Arm			13			Neat (68 mg/cm²)	3	2.5	168		0.85	*2.6*	*230*	Maibach et al. (1981)
Rat	WB					Vap	*0.13* (40 000ppm)	5	4	4		0.8	1500	19	McDougal et al. (1990)

Asessment

Due to lack of information (no e.g. area, volume, duration) in Wester et al. (2000) the duration of the exposure was assumed to be between 1 and 12h due to the small amount (5 µl/cm²) applied, resulting in wide spans for the fluxes and permeabilities.

The permeability through human skin in vitro varies tremendously between studies, with Kp values between $1 \cdot 10^{4}$ cm/h for neat benzene and 3 cm/h for saturated vapour. The only human in vivo study is that of Hanke et al. (2000) (1961, translated in 2000), with a Kp of $3 \cdot 10^{-4}$ to $5 \cdot 10^{-4}$ cm/h.

This is in agreement with the in vitro studies using human skin and neat benzene (1, 6 and $21 \cdot 10^{4}$ cm/h).

The permeability corresponds to "moderate".

Substance: Benzoapyrene
CAS: 50-32-8
Scientific basis: Not available

Skin notation: Yes
Skin permeability: Extremely low

Molecular weight: 252.3
Density: 1.351 g/cm³
Melting point: 176.5°C
Boiling point: 495°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: 6.13

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
GP	Ba	Fl	500	0.64	0.01	Ac	Neat (13 µg/cm²)	4	24	48		28	*0.0011*	*0.15*	Moody et al. (1995)
GP	Ba	Fl	200	0.64	0.01	Ac	Neat (8 µg/cm²)	5	24	24		37	*0.0009*	*0.12*	Ng et al. (1992)
GP	Ba	Fl	200	0.64	0.01	Ac	Neat (8 µg/cm²)	5	24	24		10	*0.00025*	*0.034*	Ng et al. (1992)
GP	Ba	Fl	200	0.64	0.01	Ac	Neat (74 µg/cm²)	5	24	24		7.2	*0.0016*	*0.22*	Ng et al. (1992)
GP			Full	5			Neat (10 µg)	4	24	24		*0.33*	*0.0000019*	*0.00025*	Kao et al. (1985)
HGP		Fl	200	0.64	0.01	Ac	*0.19* (3µg/cm²)	2-5	24	24		4.6	*0.31*	*0.0058*	Storm et al. (1990)
HM	Ba	Fl	Full	2	0.01-0.02	Ac	Neat (2.5 µg/cm²)	10	16	16		2.9	*0.000033*	*0.0045*	Kao et al. (1988)
HM	Ba	Fl	Full	2	0.01-0.02	Ac	Neat (2.5 µg/cm²)	9	16	16		2	*0.000023*	*0.0031*	Kao et al. (1988)
Hum	Ab	Fl	500	0.64	0.01	Ac	Neat (9.8 µg/cm²)	4	24	48		3.3	*0.000096*	*0.013*	Moody et al. (1995)
Hum	Ab	Fl	500	0.64	0.01	Ac	Neat (8.4 µg/cm²)	4	24	48		1.5	*0.000039*	*0.0053*	Moody et al. (1995)
Hum	FS/TM	Fl	300	0.64	0.01	Ac	Neat (9.1 µg/cm²)	4	24	48		0.2	*0.0000056*	*0.00076*	Moody et al. (1995)
Hum		St	350	1.8	18 mg	Soil	920 mg soil/kg	4-5	96	96			*110*	13	Stroo et al. (2005)
Hum		St	350	1.8	18 mg	Soil	140 mg soil/kg	4-5	96	96			*54*	6.7	Stroo et al. (2005)
Hum		St	350	1.8	18 mg	Soil	1700 mg soil/kg	4-5	96	96			*160*	20	Stroo et al. (2005)
Hum		St	350	1.8	18 mg	Soil	110 mg soil/kg	4-5	96	96			*27*	3.3	Stroo et al. (2005)
Hum		St	350	1.8	18 mg	Soil	38 mg soil/kg	4-5	96	96			*27*	3.3	Stroo et al. (2005)
Hum		St	350	1.8	18 mg	Soil	820 mg soil/kg	4-5	96	96			*160*	20	Stroo et al. (2005)
Hum		St	350	1.8	18 mg	Soil	630 mg soil/kg	4-5	96	96			*110*	13	Stroo et al. (2005)
Hum		Fl	500	1	40 mg	Soil	*0.014* (10 ppm)	6	24	24		0.01	*12*	*0.017*	Wester et al. (1990)
Hum		Fl	500	1	0.6	Ac	*Neat* (58 µg)	6	24	24		0.09	*0.000016*	*0.0022*	Wester et al. (1990)
Hum		Fl	200	0.64	0.01	Ac	*0.19* (3 µg/cm²)	2-5	24	24		0.8	*0.053*	*0.001*	Storm et al. (1990)
Hum	Ab	Fl	1000	0.8			4 µg/cm²					1			Hawkins et al. (1986)
Hum			Full	5			Neat (10 µg)	4	24	24		*2.7*	*0.000017*	*0.0023*	Kao et al. (1985)

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_p (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
Mon			Full	5			Neat (10 µg)	4	24	24		*3.3*	*0.000021*	*0.0028*	Kao et al. (1985)
Mou	Ba	Fl	Full	2	0.01-0.02	Ac	Neat (2.5 µg/cm²)	5	16	16		6.8	*0.000081*	*0.011*	Kao et al. (1988)
Mou	Ba	Fl	Full	2	0.01-0.02	Ac	Neat (2.5 µg/cm²)	10	16	16		6.8	*0.000081*	*0.011*	Kao et al. (1988)
Mou	Ba	Fl	Full	2	0.01-0.02	Ac	Neat (2.5 µg/cm²)	10	16	16		9.4	*0.00011*	*0.015*	Kao et al. (1988)
Mou	Ba	Fl	Full	2	0.01-0.02	Ac	Neat (2.5 µg/cm²)	10	16	16		9.2	*0.0001*	*0.014*	Kao et al. (1988)
Mou	Ba	Fl	Full	2	0.01-0.02	Ac	Neat (2.5 µg/cm²)	10	16	16		4.4	*0.00005*	*0.0068*	Kao et al. (1988)
Mou	Ba	Fl	Full	2	0.01	Ac	Neat (10 ng)		17	17		*15*	*0.00000033*	*0.000044*	Holland et al. (1984)
Mou	Ba	Fl	Full	2	0.01	Ac	Neat (100 ng)		17	17		*30*	*0.000006*	*0.00088*	Holland et al. (1984)
Mou	Ba	Fl	Full	2	0.01	Ac	Neat (1000 ng)		17	17		*25*	*0.000054*	*0.0073*	Holland et al. (1984)
Mou	Ba	Fl	Full	2	0.01	Ac	Neat (2500 ng)		17	17		*16*	*0.00009*	*0.012*	Holland et al. (1984)
Mou	Ba	Fl	Full	2	0.01	Ac	Neat (5000 ng)		17	17		*14*	*0.00016*	*0.021*	Holland et al. (1984)
Mou	Ba	Fl	Full	2	0.01	Ac	Neat (5000 ng)	20	16	16		*11*	*0.00013*	*0.017*	Holland et al. (1984)
Mou	Ba	Fl	Full	2	0.01	Ac	Neat (10000 ng)		17	17		*8*	*0.00018*	*0.024*	Holland et al. (1984)
Mou		Fl	Full	0.64	0.01	Ac	*0.19* (3µg/cm²)	2-5	24	24		3.1	*0.21*	*0.0039*	Storm et al. (1990)
Mou	Ba	Fl	Full	0.8			4 µg/cm²					6			Hawkins et al. (1986)
Mou	Ba		Full	5	0.02	Ac	Neat (5 µg)	4	24	24		24	*0.000074*	*0.01*	Kao et al. (1984)
Mou	Ba		Full	5	0.02	Ac	Neat (10 µg)	4	24	24		17	*0.0001*	*0.014*	Kao et al. (1984)
Mou	Ba		Full	5	0.02	Ac	Neat (20 µg)	4	24	24		12	*0.00015*	*0.02*	Kao et al. (1984)
Mou	Ba		Full	5	0.02	Ac	Neat (30 µg)	4	24	24		7.2	*0.00013*	*0.018*	Kao et al. (1984)
Mou			Full	5			Neat (10 µg)	4	24	24		*10*	*0.000061*	*0.0083*	Kao et al. (1985)
Pig	Ba	Fl	1000	0.8			4 µg/cm²					0.6			Hawkins et al. (1986)
Rab			Full	5			Neat (10 µg)	4	24	24		*1.7*	*0.00001*	*0.0014*	Kao et al. (1985)
Rat	Ba	Fl	500	0.64	0.01	Ac	Neat (11 µg/cm²)	4	24	48		51	*0.0017*	*0.23*	Moody et al. (1995)
Rat		Fl	200	0.64	0.01	Ac	*0.19* (3µg/cm²)	2-5	24	24		3.8	*0.25*	*0.0048*	Storm et al. (1990)
Rat	Ba	St	350	1.8		Oil	100ppm (90 µg/cm²)	5	96	96		38	*0.27*	*0.36*	Yang et al. (1989)
Rat	Ba	St	350	1.8		Soil	1% (9 mg soil/cm²)	5	96	96		8.4	*0.058*	*0.079*	Yang et al. (1989)
Rat	Ba	St	320	1.8		Solv	Neat (9.3 - 9.9 µg/cm²)	4	120	120		2.1	*0.000013*	*0.0017*	Yang et al. (1986)
Rat	Ba	St	Full	1.8		Solv	Neat (9.3 - 9.9 µg/cm²)	4	120	120		28	*0.00017*	*0.023*	Yang et al. (1986)
Rat	Ba	St	350	1.8		Solv	Neat (9.3 - 9.9 µg/cm²)	4	120	120		50	*0.0003*	*0.04*	Yang et al. (1986)
Rat		Fl	300	0.64	0.0096	Ac	*Neat?* (2-5 µg/cm²)	3	168	168		3.7	*0.000003-0.0000081*	*0.00044-0.0011*	Bronaugh et al. (1986)
Rat		Fl	300	0.64	0.0096	Ac	*Neat?* (2-5 µg/cm²)	3	168	168		56	*0.00005-0.00013*	*0.0067-0.017*	Bronaugh et al. (1986)
Rat			Full	5			Neat (10 µg)	4	24	24		*2*	*0.000013*	*0.0017*	Kao et al. (1985)

Sp	Loc	Cell	L (µm)	A (cm^2)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_p (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vivo															
GP	Ba			8	0.1	Ac	Neat (17 µg/cm^2)	4	6	6		4.1	*0.0009*	*0.12*	Chu et al. (1996)
GP	Ba			8	0.1	Ac	Neat (22 µg/cm^2)	4	24	24		17	*0.0011*	*0.15*	Chu et al. (1996)
GP	Ba			8	0.1	Ac	Neat (32 µg/cm^2)	4	24	48		23	*0.0022*	*0.3*	Chu et al. (1996)
GP	Ba			8	0.1	Ac	Neat (87 µg/cm^2)	4	24	168		24	*0.0065*	*0.87*	Chu et al. (1996)
GP	Ba			4.2	0.05	Ac	Neat (9.1 µg/cm^2)	4	24	336		68	*0.0019*	*0.26*	Moody et al. (1995)
GP	Ba			4	0.05	Ac	Neat (28 µg)	5	24	168		73	*0.0016*	*0.22*	Ng et al. (1992)
Mon	Ab			12	480 mg	Soil	*0.014* (10 ppm)	4	24	144		13	*1.6*	*0.0022*	Wester et al. (1990)
Mon	Ab			12		Ac	*Neat* (58 µg)	4	24	144		51	*0.00074*	*0.1*	Wester et al. (1990)
Mou	Ba			1.8	≤0.015	Ac	15 (130 µg/cm^2)	5-6	24	24		41	*1.4*	*2.1*	Sanders et al. (1984)
Mou	Ba			1.8	≤0.015	Ac	15 (130 µg/cm^2)	5-6	24	24		84	*0.29*	*0.43*	Sanders et al. (1984)
Mou	Ba			1.8	≤0.015	Ac	15 (130 µg/cm^2)	5-6	24	24		82	*0.029*	*0.043*	Sanders et al. (1984)
Rat	Ba			4.2	0.05	Ac	Neat (6.1 µg/cm^2)	4	24	336		69	*0.0013*	*0.17*	Moody et al. (1995)
Rat	Ba			7		Oil	100ppm (90 µg/cm^2)	5	96	96		35	*0.24*	*0.33*	Yang et al. (1989)
Rat	Ba			7		Soil	1% (9 mg soil/cm^2)	5	96	96		9.2	*0.064*	*0.086*	Yang et al. (1989)
Rat	Ba			1.2			Neat (9.2 µg/cm^2)	4	120	120		46	*0.00026*	*0.035*	Yang et al. (1986)
Rat	Ba			1.25	0.019	Ac	*Neat?* (2-5 µg/cm^2)	5	24	192		48	*0.0003-0.00074*	*0.04-0.1*	Bronaugh et al. (1986)

Asessment

Nearly all studies only report percent absorbed dose. Fluxes and Kp values were calculated assuming constant flux during the exposure.

The in vivo study by Chu et al. (1996) is preferred since a relatively large amount of benzo[a]pyrene was applied. Further it represents the mid-range of calculated Kp values.

The Kp of $1 \cdot 10^{-7}$ to $7 \cdot 10^{-7}$ cm/h suggests "extremely low" permeability

Substance: Borax
CAS: 1303-96-4
Scientific basis: AoH 1983:36

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 381.4
Density: 1.73 g/cm³
Melting point: 75°C
Boiling point: 320°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: Not available

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Hum	Leg	Fl	500	1	1	H2O	50	6	24	24		0.41	1.7	8.5	Wester et al. (1998a)
In vivo															
Hum	Ba			900	1.8	H2O	50 (2 µl/cm^2)	8	24	168		0.21	0.0018	*0.009*	Wester et al. (1998b)

Asessment

The very low flux and Kp in the in vivo study (Wester et al. (1998b)) is likely due to the small amount applied (2 µl/cm^2 or 6 µg/cm^2).

The permeability, of the in vitro study (Wester et al. (1998a)), corresponds to "moderate".

Substance: Butanol, iso-
CAS: 78-83-1
Scientific basis: AoH 1984:44

Skin notation: Yes
Skin permeability: No data

Molecular weight: 74.1
Density: 0.802 g/cm³
Melting point: -108°C
Boiling point: 107.9°C
Vapour pressure: 1.2 kPa (at 20°C)
Evaporation rate: 2
Log Kow: 0.76

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux ($\mu g/cm^2/h$)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment
The permeability properties can be assumed to be similar to that of n-butanol.

Substance: Butanol, n-
CAS: 71-36-3
Scientific basis: AoH 1984:44

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 74.1
Density: 0.81 g/cm³
Melting point: -89.5°C
Boiling point: 117.6°C
Vapour pressure: 0.7 kPa (at 20°C)
Evaporation rate: 0.46
Log Kow: 0.88

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Dog	Br	St	Full		1		*5%*	5	5	5			28	*111*	Mills et al. (2003)
Hum	Ab	St	26.6	2.5		*H2O*	*7.4*	8					25	*19*	Scheuplein et al. (1973)
Hum	Ab	St	2500	2.5		*H2O*	*7.4*	3					300	*220*	Scheuplein et al. (1973)
Hum	Ab	St	26.6	2.5			Neat	7					0.6	*48*	Scheuplein et al. (1973)
Hum	Ab	St	2500	2.5			Neat	8					10	*820*	Scheuplein et al. (1973)
Hum		Fl	250	1	0.2-0.3		Neat	3	24	24		*1.8 (9h)*	*4.1-6.2*	*330-500*	Boman et al. (2000)
Hum		Fl	250	1	0.2-0.3	Tol	50%	5	21	21		*70 (10h)*	*140-200*	*5600-8400*	Boman et al. (2000)
Hum		Fl	250	1	0.2-0.3	Chf + Me	50%	6	21	21		*22*	*21-32*	*840-1300*	Boman et al. (2000)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	0.3	0.3			65		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	4.3	4.3			82		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	7.8	7.8			120		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	11.3	11.3			120		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	14.3	14.3			120		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	1	26.3	26.3			120		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	0.3	0.3			42		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	5.8	5.8			68		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	9.8	9.8			73		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	13.8	11.3			75		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	17.8	14.3			73		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	26.3	26.3			79		Behl et al. (1980)
Mou	Ab	St	Full	0.6	0.2	NaCl		3	2	2			37		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		2	2	2			42		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		4	2	2			87		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		5	2	2			130		Behl et al. (1984)

Sp	Loc	Cell	L (µm)	A (cm^2)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
Mou	Ab	St	Full	0.6	0.2	NaCl		4	2	2			41		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		5	2	2			65		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		4	2	2			40		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		3	2	2			87		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		2	2	2			100		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		2	2	2			170		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		5	2	2			240		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		4	2	2			62		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		5	2	2			65		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		5	2	2			51		Behl et al. (1984)
Mou	Ab	St	Full	0.6		NaCl	0.0001M	5	2	2			76		Behl et al. (1981)
Mou	Ab	St	Full	0.79		NaCl	≤10-4M		2	2			29		Durrheim et al. (1980)
Mou	Ab	St	Full	0.79		NaCl	≤10-4M		2	2			44		Durrheim et al. (1980)
Mou	Ab	St	Full	0.79		NaCl	≤10-4M		2	2			150		Durrheim et al. (1980)
MP		Fl	900	3.1			Neat	6	17.5	17.5			*3.7*	300	Jacobs & Phanprasit (1993)
MP		Fl	900	3.1		Vap	0.026 (Sat.)	6	17.5	17.5			*33000*	86	Jacobs & Phanprasit (1993)
In vivo															
Dog	Br			56			Neat	2	1	8		29 mg	*6.5*	530	DiVincenzo et al. (1979)

Asessment

Based on neat solvent, the permeability is considered "moderate" with Kp values of $4{\cdot}10^{-4}$ to $1{\cdot}10^{-3}$ cm/h (human full thickness skin in vitro) and $7{\cdot}10^{-4}$ cm/h (dog in vivo).

It should be noted that there seems to be a strong vehicle effect of water. Thus, the permeability in mouse skin of n-butanol in physiological saline ranges from $4{\cdot}10^{-3}$ to $2{\cdot}10^{-2}$ cm/h. Similar values ($3{\cdot}10^{-3}$ for stratum corneum and $3{\cdot}10^{-2}$ cm/h for full thickness skin) are reported for human skin.

Substance: Butanol, sek-
CAS: 78-92-2
Scientific basis: AoH 1984:44

Skin notation: Yes
Skin permeability: No data

Molecular weight: 74.1
Density: 0.806 g/cm³
Melting point: -115°C
Boiling point: 99.5°C
Vapour pressure: 1.6 kPa (at 20°C)
Evaporation rate: 1.3
Log Kow: 0.61

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

The permeability properties can be assumed to be similar to that of n-butanol.

According to theoretical calculations by Fiserova-Bergerova et al. (1990) the potential for dermal absorption and resulting toxicity is significant.

Substance: Butanol, tert-
CAS: 75-65-0
Scientific basis: AoH 1984:44

Skin notation: Yes
Skin permeability: No data

Molecular weight: 74.1
Density: 0.786 g/cm³
Melting point: 25.5°C
Boiling point: 82.2°C
Vapour pressure: 3.4 kPa (at 20°C)
Evaporation rate: 1.1
Log Kow: 0.35

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment
The permeability properties can be assumed to be similar to that of n-butanol.

Substance: Butyl acetate, n-
CAS: 123-86-4
Scientific basis: AoH 1984:44

Skin notation: No
Skin permeability: Moderate

Molecular weight: 116.2
Density: 0.882 g/cm³
Melting point: -106.2°C
Boiling point: 126.1°C
Vapour pressure: 1.2 kPa (at 20°C)
Evaporation rate: 1
Log Kow: 1.78

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Hum	Br	St	300-600	0.64		Neat	3	6	6			*2.2*	200	Ursin et al. (1995)
In vivo														
No data available														

Asessment

Ursin et al. (1995) stretched the skin when mounting it in the diffusion cell, reaching a final thickness of about one-third of the original thickness. This procedure may give overestimates of the flux and Kp values.

The permeability corresponds to "moderate".

Substance: Butylamine, iso-
CAS: 78-81-9
Scientific basis: AoH 1983:36

Skin notation: Yes
Skin permeability: No data

Molecular weight: 73.1
Density: 0.724 g/cm³
Melting point: -85°C
Boiling point: 66°C
Vapour pressure: 13 kPa (at 18.8°C)
Evaporation rate: Not available
Log Kow: 0.73

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

According to the Swedish consensus document (AoH 1983:36) skin uptake may occur with massive exposure.
No further details are given.

See also information on n-butylamine.

Substance: Butylamine, n-
CAS: 109-73-9
Scientific basis: AoH 1983:36

Skin notation: Yes
Skin permeability: No data

Molecular weight: 73.1
Density: 0.741 g/cm³
Melting point: -50°C
Boiling point: 77°C
Vapour pressure: 11 kPa (at 20°C)
Evaporation rate: 7.3
Log Kow: 0.97

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

According to the Swedish consensus document (AoH 1983:36) skin uptake may occur with massive exposure. No further details are given.

Clayton et al. (1981) (page 3146) refers to a the dermal LD50 of 370 mg/kg bw in guinea pig. This is lower than the oral LD50 in rat (500 mg/kg bw).

Theoretical calculations by Fiserova-Bergerova et al. (1990) suggest that the potential for dermal absorption and resulting toxicity is significant.

Substance: Butylamine, sec-
CAS: 13952-84-6
Scientific basis: AoH 1983:36

Skin notation: Yes
Skin permeability: No data

Molecular weight: 73.1
Density: 0.724 g/cm³
Melting point: -85°C
Boiling point: 66°C
Vapour pressure: 18 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 0.74

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

According to the Swedish consensus document (AoH 1983:36) skin uptake may occur with massive exposure.
No further details are given.

See also information on n-butylamine.

Substance: Butylamine, tert-
CAS: 75-64-9
Scientific basis: AoH 1983:36

Skin notation: Yes
Skin permeability: No data

Molecular weight: 73.1
Density: 0.696 g/cm³
Melting point: -67.5°C
Boiling point: 44.4°C
Vapour pressure: 48 kPa (at 25°C)
Evaporation rate: 1
Log Kow: 0.40

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
No data available															

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

According to the Swedish consensus document (AoH 1983:36) skin uptake may occur with massive exposure.
No further details are given.

See also information on n-butylamine.

Substance: Carbon disulfide
CAS: 75-15-0
Scientific basis: Not available

Skin notation: Yes
Skin permeability: Very high

Molecular weight: 76.1
Density: 1.263 g/cm³
Melting point: -110°C
Boiling point: 46.2°C
Vapour pressure: 35 kPa (at 20°C)
Evaporation rate: 23
Log Kow: 1.94

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
Hum	Ha				Inf H2O	0.3-1.7	21	1	8		7-37 mg	*250-830*	20-96	Baranowska (1965)

Asessment

The only available study is that of Baranowska (1965) (in German) were the subject placed one hand in an aqueous carbon disulfide solution for 1 hour. The uptake of the substance was measured via breath monitoring.

The reported Kp values range between $3 \cdot 10^{-2}$ and $9 \cdot 10^{-2}$ cm/h, suggesting "very high" permeability.

Substance: Carbon tetrachloride
CAS: 56-23-5
Scientific basis: Not available

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 153.8
Density: 1.594 g/cm³
Melting point: -22.9°C
Boiling point: 76.7°C
Vapour pressure: 10 kPa (at 20°C)
Evaporation rate: 13
Log Kow: 2.83

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Rat	Ab	St	Full	3.7	1	Neat	24	2-4	2-4	1.4	52-210 µg	*0.13*	21	Tsuruta (1977)
In vivo														
Mou	Ab				0.5	Neat	6	0.25			360 µg	*3.1*	490	Tsuruta (1975)

Asessment

The in vitro study of Tsuruta (1977) used physiological saline as the receptor medium, this is unsuitable for highly lipophilic substances.
Tsuruta (1975) measured absorption by homogenizing the whole animal.
Dermal uptake of carbon tetrachloride has also been shown in humans (Stewart et al. (1964)), however, that study does not contain sufficient data to calculate flux of Kp.

The preferred study is Tsuruta (1975), were the calculated Kp value suggests "moderate" permeability.

Substance: Catechol
CAS: 120-80-9
Scientific basis: AoH 1992:47

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 110.1
Density: 1.3 g/cm³
Melting point: 104°C
Boiling point: 245°C
Vapour pressure: 660 Pa (at 104°C)
Evaporation rate: Not available
Log Kow: 0.88

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Ab	Fl	200-320	0.64	0.01	PHD	6	3	0.5	24		0.4	*1.6*	*0.98*	Jung et al. (2003)
Hum	Ab	Fl	200-320	0.64	0.01	HDP	6		0.5	24		1.8	*7.3*	*4.4*	Jung et al. (2003)
Rat	Ba	Fl	200-320	0.64	0.01	PHD	6		0.5	24		0.2	*0.81*	*0.49*	Jung et al. (2003)
Rat	Ba	Fl	200-320	0.64	0.01	HDP	6		0.5	24		2	*8.1*	*4.9*	Jung et al. (2003)
Rat	Ba	Fl	200-320	0.64	0.01	Et	6	8	0.5	24		6.9	*28*	*17*	Jung et al. (2003)
Rat	Ba	Fl	200-320	0.64	0.01	Et	6		24	24		42	*3.5*	*2.1*	Jung et al. (2003)
Rat	Ba	Fl	200-320	0.64	0.01	Et	6		24	72		49	*4.1*	*2.5*	Jung et al. (2003)
Rat	Ba	Fl	200-320	0.64	0.01	Et	6	4	24	24		78	*6.6*	*3.9*	Jung et al. (2003)
Rat	Ba	Fl	200-320	0.64	0.01	Et	6	4	24	24		55	*4.7*	*2.8*	Jung et al. (2003)
Rat	Ba	Fl	200-320	0.64	0.01	Et	40	9	24	24		81	*6.8*	*27*	Jung et al. (2003)
Rat	Ba	Fl	200-320	0.64	0.01	Et	40	9	24	72		81	*6.9*	*27*	Jung et al. (2003)
In vivo															
Rat	Ba			9	0.18	Et	40	3	24	24		45	*3.7*	*15*	Jung et al. (2003)
Rat	Ba			9	0.18	Et	40	3	24	72		53	*4.4*	*18*	Jung et al. (2003)

Asessment
A number of different experiments yield similar results.

The human in vitro and rat in vivo experiments give Kp values between $2 \cdot 10^{-4}$ and $7 \cdot 10^{-4}$ cm/h, corresponding to "moderate" permeability.

It should be noted that either ethanol or hair dye chemicals were used as vehicles, this may have altered the permeability.

Substance: Chlorinated biphenyls, poly- (PCB)
CAS: 1336-36-3
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No data

Molecular weight: 291.98 to 360.86
Density: 1.4 to 1.5 g/cm³
Melting point: Not available
Boiling point: 340 to 375°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: 6.34 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux ($\mu g/cm^2/h$)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No Swedish consensus document or TLV documentation is present.

Garner et al. (1998) showed that the less chlorinated PCBs penetrate the skin more rapidly. However the metabolism is more rapid for these smaller molecules, resulting in a higher body burden for the higher chlorinated PCBs.

Data on four congeners (see mono-, di-, tetra- and hexachlorobiphenyl) suggests that the permeability of PCB is "extremely low" to "very low".

Substance: Chloro-1,3-butadiene, 2-; chloroprene
CAS: 126-99-8
Scientific basis: AoH 1986:35

Skin notation: Yes
Skin permeability: No data

Molecular weight: 88.5
Density: Not available
Melting point: -130°C
Boiling point: 59.4°C
Vapour pressure: 23 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 2.53 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

According to the Swedish criteria group (AoH 1986) and ACGIH (2001) an old study (von Oettingen et al. (1936)) mentions that the substance probably can be absorbed through the skin in amounts large enough to cause acute effects.

Substance: Chlorobiphenyl, di- (DCB)
CAS: 25512-42-9
Scientific basis: Not available

Skin notation: Yes
Skin permeability: Very low

Molecular weight: Not available
Density: 1.4 g/cm³
Melting point: 149°C
Boiling point: Not available
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: 5.59 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
Rat	Ba			1	(0.15 ml/kg bw) Ac	Neat (0.4 mg/kg bw)	18	48	336		85 (24h)	*0.026*	*3.5*	Garner & Matthews (1998)
Rat	Ba			1	(0.15 ml/kg bw) Ac	Neat (0.4 mg/kg bw)	18	48	336		66 (24h)	*0.02*	*2.8*	Garner et al. (2006)

Asessment

The two studies by Garner were conducted in similar fashion except for method of measuring absorbed amount. This was done in carcass (Garner & Matthews (1998)) and in urine and faeces (Garner et al. (2006)), respectively.

The two studies show consistent results, with the calculated Kp values ranging between $2 \cdot 10^{-6}$ and $3 \cdot 10^{-6}$ cm/h, suggesting "very low" permeability.

Substance: Chlorobiphenyl, hexa- (HCB)
CAS: 26601-64-9
Scientific basis: Not available

Skin notation: Yes
Skin permeability: Extremely low

Molecular weight: 360.9
Density: 1.8 g/cm³
Melting point: 201 to 202°C
Boiling point: Not available
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: 7.75

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
Rat	Ba			1	(0.15 ml/kg bw) Ac	Neat (0.4 mg/kg bw)	18	48	336		9 (24h)	*0.002*	*0.38*	Garner & Matthews (1998)
Rat	Ba			1	(0.15 ml/kg bw) Ac	Neat (0.4 mg/kg bw)	18	48	336		19 (24h)	*0.0044*	*0.8*	Garner et al. (2006)

Asessment

The two studies by Garner were conducted in similar fashion except for method of measuring absorbed amount. This was done in carcass (Garner & Matthews (1998)) and in urine and faeces (Garner et al. (2006)), respectively.

The two studies show consistent results, with the calculated Kp values ranging between $2 \cdot 10^{-7}$ and $4 \cdot 10^{-7}$ cm/h, suggesting "extremely low" permeability.

Substance: Chlorobiphenyl, mono- (MCB)
CAS: 27323-18-8
Scientific basis: Not available

Skin notation: Yes
Skin permeability: Very low

Molecular weight: Not available
Density: 1.1 g/cm³
Melting point: 10°C
Boiling point: 365°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: 4.58

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
Rat	Ba			1	(0.15 ml/kg bw)	Ac	Neat (0.4 mg/kg bw)	18	48	336		98 (24h)	*0.037*	*4.1*	Garner & Matthews (1998)
Rat	Ba			1	(0.15 ml/kg bw)	Ac	Neat (0.4 mg/kg bw)	18	48	336		69 (24h)	*0.026*	*2.9*	Garner et al. (2006)

Asessment

The two studies by Garner were conducted in similar fashion except for method of measuring absorbed amount. This was done in carcass (Garner & Matthews (1998)) and in urine and faeces (Garner et al. (2006)), respectively.

The two studies show consistent results, with the calculated Kp values ranging between $3 \cdot 10^{-6}$ and $4 \cdot 10^{-6}$ cm/h, suggesting "very low" permeability.

Substance: Chlorobiphenyl, tetra- (TCB)
CAS: 26914-33-0
Scientific basis: Not available

Skin notation: Yes
Skin permeability: Extremely low

Molecular weight: 292.0
Density: 1.6 g/cm³
Melting point: ~170°C
Boiling point: ~360°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: 6.09

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
Rat	Ba			1	(0.15 ml/kg bw) Ac	Neat (0.4 mg/kg bw)	18	48	336		37 (24h)	*0.0096*	*1.5*	Garner & Matthews (1998)
Rat	Ba			1	(0.15 ml/kg bw) Ac	Neat (0.4 mg/kg bw)	18	48	336		8 (24h)	*0.0019*	*0.3*	Garner et al. (2006)

Asessment

The two studies by Garner were conducted in similar fashion except for method of measuring absorbed amount. This was done in carcass (Garner & Matthews (1998)) and in urine and faeces (Garner et al. (2006)), respectively.

The two studies show rather consistent results, with the calculated Kp values ranging between $2 \cdot 10^{-7}$ and $1 \cdot 10^{-6}$ cm/h, suggesting "extremely low" permeability.

Substance: Chlorocresol; 4-chloro-3-methylphenol
CAS: 59-50-7
Scientific basis: Not available

Skin notation: No
Skin permeability: Moderate

Molecular weight: 142.6
Density: 0.9 g/cm³
Melting point: 67°C
Boiling point: 235°C
Vapour pressure: 13 Pa (at 20°C)
Evaporation rate: Not available
Log Kow: 3.10

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Hum	Ab	St	Epi	2.5	Inf	H2O	4	2	8	8	0.3		550	*220*	Roberts et al. (1977)
In vivo															
GP				8	0.2	H2O + Gel	5% (10 mg)	19	24	96		75	*8.7*	*39*	Andersen et al. (1985)
GP				8	0.2	H2O	0.4% (Saturated. 0.8 mg)	20	24	96		54	*5.8*	*2.3*	Andersen et al. (1985)
GP				8	0.2	oil/ac	5% (10 mg)	20	24	96		34	*4*	*18*	Andersen et al. (1985)
GP				8	0.2	PG	5% (10 mg)	20	24	96		35	*4*	*18*	Andersen et al. (1985)

Asessment

In the experiments by Roberts et al. (1977), epidermal sheets were separated by exposing skin to ammonia vapour for 30 min. Ammonia is well known to cause severe skin damage Amshel et al. (2000). The alkaline nature of ammonia quickly saponifies the epidermal fats, thus destroying the protective structure of the epidermis. Therefore, the method used by Roberts et al. (1977) is likely to result in severe overestimates of the flux and Kp value of undamaged skin.

The preferred in vivo experiment is by Andersen et al. (1985) using water as vehicle.

The reported Kp value for saturated chlorophenol in water of $6 \cdot 10^{-4}$ cm/h, suggests "moderate" permeability.

Substance: Chloroethanol, 2-
CAS: 107-07-3
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No data

Molecular weight: 80.5
Density: 1.201 g/cm³
Melting point: -89°C
Boiling point: 130°C
Vapour pressure: 0.66 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 0.03

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment
No quantitative experimental data on dermal uptake were found in the literature.

No documentation by the Swedish consensus group or ACGIH was found for this substance.
The acute dermal toxicity is extremely high. Thus, application of 2 ml on the skin caused 80% mortality in 1 hour and a dose of 1 ml caused 80-100% mortality within 1 week in guinea pigs (Wahlberg et al. (1979)).

Substance: Chloroform; trichloromethane
CAS: 67-66-3
Scientific basis: Not available

Skin notation: No
Skin permeability: Very high

Molecular weight: 119.4
Density: 1.498 g/cm³
Melting point: -63.7°C
Boiling point: 61.7°C
Vapour pressure: 18 kPa (at 20°C)
Evaporation rate: 0.09
Log Kow: 1.97

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Ab	Fl	300	0.64	1	H2O	400 µg/l (0.62 µg/cm²)		4	4		4.1 (2h)	*320*	*0.013*	Dick et al. (1995)
Hum	Ab	Fl	300	0.64	0.05	H2O	0.9 (70 µg/cm²)		4	4		6.5 (2h)	*26*	*2.3*	Dick et al. (1995)
Hum	Ab	Fl	200-400	0.2	Inf	H2O	140-290 µg/l	19	6	6			1400		Nakai et al. (1999)
Hum	Ab	Fl	200-400	0.2	Inf	H2O	140-290 µg/l	19	6	6			1700		Nakai et al. (1999)
In vivo															
HGP	WB			~300	Inf	H2O	19-52 ppb	6	1.2	2-4w			1300		Bogen et al. (1992)
HR	WB			460	Inf	H2O	0.44	3	0.5	0.5		20 mg	2900	*130*	Islam et al. (1995)
HR	WB			510	Inf	H2O	0.44	4	0.5	6		10 mg	900	*40*	Islam et al. (1996)
HR	Ba			5.46	0.35		Neat	3	1 min	6		2.8 mg	*210*	*31000*	Islam et al. (1999)
HR	Ba			5.46	0.35		Neat	3	3 min	6		3.5 mg	*85*	*13000*	Islam et al. (1999)
HR	Ba			5.46	0.35		Neat	3	8 min	6		13 mg	*120*	*18000*	Islam et al. (1999)
Hum	Arm			3.1	0.05	H2O	1 (50 µg)	3	8	72		8.2	*1.7*	*0.17*	Dick et al. (1995)
Hum	Arm			3.1	0.05	Et	5 (250 µg)	4	8	72		1.7	*0.34*	*0.17*	Dick et al. (1995)
Hum	WB				Inf	H2O	40 µg/l	6	0.5	2.5			150	*0.0006*	Xu et al. (2005)
Hum	WB				Inf	H2O	*60-150 µg/l* (40-97 ppb)	9	0.5	~1		12-44 µg	600	*0.0036-0.009*	Corley et al. (2000)
Mou	Ab			2.9	0.5		Neat	10	0.25			1700 µg	*16*	2400	Tsuruta (1975)

Asessment

The experiment using ethanol as vehicle is disregarded as skin permeability may be affected.
The in vitro Kp value of Dick et al. (1995) is calculated during the first 2h of exposure, due to possible depletion.
The in vivo study of Dick et al. (1995) was performed unoccluded, hence the low absorption/Kp values.
Tsuruta (1975) measured absorption by homogenizing the whole animal. This method may severely underestimate skin permeability.
The preferred experiment is that of Islam et al. (1999), using neat chloroform and hairless rat in vivo and the longest exposure duration (8 min). The Kp value of $1 \cdot 10^{-2}$ suggest "very high" permeability.

Substance: Chromate, potassium di-
CAS: 7778-50-9
Scientific basis: AoH 2000:22

Skin notation: No
Skin permeability: Very low

Molecular weight: 294.2
Density: 2.676 g/cm³
Melting point: 398°C
Boiling point: 500°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: -3.59 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Hum	Ab	St	Full	0.7/1.8	556 µl/cm^2	H2O	0.5% (0.034 M)	3	190	190			*0.00014*	0.00019	Gammelgaard et al. (1992)
In vivo															
Hum	WB			~13000	Inf	H2O	0.022	4	3	96			*0.068*	0.00015	Corbett et al. (1997)

Asessment

Only one study was found on potassium dichromate. In Gammelgaard et al. (1992), human abdominal skin was exposed to aqueous solution.

The reported Kp value suggests "extremely low" permeability.

It should be noted that the reported Kp value of sodium chromate is two orders of magnitude higher.

Substance: Chromate, sodium di-
CAS: 7775-11-3
Scientific basis: AoH 2000:22

Skin notation: No
Skin permeability: High

Molecular weight: 162.0
Density: 2.7 g/cm^3
Melting point: 792°C
Boiling point: Not available
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: Not available

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
GP	Ba	Fl	Full	3.1		H2O	*5.5* (0.034 M)	10	48	48			*11*	6.2	Wahlberg (1965)
GP	Ba		Full	3.1	1	H2O	*2.8* (0.017 M)	5	24	24			*19*	5.2	Wahlberg (1970)
GP	Ba		Full	3.1	1	H2O	*13* (0.080 M)	5	24	24			*15*	20	Wahlberg (1970)
GP	Ba		Full	3.1	1	H2O	*39* (0.239 M)	5	24	24			*14*	54	Wahlberg (1970)
GP	Ba		Full	3.1	1	H2O	*65* (0.398 M)	5	24	24			*12*	75	Wahlberg (1970)
Hum	Ab	Fl	Full	3.1		H2O	*5.5* (0.034 M)	10	48	48			*3.3*	1.8	Wahlberg (1965)
Hum	Ab		Full	3.1	1	H2O	*2.8* (0.017 M)	5	24	24			*8.7*	2.4	Wahlberg (1970)
Hum	Ab		Full	3.1	1	H2O	*13* (0.080 M)	5	24	24			*13*	17	Wahlberg (1970)
Hum	Ab		Full	3.1	1	H2O	*39* (0.239 M)	5	24	24			*14*	54	Wahlberg (1970)
Hum	Ab		Full	3.1	1	H2O	*65* (0.398 M)	5	24	24			*15*	97	Wahlberg (1970)
In vivo															
GP						H2O	2.8-65 (0.017-0.398 M)	20	5	5			*17-18*	4.9-120	Wahlberg et al. (1965)
GP	Ba			3.1		H2O	*5.5* (0.034 M)	10	48	48			*12*	6.8	Wahlberg (1965)
GP	Ba				1	H2O	*2.8* (0.017 M)	5	24	24			*18*	4.9	Wahlberg et al. (1963)
GP	Ba				1	H2O	*13* (0.080 M)	5	24	24			*13*	17	Wahlberg et al. (1963)
GP	Ba				1	H2O	*42* (0.261 M)	5	24	24			*26*	110	Wahlberg et al. (1963)
GP	Ba				1	H2O	*65* (0.398 M)	5	24	24			*18*	120	Wahlberg et al. (1963)
Hum	Arm					H2O	*1.6* (0.01M)	9	1	1			*6.9*	1.1	Baranowska-Dutkiewicz (1981)
Hum	Arm					H2O	*16* (0.1M)	9	1	1			*4.1*	6.5	Baranowska-Dutkiewicz (1981)
Hum	Arm					H2O	*32* (0.2M)	9	1	1			*3.1*	10	Baranowska-Dutkiewicz (1981)

Asessment

Human and guinea pig data suggest "high" permeability of sodium dichromate,
with Kp values between $3 \cdot 10^{-4}$ and $3 \cdot 10^{-3}$ cm/h.
It should be noted that the reported Kp value for potassium dichromate is two orders of magnitude lower.

Substance: Chromic chloride
CAS: 10025-73-7
Scientific basis: AoH 2000:22

Skin notation: No
Skin permeability: High

Molecular weight: 158.4
Density: 2.76 g/cm³
Melting point: 1152°C
Boiling point: Not available
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: 1.16 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
GP	Ba		Full	3.1	1	H2O	*2.7* (0.017 M)	5	24	24			*20*	5.5	Wahlberg (1970)
GP	Ba		Full	3.1	1	H2O	*13* (0.080 M)	5	24	24			*20*	26	Wahlberg (1970)
GP	Ba		Full	3.1	1	H2O	*38* (0.239 M)	5	24	24			*21*	81	Wahlberg (1970)
GP	Ba		Full	3.1	1	H2O	*63* (0.398 M)	5	24	24			*15*	91	Wahlberg (1970)
GP	Ba	Fl	Full	3.1		H2O	*2.7* (0.017 M)	10	48	48			*15*	4	Wahlberg (1965)
GP	Ba	Fl	Full	3.1		H2O	*13* (0.080 M)	10	48	48			*10*	13	Wahlberg (1965)
GP	Ba	Fl	Full	3.1		H2O	*20* (0.126 M)	10	48	48			*12*	24	Wahlberg (1965)
GP	Ba	Fl	Full	3.1		H2O	*38* (0.239 M)	10	48	48			*13*	50	Wahlberg (1965)
GP	Ba	Fl	Full	3.1		H2O	*41* (0.261 M)	10	48	48			*13*	52	Wahlberg (1965)
Hum	Ab		Full	3.1	1	H2O	*2.7* (0.017 M)	5	24	24			*15*	4	Wahlberg (1970)
Hum	Ab		Full	3.1	1	H2O	*13* (0.080 M)	5	24	24			*13*	16	Wahlberg (1970)
Hum	Ab		Full	3.1	1	H2O	*38* (0.239 M)	5	24	24			*11*	40	Wahlberg (1970)
Hum	Ab		Full	3.1	1	H2O	*63* (0.398 M)	5	24	24			*12*	75	Wahlberg (1970)

In vivo

No data available

Asessment

The calculated Kp values (two studies only) on chromate chloride are consistent.
The preferred experiments are those on human skin, with calculated Kp values corresponding to "high" permeability.

Substance: Cobalt
CAS: 7440-48-4
Scientific basis: AoH 2004:16

Skin notation: No
Skin permeability: Extremely low

Molecular weight: 58.9
Density: 8.92 g/cm³
Melting point: 1495°C
Boiling point: 2870°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: 0.23 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Hum	Ab	St	Full		1	NaCl	50	7	24	24	1.55		*0.0025*	0.012	Larese Filon et al. (2004)
In vivo															
Hum	Ha			*390*	Inf	Powder	5-15% (0.05-0.25 mg/m³)	4	1.5	72			*0.0003-0.0009*	*0.04*	Scansetti et al. (1994)

Asessment

The two found studies report fairly consistent Kp values, ranging between $3 \cdot 10^{-7}$ and $3 \cdot 10^{-8}$ cm/h.

The preferred study is that of Scansetti et al. (1994). The Kp value corresponds to "extremely low" permeability.

Substance: Cobalt dichloride
CAS: 7646-79-9
Scientific basis: AoH 2004:16

Skin notation: No
Skin permeability: Moderate

Molecular weight: 129.8
Density: 3.356 g/cm³
Melting point: 735°C
Boiling point: 1049°C
Vapour pressure: 5.3 kPa (at 770°C)
Evaporation rate: Not available
Log Kow: 0.85 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
GP	Ba	Fl	Full	3.1		H2O	*5.0* (0.085M)	10	48	48			*12*	6.2	Wahlberg (1965)
Hum	Ab/Br	Fl	Full	3.1		H2O	*5.0* (0.085M)	10	48	48			*4.4*	2.2	Wahlberg (1965)
In vivo															
GP	Ba			3.1		H2O	*5.0* (0.085M)	10	48	48			*13-22*	6.6-11	Wahlberg (1965)
Ham	Ba				0.1	NaCl/Et	20	4	48	48		*60*			Lacy et al. (1996)

Asessment

The study by Lacy et al. (1996) gives no area of exposure, therefore no Kp or flux value can be calculated.
The high absorption shows that cobalt dichloride readily penetrates the skin.

The three studies of Wahlberg (1965) show consistent results.
The preferred experiment is that with human skin. The Kp value corresponds to "moderate" permeability.

Substance: Cresol, m-
CAS: 108-39-4
Scientific basis: AoH 1998:25

Skin notation: No
Skin permeability: Very high

Molecular weight: 108.1
Density: 1.034 g/cm³
Melting point: 11.5°C
Boiling point: 202.2°C
Vapour pressure: 13 Pa (at 20°C)
Evaporation rate: Not available
Log Kow: 1.96

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Hum	Ab	St	Epi	2.5	Inf	H2O	4	2	8	8	0.25		150	*60*	Roberts et al. (1977)
Sn	Ba	St	Full	1.8		PBS	1-3	4	6	6			99	*9.9-30*	Itoh et al. (1990)
In vivo															
No data available															

Asessment

In the study by Itoh et al. (1990), snake skin was used. As this is very different from human skin, this data is disregarded.

The preferred study is that of Roberts et al. (1977), where the reported Kp value of $2 \cdot 10^{-2}$ cm/h suggest "high" permeability.

It should be noted that in the experiments by Roberts et al. (1977), epidermal sheets were separated by exposing skin to ammonia vapour for 30 min. Ammonia is well known to cause severe skin damage Amshel et al. (2000). The alkaline nature of ammonia quickly saponifies the epidermal fats, thus destroying the protective structure of the epidermis. Therefore, the method used by Roberts et al. (1977) is likely to result in severe overestimates of the flux and Kp value of undamaged skin.

Substance: Cresol, o-
CAS: 95-48-7
Scientific basis: AoH 1998:25

Skin notation: No
Skin permeability: Very high

Molecular weight: 108.1
Density: 1.048 g/cm³
Melting point: 30.9°C
Boiling point: 191°C
Vapour pressure: 33 Pa (at 25°C)
Evaporation rate: Not available
Log Kow: 1.95

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Hum	Ab	St	Epi	2.5	Inf H2O	4	2	8	8	0.25		160	*64*	Roberts et al. (1977)
In vivo														
No data available														

Asessment

Only one study was found on o-cresol. The study by Roberts et al. (1977) reported a Kp value of $2 \cdot 10^{-2}$ cm/h, suggesting "high" permeability.

It should be noted that in the experiments by Roberts et al. (1977), epidermal sheets were separated by exposing skin to ammonia vapour for 30 min. Ammonia is well known to cause severe skin damage Amshel et al. (2000). The alkaline nature of ammonia quickly saponifies the epidermal fats, thus destroying the protective structure of the epidermis. Therefore, the method used by Roberts et al. (1977) is likely to result in severe overestimates of the flux and Kp value of undamaged skin.

Substance: Cresol, p-
CAS: 106-44-5
Scientific basis: AoH 1998:25

Skin notation: No
Skin permeability: Very high

Molecular weight: 108.1
Density: 1.034 g/cm³
Melting point: 32 to 34°C
Boiling point: 201.8°C
Vapour pressure: 15 Pa (at 25°C)
Evaporation rate: Not available
Log Kow: 1.94

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Hum	Ab	St	Epi	2.5	Inf H2O	4	2	8	8	0.27		180	*72*	Roberts et al. (1977)
In vivo														
No data available														

Asessment

Only one study was found on o-cresol. The study by Roberts et al. (1977) reported a Kp value of $2 \cdot 10^{-2}$ cm/h, suggesting "high" permeability.

It should be noted that in the experiments by Roberts et al. (1977), epidermal sheets were separated by exposing skin to ammonia vapour for 30 min. Ammonia is well known to cause severe skin damage Amshel et al. (2000). The alkaline nature of ammonia quickly saponifies the epidermal fats, thus destroying the protective structure of the epidermis. Therefore, the method used by Roberts et al. (1977) is likely to result in severe overestimates of the flux and Kp value of undamaged skin.

Substance: Cyanamide, hydrogen
CAS: 420-04-2
Scientific basis: AoH 1999:25

Skin notation: No
Skin permeability: High

Molecular weight: 42.0
Density: 1.06 g/cm³
Melting point: 42°C
Boiling point: 260°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: -0.82

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
Hum	Arm			16	1	H2O	1% (10mg)	6	6	48		7.7 (2.3 mg)	*24*	*24*	Mertschenk et al. (1991)

Asessment
The only study found on cyanamide was that by Mertschenk et al. (1991) where the calculated Kp value corresponds to "high" permeability.

Substance: Cyclohexanone
CAS: 108-94-1
Scientific basis: AoH 1999:25

Skin notation: Yes
Skin permeability: Low

Molecular weight: 98.1
Density: 0.947 g/cm³
Melting point: -47°C
Boiling point: 155.6°C
Vapour pressure: 0.69 kPa (at 25°C)
Evaporation rate: 0.23
Log Kow: 0.81

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
Hum	Ha				Inf		Neat	3	0.5	72			*0.59*	56	Mraz et al. (1994)

Asessment
A single human in vivo study was found (Mraz et al. (1994)).
The flux was obtained by analyzing the urinary excretion of 1,4-cyclohexanediol after both dermal and inhalational exposure.

The calculated Kp value of $6 \cdot 10^{-5}$ cm/h, suggests "low" permeability.

Substance: Di-(2-ethylhexyl)phthalate (DEHP)
CAS: 117-81-7
Scientific basis: AoH 1983:36

Skin notation: No
Skin permeability: Extremely low

Molecular weight: 390.6
Density: 0.973 g/cm³
Melting point: -50°C
Boiling point: 286.9°C
Vapour pressure: 1 Pa (at 20°C)
Evaporation rate: <0.005
Log Kow: 7.60

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
GP	Ba	Fl	200	0.64	0.01	Ac	0.89	5	24	24		6.1	*0.4*	*0.035*	Ng et al. (1992)
GP	Ba	Fl	200	0.64	0.01	Ac	0.89	5	24	24		5	*0.33*	*0.029*	Ng et al. (1992)
GP	Ba	Fl	200	0.64	0.01	Ac	3.8	5	24	24		2.4	*0.16*	*0.06*	Ng et al. (1992)
GP	Ba	Fl	200	0.64	0.01	Ac	7.8	5	24	24		2.5	*0.16*	*0.12*	Ng et al. (1992)
Hum		St	Epi	0.64/1.0			Neat	4	32	32	*1-2*		0.0011	100	Barber et al. (1992)
Hum	Ab	St	Epi	1.8	0.5		Neat	9	72	72	3.1		0.057	5.6	Scott et al. (1987)
Pig			Full	10	0.05	Et	3.7	5	8	8		0.1	*0.0088*	*0.0032*	Wester et al. (1998d)
Rat		St	Full	0.64/1.0			Neat	11	32	32	*1-2*		0.0043	420	Barber et al. (1992)
Rat	Ba	Fl	Epi	0.64	0.05	Ac	1.6	8	72	72	2.58	51	9.5	*1.5*	Pelling et al. (1998)
Rat	Ba	Fl	Derm	0.64	0.05	Ac	1.6	11	72	72	1.17	5.6	0.98	*0.15*	Pelling et al. (1998)
Rat	Ba	Fl	Epi	0.64	0.05	Ac	1.6	9	72	72	2.47	1.2	0.13	*0.021*	Pelling et al. (1998)
Rat	Ba	Fl	Derm	0.64	0.05	Ac	1.6	9	72	72	0.91	1.7	0.48	*0.076*	Pelling et al. (1998)
Rat	Ba	St	Epi	1.8	0.5		Neat	9	53	53	3.9		0.23	22	Scott et al. (1987)
In vivo															
GP	Ba			8	0.1	Ac	9.5	4	24	24		13	*0.67*	*0.63*	Chu et al. (1996)
GP	Ba			8	0.1	Ac	8.6	4	24	48		19	*0.97*	*0.83*	Chu et al. (1996)
GP	Ba			8	0.1	Ac	35	4	24	168		19	*0.98*	*3.5*	Chu et al. (1996)
GP	Ba			8	0.1	Ac	42	4	24	336		9.7	*0.51*	*2.1*	Chu et al. (1996)
GP	Ba			4	0.05	Ac	4.2	5	24	168		53	*2.8*	*1.2*	Ng et al. (1992)
Hum	Arm			10	0.05	Et	3.7	6	24	168		1.8	*0.038*	*0.014*	Wester et al. (1998d)
Rat	Ba			15		Film	400mg	4	24	24		0.1	*0.0025*	0.24	Deisinger et al. (1998)
Rat	Ba			1.3			5-8 mg/cm²	3	168	168		7	*0.034*	*3.3*	Elsisi et al. (1989)

Asessment

The dermal absorption of DEHP shows huge variability between studies with Kp values ranging from $1 \cdot 10^{-7}$ to $2 \cdot 10^{-5}$ cm/h (data with neat DEHP only).
Scott et al. (1987) used physiological saline/ethanol (50/50) as receptor medium. The ethanol may severely affect skin permeability.

The preferred study is that of Barber et al. (1992) who used buffered isotonic water with an addition of polyethylene glycol 20 oleyl ether to achieve sufficient solubility of DEHP in the receptor medium.

The Kp value of $1 \cdot 10^{-7}$ cm/h for human skin corresponds to "extremely low" permeability.

Substance: Dibutyl phthalate (DBP)
CAS: 84-74-2
Scientific basis: AoH 1983:36

Skin notation: No
Skin permeability: Very low

Molecular weight: 278.3
Density: 1.043 g/cm³
Melting point: -35°C
Boiling point: 340°C
Vapour pressure: <10 Pa (at 20°C)
Evaporation rate: <0.005
Log Kow: 4.50

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
HR	Ba	St	Full	1.8	Inf		Neat	9	24	24			*0.37*	39	Payan et al. (2001)
Hum	Ab	St	Epi	1.8	0.5		Neat	15	30	30	2.9		0.023	0.07	Scott et al. (1987)
Hum	Leg	St		7.1	0.5	Ac	20	2	48	48	3.1		*0.2*	0.4	Sherertz et al. (1988)
Mou		St	Full	7.1	0.5	Ac	20	3	48	48	2.3	33	*8.5*	17	Sherertz et al. (1988)
Rat	Ba	St	Full	1.8	Inf		Neat	9	24	24			*0.25*	26	Payan et al. (2001)
Rat	Ba	St	Epi	1.8	0.5		Neat	9	8	8	0.4		0.9	9.3	Scott et al. (1987)
In vivo															
Hum	Arm			14-16	2-6	PG + H2O	Saturated	12	6	6			520	3.8	Hagedorn-Leweke et al. (1995)
Rat	Ba			10	0.1		Neat	8	72	72		74	*1.1*	110	Payan et al. (2001)
Rat	Ba			10	0.1		Neat	8	48	48		63	*1.3*	140	Payan et al. (2001)
Rat	Ba			10	0.1		Neat	8	24	24		31	*1.2*	130	Payan et al. (2001)
Rat	Ba			10	0.1		Neat	8	8	8		3.3	*0.38*	40	Payan et al. (2001)
Rat	Ba			10	0.1		Neat	8	4	4		1.9	*0.38*	40	Payan et al. (2001)
Rat	Ba			10	0.1		Neat	3	2	2		1.1	*0.57*	60	Payan et al. (2001)
Rat	Ba			10	0.1		Neat	3	1	1		0.5	*0.57*	60	Payan et al. (2001)
Rat	Ba			10	0.1		Neat	3	0.5	0.5		0.3	*0.57*	60	Payan et al. (2001)

Asessment

The most relevant study is that of Scott et al. (1987), using human skin in vitro.
The other studies used rodent skin and/or vehicles (acetone, propylene glycol) that may affect skin permeability.

The Kp value of $2 \cdot 10^{-6}$ cm/h for human skin corresponds to "very low" permeability.

Substance: Dichloroethane, 1,2-
CAS: 107-06-2
Scientific basis: AoH 1981:21

Skin notation: Yes
Skin permeability: High

Molecular weight: 99.0
Density: 1.253 g/cm³
Melting point: -35.3°C
Boiling point: 83.5°C
Vapour pressure: 8.7 kPa (at 20°C)
Evaporation rate: 6.5
Log Kow: 1.48

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Rat	Ab	St	Full	3.7	1	Neat	27	1-3	1-3	0.6	1-9 mg	*8*	1000	Tsuruta (1977)
In vivo														
Mou	Ab			2.9	0.5	Neat	3	0.3			2100 µg	*23*	2800	Tsuruta (1975)

Asessment
Physiological saline was used as receptor medium in the in vitro study, this may result in underestimates of flux and Kp.
The in vivo study with mice is preferred.

The Kp value of $2 \cdot 10^{-3}$ corresponds to "high" permeability.

Substance: Diethanolamine
CAS: 111-42-2
Scientific basis: AoH 1992:47

Skin notation: Yes
Skin permeability: Low

Molecular weight: 105.1
Density: 1.09 g/cm³
Melting point: 28°C
Boiling point: 268.8°C
Vapour pressure: <2 Pa (at 20°C)
Evaporation rate: <0.001
Log Kow: -1.43

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Br	Fl	Full	1.8	0.04		Neat	6	6	6	3.2	0.1	0.05	5.7	Sun et al. (1996)
Hum	Br	Fl	Full	1.8	0.1	H2O	20 mg/cm²	6	6	6	2.4	0.2	0.34	13	Sun et al. (1996)
Hum	Br	St	~1000	1	0.2	H2O	1%	22	24	24	*~6*	0.4	*0.5*	*0.55*	Brain et al. (2005)
Hum	Br	St	~1000	1	0.2	H2O	1%	20	24	24	*~8*	0.1	*0.088*	*0.096*	Brain et al. (2005)
Mou		Fl	Full	1.8	0.04		Neat	3	6	6	0.9	1.3	0.42	46	Sun et al. (1996)
Mou		Fl	Full	1.8	0.1	H2O	20 mg/cm²	3	6	6	0.8	6.7	7.6	290	Sun et al. (1996)
Rab		Fl	Full	1.8	0.04		Neat	3	6	6	1.3	0	0.01	0.9	Sun et al. (1996)
Rab		Fl	Full	1.8	0.1	H2O	20 mg/cm²	3	6	6	1.5	2.8	3.4	130	Sun et al. (1996)
Rat		Fl	Full	1.8	0.04		Neat	3	6	6	0.6	0	0.02	1.8	Sun et al. (1996)
Rat		Fl	Full	1.8	0.1	H2O	20 mg/cm²	3	6	6	0.8	0.6	0.6	23	Sun et al. (1996)
In vivo															
Mou				1	0.02	95% Et	13	4	48	48		58	*2.4*	*3.2*	Mathews et al. (1997)
Mou				1	0.02	95% Et	38	5	48	48		34	*1.4*	*5.4*	Mathews et al. (1997)
Mou				1	0.02	95% Et	140	5	48	48		2.9	*0.12*	*1.6*	Mathews et al. (1997)
Rat				2	0.03	95% Et	14	5	48	48		2.9	*0.091*	*0.13*	Mathews et al. (1997)
Rat				2	0.03	95% Et	50	5	48	48		11	*0.33*	*1.6*	Mathews et al. (1997)
Rat				2	0.03	95% Et	180	4	48	48		16	*0.51*	*9.2*	Mathews et al. (1997)

Asessment

The in vivo studies (Mathews et al. (1997)) used 95% ethanol as vehicle and cannot be used.

The reported permeabilities using neat diethanolamine are contradictive with Kp values ranging from $1 \cdot 10^{-6}$ to $4 \cdot 10^{-5}$ cm/h.

The permeability of diethanolamine in water solution is higher with Kp values between $1 \cdot 10^{-5}$ and $8 \cdot 10^{-4}$ cm/h.

The preferred study is that of Brain et al. (2005) who applied excess volume of 1% diethanolamine in water using a static diffusion cell and fresh or frozen human breast.

The Kp values of $9 \cdot 10^{-6}$ (fresh skin) and $5 \cdot 10^{-5}$ (frozen skin) cm/h correspond to "low" permeability.

Substance: Diethyl phthalate (DEP)
CAS: 84-66-2
Scientific basis: Not available

Skin notation: No
Skin permeability: Low

Molecular weight: 222.2
Density: 1.118 g/cm³
Melting point: -3°C
Boiling point: 298°C
Vapour pressure: 0.3 Pa (at 20°C)
Evaporation rate: <0.005
Log Kow: 2.42

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
GP	Ab	St	350	0.64	Inf	PB	0.44	6	5	5	0.67		210	*9.2*	Frasch et al. (2005)
Hum	Br	Fl	Full	0.32	0.01		Neat (17mg/cm^2)	4	72	72			*0.098*	11	Mint et al. (1994)
Hum	Ab	St	Epi	1.8	0.5		Neat	11	30	30	6		0.11	1.3	Scott et al. (1987)
Hum*	Br	Fl	Full	0.32	0.01		Neat (17mg/cm^2)	3	72	72			*0.13*	14	Mint et al. (1994)
Rat	Ba	Fl	Full	0.32	0.01		Neat (17mg/cm^2)	4	72	72			*0.84*	94	Mint et al. (1994)
Rat	Ba	St	Epi	1.8	0.5		Neat	11	8	8	1.1		3.7	41	Scott et al. (1987)
Rat*	Ba	Fl	Full	0.32	0.01		Neat (17mg/cm^2)	3	72	72			*0.92*	103	Mint et al. (1994)
In vivo															
No data available															

Asessment

Two different studies (Mint et al. (1994), Scott et al. (1987)) using human skin in vitro, report consistent results.
The two data sets from Mint et al. (1994) for rat and human skin represent non-occluded (*) and occluded application of diethyl phthalate.

The Kp value of $1 \cdot 10^{-5}$ corresponds to "low" permeability.

Substance: Diethylamine
CAS: 109-89-7
Scientific basis: AoH 1983:36

Skin notation: Yes
Skin permeability: No data

Molecular weight: 73.1
Density: 0.707 g/cm³
Melting point: -50°C
Boiling point: 55.5°C
Vapour pressure: 26 kPa (at 20°C)
Evaporation rate: 17
Log Kow: 0.58

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The dermal LD50 in rabbits is 820 mg/kg bw, as compared to an oral LD50 of 130 mg/kg bw in mice (ACGIH (2001)).

Substance: Diethylaminoethanol, 2-
CAS: 100-37-8
Scientific basis: AoH 1995:19

Skin notation: Yes
Skin permeability: No data

Molecular weight: 117.2
Density: 0.884 g/cm³
Melting point: -70°C
Boiling point: 162°C
Vapour pressure: 0.19 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 0.05 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
No data available															

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The skin notation by ACGIH (2001) is based on the reported dermal LD50 of 0.9 g/kg bw in rabbits.
For comparison, the oral LD50 in rats is in the range of 1.3 to 5.7 g/kg bw.

According to theoretical calculations (based on the physical properties of the substance)
by Fiserova-Bergerova et al. (1990), the potential for dermal absorption and resulting toxicity is significant.

Substance: Diethylene glycol
CAS: 111-46-6
Scientific basis: Not available

Skin notation: Yes
Skin permeability: Very low

Molecular weight: 106.1
Density: 1.118 g/cm³
Melting point: -10°C
Boiling point: 245°C
Vapour pressure: 0.5 Pa (at 20°C)
Evaporation rate: Not available
Log Kow: -1.47 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
Rat	Ba			12	*0.045*	Neat (50 mg)	5	72	72		9.1	*0.047*	*5.3*	Mathews et al. (1991)

Asessment
Neat labelled diethylene glycol was applied to the clipped back of rats and total radioactivity was measured in breath and urine up to 72h.

The calculated permeability is considered as "very low".

Substance: Diethylene glycol monobutyl ether (DEGBE)
CAS: 112-34-5
Scientific basis: AoH 1995:19

Skin notation: No
Skin permeability: Moderate

Molecular weight: 162.2
Density: 0.967 g/cm³
Melting point: -68.1°C
Boiling point: 230.4°C
Vapour pressure: 4.4 Pa (at 20°C)
Evaporation rate: 0.003
Log Kow: 0.56

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Hum		St	Epi	0.64/1.0		Neat	10	8	8	*1-2*		3.1	290	Barber et al. (1992)
Hum	Ab	St	Epi	1.8	1-5	Neat	9	8	8	2		0.36	35	Dugard et al. (1984)
Rat		St	Full	0.64/1.0		Neat	12	8	8	*1-2*		5.3	510	Barber et al. (1992)
In vivo														
Rat	Ba			4.3		Neat	4	24	168			*7.7-16*	730-1500	Boatman et al. (1993)

Asessment

All three studies used similar techniques; static Franz cells, heat-separated epidermis (60°C in water), frozen and thawed human or rat skin. The results of Barber et al. (1992) and Boatman et al. (1993) are consistent, whereas Dugard et al. (1984) reports 10-fold lower flux and Kp.

The preferred study is that of Barber et al. (1992) using human skin.

The Kp value of $3 \cdot 10^{-4}$ cm/h corresponds to "moderate" permeability.

Substance: Diethylene glycol monobutyl ether acetate (DEGBEA)
CAS: 124-17-4
Scientific basis: AoH 1995:19

Skin notation: No
Skin permeability: High

Molecular weight: 204.3
Density: 0.98 g/cm³
Melting point: -32°C
Boiling point: 246°C
Vapour pressure: 5.3 Pa (at 20°C)
Evaporation rate: 0.001
Log Kow: 1.30 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
Rat	Ba			4.3		Neat	4	24	168			*13-16*	1300-1600	Boatman et al. (1993)

Asessment
Only rat in vivo data are available. Notably, the flux and Kp of DEGBEA is similar to that of DEGBE.

The Kp value for rat skin corresponds to "high" permeability.

Substance: Diethylene glycol monoethyl ether (DEGEE)
CAS: 111-90-0
Scientific basis: AoH 1997:24

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 134.2
Density: 0.999 g/cm³
Melting point: -76°C
Boiling point: 197°C
Vapour pressure: 19 Pa (at 25°C)
Evaporation rate: 0.02
Log Kow: -0.54

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Hum	Ab	St	Epi	1.8	1-5	Neat	10	8	8	<1		1.3	130	Dugard et al. (1984)
In vivo														
No data available														

Asessment

The only study found is that of Dugard et al. (1984) were human skin was exposed to neat DEGEE in vitro.
The reported Kp value of $1 \cdot 10^{-4}$ cm/h, corresponds to "moderate" permeability.

It should be noted that Dugard et al. (1984) has also presented Kp data on some related glycol ethers,
e.g. DEGBE, that were approximately ten times lower that that of other investigators.

Substance: Diethylene glycol monoethyl ether acetate (DEGEEA)
CAS: 112-15-2
Scientific basis: AoH 1997:24

Skin notation: Yes
Skin permeability: No data

Molecular weight: 176.2
Density: 1.01 g/cm³
Melting point: -25°C
Boiling point: 210 to 220°C
Vapour pressure: 7 Pa (at 20°C)
Evaporation rate: 0.008
Log Kow: 0.32 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
No data available															

Asessment
No quantitative experimental data on dermal uptake were found in the literature.

The Swedish consensus report (AoH 1997:25) states that "… it is reasonable to assume that (DEGEEA), like other glycol ethers, are efficiently absorbed via both skin and inhalation".

Substance: Diethylentriamine
CAS: 111-40-0
Scientific basis: AoH 1995:19

Skin notation: Yes
Skin permeability: No data

Molecular weight: 103.2
Density: 0.951 g/cm³
Melting point: -33°C
Boiling point: 207°C
Vapour pressure: 0.05 kPa (at 20°C)
Evaporation rate: 0.01
Log Kow: -2.13 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The Swedish consensus report (AoH 1995:19) states that the substance can be taken up by skin, without further details.

The oral (2.33 and 1.08 g/kg bw in rats, Smyth et al. (1949) and Hine et al. (1958)) and dermal (1.09 g/kg bw in rabbit, Smyth et al. (1949)) LD50 are not very different from one another, suggesting extensive dermal uptake.

According to theoretical calculations by Fiserova-Bergerova et al. (1990) the potential for dermal absorption and resulting toxicity is significant.

Substance: Diisopropylamine
CAS: 108-18-9
Scientific basis: AoH 1991:8

Skin notation: Yes
Skin permeability: No data

Molecular weight: 101.2
Density: 0.722 g/cm³
Melting point: -61°C
Boiling point: 84°C
Vapour pressure: 8 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 1.40

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The Swedish consensus report (AoH 1991:8) states that diisopropylamine can be taken up by the skin. No further details are given. The source (Andersson et al. (1985)) contains no information on dermal absorption.

According to theoretical calculations by Fiserova-Bergerova et al. (1990) the potential for dermal absorption and resulting toxicity is significant.

Substance: Dimethyl phthalate
CAS: 131-11-3
Scientific basis: AoH 1983:36

Skin notation: No
Skin permeability: Low

Molecular weight: 194.2
Density: 1.19 g/cm³
Melting point: 2°C
Boiling point: 283.7°C
Vapour pressure: 0.8 Pa (at 20°C)
Evaporation rate: <0.005
Log Kow: 1.60

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Hum	Ab	St	Epi	1.8	0.5		Neat	14	30	30	0.1		0.33	4	Scott et al. (1987)
Rat	Ab	St	Epi	1.8	0.5		Neat		8	8	0.5		3.5	42	Scott et al. (1987)
In vivo															
No data available															

Asessment

The only available study (Scott et al. (1987)) reports 10-fold different permeabilities for human and rat skin.
Human epidermal membranes were prepared by heating in water (60°C), whereas rat membranes were prepared using 2M NaBr.
However, the authors claim that the two preparation techniques give the same permeability properties.

The human in vitro data suggests "low" permeability.

Substance: Dimethylacetamide, N-
CAS: 127-19-5
Scientific basis: AoH 1994:30

Skin notation: Yes
Skin permeability: Very high

Molecular weight: 87.1
Density: 0.937 g/cm³
Melting point: -20°C
Boiling point: 166.1°C
Vapour pressure: 0.2 kPa (at 20°C)
Evaporation rate: 0.14
Log Kow: -0.77

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Hum	Br	St	300-600	0.64		Neat	3	6	6			*120*	11000	Ursin et al. (1995)
In vivo														
No data available														

Asessment

The only study found was that of Ursin et al. (1995) where human skin was exposed to neat n-dimethylacetamide in vitro.

The reported Kp value of $1 \cdot 10^{-2}$ cm/h, suggests "very high" permeability

Substance: Dimethylanilline, N,N-
CAS: 121-69-7
Scientific basis: AoH 1991:8

Skin notation: Yes
Skin permeability: No data

Molecular weight: 121.2
Density: 0.956 g/cm³
Melting point: 2.5°C
Boiling point: 194°C
Vapour pressure: 0.067 kPa (at 20°C)
Evaporation rate: <1
Log Kow: 2.31

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
No data available															

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The Swedish consensus report (AoH 1991:8) states that dimethylaniline can be absorbed via the skin. No additional data are given.

According to theoretical calculations by Fiserova-Bergerova et al. (1990) the potential for dermal absorption and resulting toxicity is significant.

Substance: Dimethylethylamine
CAS: 598-56-1
Scientific basis: AoH 1992:6

Skin notation: No
Skin permeability: High

Molecular weight: 73.1
Density: 0.675 g/cm³
Melting point: -140°C
Boiling point: 36°C
Vapour pressure: 55 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 0.70

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
GP		Fl	Full		0.1	H2O	0.67	6	48	48	7		10	8	Lundh et al. (1997)
GP		Fl	Full		0.1	H2O	0.67	6	48	48			10	5	Lundh et al. (1997)
GP		Fl	Full		0.1	NaCl	0.67	6	48	48	3		40	25	Lundh et al. (1997)
GP		Fl	Full		0.1	NaCl	0.67	6	48	48	8		20	9	Lundh et al. (1997)
Hum		Fl	250		0.1	H2O	0.67	6					40	26	Lundh et al. (1997)
Hum		Fl	250		0.1	H2O	0.67	6					20	11	Lundh et al. (1997)
Hum		Fl	250		0.1	NaCl	0.67	6			1		20	16	Lundh et al. (1997)
In vivo															
Hum	Arm			870	Inf	Vap	0.00027	3	4	8		44 µg	500	0.013	Lundh et al. (1997)
Hum	Arm			870	Inf	Vap	0.00053	3	4	8		64 µg	320	0.02	Lundh et al. (1997)
Hum	Arm			870	Inf	Vap	0.001	3	4	8		88 µg	250	0.026	Lundh et al. (1997)

Asessment

The one found study by Lundh et al. (1997) shows consistent results between vapour and aqueous solutions.

The preferred experiments are those on human skin in vitro with reported Kp values between $2 \cdot 10^{-3}$ to $4 \cdot 10^{-3}$ cm/h, which corresponds to "high" permeability.

Substance: Dimethylformamide
CAS: 68-12-2
Scientific basis: AoH 1983:36

Skin notation: Yes
Skin permeability: Very high

Molecular weight: 73.1
Density: 0.944 g/cm³
Melting point: -61°C
Boiling point: 153°C
Vapour pressure: 0.49 kPa (at 25°C)
Evaporation rate: 0.17
Log Kow: -1.01

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Hum	Ab	St	Full	3.1	0.2	Neat	6?	4	4	1		96	8400	Larese et al. (1994)
Hum	Br	St	300-600	0.64		Neat	3	6	6			*140*	13000	Ursin et al. (1995)
In vivo														
Hum	Ha				Inf	Neat	18	0.033-0.33	24			*100*	9400	Mraz et al. (1992)

Asessment

The three different studies show consistent results. The preferred study is the human in vivo study by Mraz et al. (1992).

The Kp value of $1 \cdot 10^{-2}$ cm/h corresponds to "very high" permeability.

Substance: Dimethylsulfoxide
CAS: 67-68-5
Scientific basis: AoH 1992:47

Skin notation: Yes
Skin permeability: Very high

Molecular weight: 78.1
Density: 1.096 g/cm³
Melting point: 18.5°C
Boiling point: 189°C
Vapour pressure: 0.049 kPa (at 20°C)
Evaporation rate: 4.3
Log Kow: -1.35

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro														
Hum	Br	St	300-600	0.64		Neat	3	6	6			*160*	18000	Ursin et al. (1995)
In vivo														
Hum	EB			250		*880* (80%. 17 g)		0.5	504		25-40	*380-610*	*33000-53000*	Wong et al. (1971)
Hum	WB			*20000*	H2O	*770* (70%. 1 g/kg BW)	2	*8*	20		13	*0.74*	57	Hucker et al. (1967)
MP	Ba			250		*880* (80%. 17 g)		4	144		100	*190*	*17000*	Wong et al. (1971)
Rat	Ab			25		Neat (260 mg)		0.25	48		37	*140*	*16000*	McDermot et al. (1967)
Rat	Ab			25		Neat (240 mg)		0.5	48		67	*120*	*13000*	McDermot et al. (1967)
Rat	Ab			25		Neat (350 mg)		0.75	48		90	*160*	*17000*	McDermot et al. (1967)
Rat	Ab			25		Neat (270 mg)		1	48		94	*92*	*10000*	McDermot et al. (1967)

Asessment

The different studies show consistent results with Kp values ranging from $1 \cdot 10^{-3}$ to $6 \cdot 10^{-2}$ cm/h, with a preferred study of Ursin et al. (1995) were human skin was exposed to neat chemical.

These Kp values correspond to "high" permeability.

Substance: Dinitrobenzene
CAS: 25154-54-5
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No data

Molecular weight: 168.1
Density: 1.368 g/cm³
Melting point: 88 to 90°C
Boiling point: ~300°C
Vapour pressure: <100 Pa (at 20°C)
Evaporation rate: Not available
Log Kow: Not available

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux Reference (µg/cm^2/h)
In vitro													
No data available													
In vivo													
No data available													

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The contribution of dermal exposure to the systemic toxicity of dinitrobenzene is well established (ACGIH (2001)).

Substance: Dinitrotoluene
CAS: 25321-14-6
Scientific basis: AoH 1992:6

Skin notation: Yes
Skin permeability: No data

Molecular weight: 182.1
Density: 1.321 g/cm³
Melting point: 70°C
Boiling point: 250°C
Vapour pressure: 2.4 Pa (at 20°C)
Evaporation rate: Not available
Log Kow: 2.18 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

Biomonitoring studies in workers show higher urine levels of metabolites than would be expected from inhalation exposure only (AoH 1992:6, ACGIH (2001), Tchounwou et al. (2003)).

Substance: Dinitrotoluene, 2,4-
CAS: 121-14-2
Scientific basis: AoH 1992:6

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 182.1
Density: 1.521 g/cm³
Melting point: 69°C
Boiling point: 300°C
Vapour pressure: 130 Pa (at 103°C)
Evaporation rate: Not available
Log Kow: 1.98

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Pig	Ba	St	500-900	0.8	11 mg/cm²	Soil (Ti)	*0.93* (6.8 µg/cm²)	6	8	8		5.3	*0.49*	*0.045*	Reifenrath et al. (2002)
Pig	Ba	St	500-900	0.8	12 mg/cm²	Soil (Yo)	*1.5* (12 µg/cm²)	6	8	8		14	*1.4*	*0.21*	Reifenrath et al. (2002)
Pig	Ba	St	500-900	0.8	0.005	Ac	*2.4* (12 µg/cm²)	6	8	8		34	*2.1*	*0.49*	Reifenrath et al. (2002)
In vivo															
No data available															

Asessment

The only found study was that of Reifenrath et al. (2002), where pig skin was exposed to 2,4-dinitrotoluene and 2,6-dinitrotoluene with soil or acetone as vehicle. It should be noted that the use of acetone as vehicle may have severely affected the skin properties.

The reported Kp values are consistent between experiments and isomers, and range between $1 \cdot 10^{-4}$ and $2 \cdot 10^{-4}$ cm/h, suggesting a "moderate" permeability.

Substance: Dinitrotoluene, 2,6-
CAS: 606-20-2
Scientific basis: AoH 1992:6

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 182.1
Density: 1.283 g/cm³
Melting point: 65°C
Boiling point: 300°C
Vapour pressure: 130 Pa (at 20°C)
Evaporation rate: Not available
Log Kow: 2.10

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro														
Pig	Ba	St	500-900	0.8	17 mg/cm² Soil (Ti)	*0.47* (6.1 µg/cm²)	6	8	8		3.7	*0.94*	*0.044*	Reifenrath et al. (2002)
Pig	Ba	St	500-900	0.8	11 mg/cm² Soil (Yo)	*1.1* (9.7 µg/cm²)	6	8	8		15	*1.7*	*0.2*	Reifenrath et al. (2002)
Pig	Ba	St	500-900	0.8	0.005 Ac	*1.9* (9.6 µg/cm²)	6	8	8		22	*1.5*	*0.29*	Reifenrath et al. (2002)
In vivo														
No data available														

Asessment

The only found study was that of Reifenrath et al. (2002), where pig skin was exposed to 2,4-dinitrotoluene and 2,6-dinitrotoluene with soil or acetone as vehicle. It should be noted that the use of acetone as vehicle may have severely affected the skin properties.

The reported Kp values are consistent between experiments and isomers, and range between $1 \cdot 10^{-4}$ and $2 \cdot 10^{-4}$ cm/h, suggesting a "moderate" permeability.

Substance: Dioxane
CAS: 123-91-1
Scientific basis: AoH 1992:47

Skin notation: Yes
Skin permeability: No conclusion

Molecular weight: 88.1
Density: 1.033 g/cm³
Melting point: 11.8°C
Boiling point: 101.1°C
Vapour pressure: 4.9 kPa (at 25°C)
Evaporation rate: 2.7
Log Kow: -0.27

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
No data available															
In vivo															
Mon	Arm			3-15		Me	4 µg/cm²	3-6	24	120		2.3	*0.000037*	*0.0038*	Marzulli et al. (1981)
Mon	Arm			3-15		Cream	4 µg/cm²	3-6	24	120		3.4		*0.0057*	Marzulli et al. (1981)

Asessment

Marzulli et al. (1981) studied dermal uptake in vivo in Rhesus monkeys. The small amount applied and the non-occluded condition most possibly led to massive losses of dioxane via evaporation. Thus the calculated fluxes and Kp values are not reliable.

Substance: Dipropylene glycol monomethyl ether (DPGME)
CAS: 34590-94-8
Scientific basis: AoH 1992:6

Skin notation: Yes
Skin permeability: No data

Molecular weight: 148.2
Density: 0.95 g/cm³
Melting point: -83°C
Boiling point: 190°C
Vapour pressure: 0.05 kPa (at °C)
Evaporation rate: 0.02
Log Kow: -0.35 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

According to Smyth et al. (1962) the rat oral LD50 is 5.7 g/kg bw. For comparison, the rabbit dermal LD50 is 10 g/kg bw.

Substance: Epichlorohydrin
CAS: 106-89-8
Scientific basis: AoH 1981:10

Skin notation: Yes
Skin permeability: No data

Molecular weight: 92.5
Density: 1.183 g/cm³
Melting point: -57°C
Boiling point: 117.9°C
Vapour pressure: 1.5 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 0.45

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
No data available															

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

According to NEG (1981) epichlorohydrin penetrates the skin and mucous membranes. No further details are given.
According to ACGIH (2001) the rabbit dermal LD50 is 755 mg/kg bw. For comparison, the rat and mouse oral LD50 values are 260 and 237 mg/kg bw, respectively.

Substance: Ethanol
CAS: 64-17-5
Scientific basis: AoH 1991:8

Skin notation: No
Skin permeability: High

Molecular weight: 46.1
Density: 0.789 g/cm³
Melting point: -114.1°C
Boiling point: 78.3°C
Vapour pressure: 6.7 kPa (at 25°C)
Evaporation rate: Not available
Log Kow: -0.31

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Dog	Br	St	Full	3.1	1	PBS		5	5	5			6.2		Mills et al. (2004)
Dog	Ne	St	Full	3.1	1	PBS		5	5	5			7.9		Mills et al. (2004)
Dog	Ba	St	Full	3.1	1	PBS		5	5	5			9.1		Mills et al. (2004)
Dog	Th	St	Full	3.1	1	PBS		5	5	5			4.8		Mills et al. (2004)
Dog	Ax	St	Full	3.1	1	PBS		5	5	5			8.4		Mills et al. (2004)
GP	Ba	Fl	Full	5	0.1		Neat	9	19	19		27	*2.9*	*225*	Gummer et al. (1986)
Hum	Ab	St	27	2.5		*H2O*	*7.4*	35					8	*3.7*	Scheuplein & Blank (1973)
Hum	Ab	St	2500	2.5		*H2O*	*7.4*	8					350	*160*	Scheuplein & Blank (1973)
Hum	Ab	St	27	2.5			Neat	19					7.2	*570*	Scheuplein & Blank (1973)
Hum	Ab	St	2500	2.5			Neat	4					70	*5500*	Scheuplein & Blank (1973)
Hum	Ab	St	Full	2.5	0.1	H2O		5	6	6			3.2		Scott et al. (1991)
Hum	Br	St	300-600	0.64			Neat	3	6	6			*15*	1500	Ursin et al. (1995)
Hum	Ba	St	SC	0.5		H2O	45-75%	9					*23-61*	800-3600	Berner et al. (1989)
Hum	Ba	St	SC	0.5		H2O	20%	9					*25*	400	Berner et al. (1989)
Ma	Ab	St	Full	2.5	0.1	H2O		3	6	6			3.8		Scott et al. (1991)
Ma	Ba	St	Full	2.5	0.1	H2O		3	6	6			3.2		Scott et al. (1991)
Ma	Arm	St	Full	2.5	0.1	H2O		6	6	6			8		Scott et al. (1991)
Ma	Leg	St	Full	2.5	0.1	H2O		6	6	6			5.6		Scott et al. (1991)
Ma	Sc	St	Full	2.5	0.1	H2O		4	6	6			3.9		Scott et al. (1991)
Ma	Leg	St	Full	2.5	0.1	H2O		3	6	6			4.1		Scott et al. (1991)
Ma	Br	St	Full	2.5	0.1	H2O		3	6	6			5.8		Scott et al. (1991)
Ma	Arm	St	Full	2.5	0.1	H2O		5	6	6			6.5		Scott et al. (1991)

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_p (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	8	0.5	0.5			21		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	8	5.5	5.5			22		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	8	10.5	10.5			23		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	8	15.5	15.5			22		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	8	20.5	20.5			21		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	8	25.5	25.5			20		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	8	29.5	29.5			19		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	0.3	0.3			20		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	5.8	5.8			20		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	9.8	9.8			21		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	13.8	13.8			23		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	17.8	17.8			21		Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	0.0001M	4	26.3	26.3			22		Behl et al. (1980)
Mou	Ab	St	Full	0.6	0.2	NaCl		3	2	2			9		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		2	2	2			9		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		4	2	2			25		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		5	2	2			35		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		6	2	2			13		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		4	2	2			9		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		5	2	2			12		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		5	2	2			9		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		4	2	2			24		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		2	2	2			29		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		4	2	2			44		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		5	2	2			75		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		4	2	2			14		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		5	2	2			12		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		5	2	2			10		Behl et al. (1984)
Mou	Ab	St	Full	0.6		NaCl	0.0001M	5	2	2			32		Behl & Barrett (1981)
Mou	Ab	St	Full	0.79		NaCl	≤10-4M		2	2			7.2		Durrheim et al. (1980)
Mou	Ab	St	Full	0.79		NaCl	≤10-4M		2	2			12		Durrheim et al. (1980)
Mou	Ab	St	Full	0.79		NaCl	≤10-4M		2	2			48		Durrheim et al. (1980)

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_p (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
Pig[1]	Ba	Fl	Full	0.39	0.01	Neat	3	24	24		1	*0.052*	*4.1*	Pendlington et al. (2001)
Pig[2]	Ba	Fl	Full	0.39	0.01	Neat	3	24	24		21	*1.1*	*89*	Pendlington et al. (2001)
Rat	Ba	St	Full	2.5	0.1 H2O		8	6	6			4.2		Scott et al. (1991)
In vivo														
Hum	Fi				Inf H2O	1%	12	15s	0.3			*0.23*	0.18	Naitoh et al. (2002)
Hum	Fi				Inf H2O	1%	12	15s	0.3			*30*	24	Naitoh et al. (2002)

Asessment

[1]Non occluded [2]Occluded

The only available in vivo study is that of Naitoh et al. (2002). An unconventional technique was used in that one thumb was dipped once or several times (15 sec/occasion) in an aqueous solution. The flux was calculated from the evaporation from the thumb. The evaporation profile was biphasic, thus two different fluxes were reported. The reported fluxes reflects absorption into (and out of) rather than through skin. Thus the calculated Kp may represent an serious overestimate of the "true" value.

Most in vitro studies report Kp values in the range $3 \cdot 10^{-4}$ to $8 \cdot 10^{-3}$ cm/h, although lower and higher values have occasionally been given.

The higher end, $7 \cdot 10^{-3}$ cm/h, corresponds to "high" permeability.

Substance: Ethanolamine
CAS: 141-43-5
Scientific basis: AoH 1992:47

Skin notation: Yes
Skin permeability: Low

Molecular weight: 61.1
Density: 1.012 g/cm³
Melting point: 10.3°C
Boiling point: 171°C
Vapour pressure: 0.05 kPa (at 20°C)
Evaporation rate: 0.015
Log Kow: -1.31

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Br	Fl	Full	1.8	0.03	H2O	4 mg/cm²	6	6	6	2.4	1.1	0.43	9.7	Sun et al. (1996)
Hum	Br	Fl	Full	1.8	0.01		Neat	6	6	6	3.8	0.6	0.08	7.9	Sun et al. (1996)
Mou		Fl	Full	1.8	0.03	H2O	4 mg/cm²	3	6	6	0.1	25	4.6	170	Sun et al. (1996)
Mou		Fl	Full	1.8	0.01		Neat	3	6	6	0.4	17	1.2	120	Sun et al. (1996)
Pig	Ba	Fl	1000	0.8	0.01	Et	*0.8* (4 µg/cm²)		50	50		5	*0.063*	*0.005*	Klain et al. (1985)
Rab		Fl	Full	1.8	0.01		Neat	3	6	6	1.3	8.7	0.72	74	Sun et al. (1996)
Rab		Fl	Full	1.8	0.03	H2O	4 mg/cm²	3	6	6	3.1	1.9	1.1	25	Sun et al. (1996)
Rat		Fl	Full	1.8	0.01		Neat	3	6	6	1.5	6	0.42	43	Sun et al. (1996)
Rat		Fl	Full	1.8	0.03	H2O	4 mg/cm²	3	6	6	1.7	1.3	0.53	12	Sun et al. (1996)

In vivo

No data available

Asessment

The study by Klain et al. (1985) used ethanol as vehicle and is therefore disregarded as it may affect skin permeation.
The study by Sun et al. (1996) shows consistent results considering known species differences and effect of dilution.

The experiment using human skin and aqueous dilution reported a Kp of $4 \cdot 10^{-5}$ cm/h suggesting "low" permeability.

Substance: Ethyl 2-cyanoacrylate
CAS: 7085-85-0
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No data

Molecular weight: 125.1
Density: 1.06 g/cm³
Melting point: -22.5°C
Boiling point: Not available
Vapour pressure: 17 Pa (at 20°C)
Evaporation rate: Not available
Log Kow: 1.42 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment
No quantitative experimental data on dermal uptake were found in the literature.

In Ousterhout et al. (1968), the radiolabelled homologous substances methyl α-cyanoacrylate and n-butyl α-cyanoacrylate were studied. The neat substances (50 ml/500 000 µg) were placed on the back of rats (29 cm²) and the urine was analyzed for radioactivity. The exposure and observation time was 6 days (144 h). From figure 1, the % radioactivity in urine was ~4 and 0.25%, respectively.

From these figures the steady-state flux and permeability can be calculated (e.g. for methyl α-cyanoacrylate):

$$\text{Flux} = \frac{\%\text{Absorbed}\cdot\text{Applied amount}}{\text{Area}\cdot\text{Duration}\cdot 100} = \frac{0.04\cdot 500000}{29\cdot 144} = 5\ \mu g/cm^2/h$$

$$Kp = \frac{\text{Flux}}{\text{Conc.}} = \frac{4.8}{1000000} = 5\cdot 10^{-6}\ cm/h$$

The corresponding values for n-butyl α-cyanoacrylate are 0.3 µg/cm²/h and $3\cdot 10^{-7}$ cm/h.

These permeabilities correspond to "very low" and "extremely low", respectively.

Substance: Ethyl acrylate
CAS: 140-88-5
Scientific basis: AoH 1985:32

Skin notation: Yes
Skin permeability: No data

Molecular weight: 100.1
Density: 0.924 g/cm³
Melting point: -71.2°C
Boiling point: 99.8°C
Vapour pressure: 3.5 kPa (at 20°C)
Evaporation rate: 3.3
Log Kow: 1.32

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
No data available															

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

According to the Swedish consensus report (AoH 1985:32) acrylates are taken up fairly slowly via the skin. No further details are given on ethyl acrylate.

The rat oral LD50 is reported to be approximately 1020 mg/kg bw. The dermal LD50 for rabbits is in the same range (1790 mg/kg bw) suggesting that skin absorption may be extensive (ACGIH (2001)).

Substance: Ethyl benzene
CAS: 100-41-4
Scientific basis: AoH 1987:39

Skin notation: No
Skin permeability: High

Molecular weight: 106.2
Density: 0.867 g/cm³
Melting point: -94.9°C
Boiling point: 136.2°C
Vapour pressure: 2 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 3.15

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Rat	Ba	St	560	4.9	2	JP-8	0.15%	8	4	4	0.5		3.1	0.38	McDougal et al. (2000)
Rat	Ab	St	Full	2.6	1		Neat	31	3-6	3-6	2	18-68 µg	*0.07*	6.3	Tsuruta (1982)
In vivo															
HM	Ba			0.8	0.01		Neat	11	0.083	4		3.4 (150 µg)	*26*	2200	Susten et al. (1990)
Hum	Arm			17	0.2		Neat	7	0.17-0.25	1		99 mg	*320*	28000	Dutkiewicz et al. (1967)
Hum	Ha			*400*	Inf	H2O	0.11	7	1	14		39 mg	*11000*	120	Dutkiewicz et al. (1967)
Hum	Ha			*400*	Inf	H2O	0.16	7	1	14		71 mg	*14000*	220	Dutkiewicz et al. (1967)
Hum	Has			*800*		H2O	0.14	5	2	24		*11 mg*	*500*	*7*	Dutkiewicz et al. (1967)

Asessment

Tsuruta (1982) used physiological saline as the receptor medium, this is unsuitable for highly lipophilic substances like ethyl benzene. McDougal et al. (2000) used jet fuel as vehicle, this may have affected the permeation of ethyl benzene. In the first three experiments by Dutkiewicz et al. (1967), absorbed amount was obtained as the difference between applied and remaining amount after dipping one hand in a beaker for 1h. These measures includes absorption into the skin as well as evaporation and may heavily overestimate the systemic absorption. In the 4th, absorption rate was obtained from measuring the metabolite mandelic acid, in urine. The extremely high Kp value is unrealistic.

The Susten et al. (1990) study, although using hairless mice in vivo, is chosen as the preferred study.

The Kp value of $3 \cdot 10^{-3}$ cm/h corresponds to "high" permeation.

Substance: Ethyl ether
CAS: 60-29-7
Scientific basis: Not available

Skin notation: No
Skin permeability: No conclusion

Molecular weight: 74.1
Density: 0.713 g/cm³
Melting point: -116.3°C
Boiling point: 34.6°C
Vapour pressure: 48 kPa (at 20°C)
Evaporation rate: 38
Log Kow: 0.89

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
Hum	Fi				Inf	H2O	0.05%	12	15s	0.3			*9.8*	0.35	Naitoh et al. (2002)
Hum	Fi				Inf	H2O	0.05%	12	15s	0.3			*210*	7.6	Naitoh et al. (2002)

Asessment

The only available study is that of Naitoh et al. (2002). An unconventional technique was used in that one thumb was dipped once or several times (15 sec/occasion) in an aqueous solution. The flux was calculated from the evaporation from the thumb. The evaporation profile was biphasic, thus two different fluxes were reported. The reported fluxes reflects absorption into (and out of) rather than through skin.

Thus the calculated Kp may represent an serious overestimate of the "true" value.

Substance: Ethyl morpholine, N-
CAS: 100-74-3
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No data

Molecular weight: 115.2
Density: 0.905 g/cm³
Melting point: -63°C
Boiling point: 138°C
Vapour pressure: 0.8 kPa (at 20°C)
Evaporation rate: 0.74
Log Kow: 0.14 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

ACGIH has assigned a skin notation by analogy with morpholine (ACGIH (2001)).

Substance: Ethylamine
CAS: 75-04-7
Scientific basis: AoH 1983:36

Skin notation: Yes
Skin permeability: No data

Molecular weight: 45.1
Density: 0.8 g/cm³
Melting point: -81°C
Boiling point: 16.6°C
Vapour pressure: 120 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: -0.13

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The Swedish consensus document (AoH 1983:36) states that dermal uptake of amines may occur following very high exposures, without further specification.

The skin notation by ACGIH (2001) is based on the low dermal LD50 in rabbits of 390 mg/kg bw, which is similar to the oral LD50 (400 mg/kg bw in rats).

According to theoretical calculations by Fiserova-Bergerova et al. (1990) the potential for dermal absorption and resulting toxicity is significant.

Substance: Ethylene glycol
CAS: 107-21-1
Scientific basis: AoH 1982:24

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 62.1
Density: 1.116 g/cm³
Melting point: -13°C
Boiling point: 195°C
Vapour pressure: 13 Pa (at 25°C)
Evaporation rate: 0.01
Log Kow: -1.36

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Br	Fl	Full				Neat	8	16.5	16.5	*~0.5*		*1.1*	120	Loden (1986b)
Hum	Leg	Fl	500	1		Ac	1.6	3	24	24		18	*0.56*	0.09	Driver et al. (1993)
Hum		St	900	0.64	0.13	H2O	10%		8	8	2	*9 µg*	*0.21*	*2.3*	Korinth et al. (2003)
Hum		St	900	0.64	0.13	H2O	50%		8	8	2	*30 µg*	*0.14*	*7.8*	Korinth et al. (2003)
In vivo															
Mou	Ba			1			Neat (10 mg/kg bw)	4	96	96		77	*0.014*	*1.6*	Frantz et al. (1996a)
Mou	Ba			1			Neat (1000 mg/kg bw)	4	96	96		84	*1.6*	*180*	Frantz et al. (1996a)
Mou	Ba			1		H2O	50% (1000 mg/kg bw)	4	96	96		60	*2.2*	*130*	Frantz et al. (1996a)
Rat	Ba			1			Neat (10 mg/kg bw)	4	96	96		32	*0.059*	*6.6*	Frantz et al. (1996a)
Rat	Ba			1			Neat (1000 mg/kg bw)	4	96	96		29	*5.5*	*610*	Frantz et al. (1996a)
Rat	Ba			1		H2O	50% (1000 mg/kg bw)	4	96	96		26	*9.7*	*540*	Frantz et al. (1996a)
Rat	Ba			1			Neat (10 mg/kg bw)	4	96	96		32	*0.059*	*6.6*	Frantz et al. (1996b)
Rat	Ba			1			Neat (1000 mg/kg bw)	4	96	96		36	*6.6*	*740*	Frantz et al. (1996b)
Rat	Ba			1		H2O	50% (1000 mg/kg bw)	4	96	96		22	*8.3*	*460*	Frantz et al. (1996b)

Asessment

The experiment using acetone as vehicle is disregarded, as skin permeability may be affected.

The preferred study is that of Loden (1986b) using neat ethylene glycol and human skin.
The Kp value of $1 \cdot 10^{-4}$ cm/h, corresponds to "moderate" permeability.

Substance: Ethylene glycol dinitrate
CAS: 628-96-6
Scientific basis: AoH 1985:32

Skin notation: Yes
Skin permeability: High

Molecular weight: 152.1
Density: 1.49 g/cm³
Melting point: -23°C
Boiling point: 114°C
Vapour pressure: 5-6.6 Pa (at 20°C)
Evaporation rate: Not available
Log Kow: 1.16

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
No data available															
In vivo															
Hum	Arm			1	22 mg	SpSt	22%	6	7	7		2.3-2.8 mg	*10-12*	*330-400*	Gross et al. (1960)
Rat	Br/Ab			1	100 mg	NC	93%	36	192	192		35 mg (12h)	*21*	*2900*	Gross et al. (1960)
Rat	Br/Ab			1	200 mg	NC	93%	36	192	192		43 mg (12h)	*26*	*3600*	Gross et al. (1960)
Rat	Br/Ab			1	300 mg	NC	93%	36	192	192		59 mg (12h)	*36*	*4900*	Gross et al. (1960)
Rat	Br/Ab			1	400 mg	NC	93%	36	192	192		60 mg (12h)	*36*	*5000*	Gross et al. (1960)
Rat	Br/Ab			1	500 mg	NC	93%	36	192	192		80 mg (12h)	*48*	*6700*	Gross et al. (1960)
Rat	Br/Ab			1	600 mg	NC	93%	36	192	192		85 mg (12h)	*51*	*7100*	Gross et al. (1960)

Asessment

The only available study is a German publication by Gross et al. (1960) were the skin absorption in vivo in rats and humans was measured after application of ethylene glycol dinitrate in "gelatin" (nitrocellulose, NC) and "sprengstoff" (SpSt).

The absorption was obtained as the difference between applied and recovered amount. The calculated fluxes (and Kp values) increased with applied dose, in spite of using the same concentration within the experiment. This suggest that depletion of ethylene glycol dinitrate occurs in the layers closest to the skin.

The preferred experiment is that of humans in vivo, were a calculated Kp value of $1 \cdot 10^{-3}$ cm/h corresponds to "high" permeability.

Substance: Ethylene glycol monobutyl ether (EGBE)
CAS: 111-76-2
Scientific basis: AoH 1983:36

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 118.2
Density: 0.903 g/cm³
Melting point: -70°C
Boiling point: 171°C
Vapour pressure: 0.12 kPa (at 25°C)
Evaporation rate: 0.07
Log Kow: 0.83

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
HR	Ba	St	Full	5	0.03		Neat	3	1	1		19	*12*	*1100*	Bartnik et al. (1987)
HR	Ba	St	Full	5	0.03		Neat	3	1	1		5.6	*3.4*	*303*	Bartnik et al. (1987)
HR	Ba	St	Full	5	0.03	H2O	10%	3	1	1		63	*38*	*340*	Bartnik et al. (1987)
HR	Ba	St	Full	5	0.03	H2O	10%	3	1	1		10	*6.2*	*56*	Bartnik et al. (1987)
HR	Ba	St	Full	5	0.03	H2O	3.50%	3	1	1		46	*26*	*82*	Bartnik et al. (1987)
HR	Ba	St	Full	5	0.03	H2O	3.50%	3	1	1		11	*6.3*	*20*	Bartnik et al. (1987)
HR	Ba	St	Full	5	0.05	H2O	10% (1000 µg/cm²)	3	1	1		11	*2.4*	*22*	Bartnik et al. (1987)
HR	Ba	St	Full	5	0.05	H2O	10% (1000 µg/cm²)	3	1	1		43	*9.6*	*87*	Bartnik et al. (1987)
HR	Ba	St	Full	5	0.03	H2O	10% (600 µg/cm²)	3	1	1		15	*2*	*18*	Bartnik et al. (1987)
HR	Ba	St	Full	5	0.03	H2O	10% (600 µg/cm²)	3	1	1		63	*8.3*	*75*	Bartnik et al. (1987)
Hum	Ab	St	Epi	1.8	1-5		Neat	8	8	8	<1		2.1	200	Dugard et al. (1984)
Hum	Br	Fl	300	0.64	0.2	H2O	6	5	24	7		23	*180*	110	Wilkinson et al. (2002)
Hum	Br	Fl	300	0.64	0.1	H2O	3	5	24	7	0.36	16	*100*	31	Wilkinson et al. (2002)
Hum	Br	Fl	300	0.64	0.2	H2O	3	5	24	24	0.3	27	*210*	64	Wilkinson et al. (2002)
Hum	Br	Fl	300	0.64	0.011		Neat	5	24	24			*9.5*	851	Wilkinson et al. (2002)
Hum	Arm	St	Full	3	0.03	H2O	10% (1000 µg/cm²)	3	1	1		6.9	*2.5*	*23*	Bartnik et al. (1987)
Hum	Arm	St	Full	3	0.03	H2O	10% (1000 µg/cm²)	3	1	1		17	*6.4*	*58*	Bartnik et al. (1987)
Hum	Br	Fl	330	0.64	0.01	Me	50%	5	24	24		11	0.48	*22*	Lockley et al. (2004)
Hum	Br	Fl	280	0.64	0.01		Neat	5	24	24		3.9	0.19	*18*	Lockley et al. (2004)
Pig	Ba	St	Full	5	0.03		Neat	3	6	6		11	*1.1*	*101*	Bartnik et al. (1987)
Pig	Ba	St	Full	5	0.03	H2O	10%	3	6	6		37	*3.7*	*33*	Bartnik et al. (1987)
Pig	Ba	St	Full	5	0.03	H2O	3.50%	3	6	6		48	*4.4*	*14*	Bartnik et al. (1987)
Pig	Ba	St	Full	5	0.05	H2O	10% (1000 µg/cm²)	3	1	1		8.6	*1.9*	*17*	Bartnik et al. (1987)
Pig	Ba	St	Full	5	0.05	H2O	10% (1000 µg/cm²)	3	1	1		18	*3.9*	*35*	Bartnik et al. (1987)
Pig	Ba	St	Full	5	0.03	H2O	10% (600 µg/cm²)	3	1	1		13	*7.8*	*16*	Bartnik et al. (1987)
Pig	Ba	St	Full	5	0.03	H2O	10% (600 µg/cm²)	3	1	1		21	*2.8*	*25*	Bartnik et al. (1987)

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_p (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
Rat	Ba	Fl	Full	0.64	0.01	Me	50%	5	24	24		15	0.81	*37*	Lockley et al. (2004)
Rat	Ba	Fl	280	0.64	0.01	Me	50%	5	24	24		23	1.4	*64*	Lockley et al. (2004)
Rat	Ba	Fl	Full	0.64	0.01		Neat	5	24	24		7.9	0.32	*29*	Lockley et al. (2004)
Rat	Ba	Fl	280	0.64	0.01		Neat	5	24	24		16	0.92	*83*	Lockley et al. (2004)
Rat	Ba	Fl	280	0.64	0.01		Neat	5	24	24		18	1.1	*99*	Lockley et al. (2004)
In vivo															
GP	Ba			6.3			Neat	10	2	4.5	0.35-1		*20*	1800	Johanson et al. (1986)
GP	Ba			3.1	1	H2O	5%	2	2	4			100	525	Johanson et al. (1988c)
GP	Ba			3.1	1	H2O	10%	2	2	4			60	525	Johanson et al. (1988c)
GP	Ba			3.1	1	H2O	20%	2	2	4			40	700	Johanson et al. (1988c)
GP	Ba			3.1	1	H2O	40%	2	2	4			20	700	Johanson et al. (1988c)
GP	Ba			3.1	1	H2O	80%	2	2	4			8	600	Johanson et al. (1988c)
GP	Ba			3.1	1		Neat	14	2	2			3	350	Johanson et al. (1988c)
Hum	Fi			79-190	Inf		Neat	12	2	24		15-220 mg	*1.5*	*50-680*	Johanson et al. (1988a)
Hum	WB					Vap	0.00024	4	2	4			*590000*	*14*	Johanson et al. (1991)
Hum	WB			*20000*			49ppm	18	2	34		11			Jones et al. (2003)
Hum	Arm			40		H2O	50%	6	4	8			18-30	920-1340	Jakasa et al. (2004)
Hum	Arm			40		H2O	90%	3	4	8			8.8-11	740-920	Jakasa et al. (2004)
Hum	Arm			40			Neat	6	4	8			*2.9*	260	Jakasa et al. (2004)
Hum	Arm			40	8	H2O	50%	6	4	48			*53*	2400	Kezic et al. (2004b)
Rat	Ba			12	0.072		*Neat* (200 mg/kg BW)	12	48	48		27	*0.26*	*23*	Bartnik et al. (1987)
Rat	Ba			9.4	0.09	Ac	*0.00016* (120 µmol/rat)	4	72	72		25	*0.34*	*0.0000054*	Sabourin et al. (1992)
Rat	Ba			9.4	0.09	Ac	*0.00048* (370 µmol/rat)	4	72	72		26	*0.35*	*0.000017*	Sabourin et al. (1992)
Rat	Ba			9.4	0.09	Ac	*0.00085* (650 µmol/rat)	4	72	72		21	*0.27*	*0.000023*	Sabourin et al. (1992)
Rat	Ba			9.6	0.1		Neat	5	24	24		28	*1.2*	*111*	Lockley et al. (2004)

Asessment

The studies using acetone or methanol as vehicle are excluded as they may affect skin permeation.

10^{-5}	10^{-4}	10^{-3}	10^{-2}	10^{-1}	10^{0}	10^{1}	10^{2}
Neat	Aq. dilution					Vapour	

The Kp for vapour is an overestimate of the "true" Kp, since EGBE has an extremely high water:air partition coefficient of 7000 (Johanson et al. (1988b)) and is therefore concentrated on the skin.

The preferred study is that of Jakasa et al. (2004) were human skin in vivo is used, with a reported Kp value of neat EGBE is $3 \cdot 10^{-4}$ cm/h, which corresponds to "moderate" permeability.

It should be noted that the permeability of EGBE in aqueous solutions is approximately one order of magnitude higher.

Substance: Ethylene glycol monobutyl ether acetate (EGBEA)
CAS: 112-07-2
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No data

Molecular weight: 160.2
Density: 0.94 g/cm³
Melting point: 5.5°C
Boiling point: 192°C
Vapour pressure: 31 Pa (at 20°C)
Evaporation rate: 0.03
Log Kow: 1.57 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The substance has not been assessed by the Swedish Criteria Group, nor the ACGIH-TLV committee.

Based on comparison between ethylene glycol monoethyl ether (EGEE) and ethylene glycol monoethyl ether acetate (EGEEA) Johanson (1996), it may be assumed that the skin permeability of ethylene glycol monobutyl ether acetate (EGBEA) is similar to that of ethylene glycol monobutyl ether (EGBE).

Substance: Ethylene glycol monoethyl ether (EGEE)
CAS: 110-80-5
Scientific basis: AoH 1983:36

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 90.1
Density: 0.931 g/cm^3
Melting point: -90°C
Boiling point: 135.6°C
Vapour pressure: 0.71 kPa (at 25°C)
Evaporation rate: 0.3
Log Kow: -0.32

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_p (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Ab	St	Epi	1.8	1-5		Neat	11	8	8	<1		8.4	800	Dugard et al. (1984)
Hum	Ab	Fl	Full	3.1	0.02		Neat		4	4	1		8.8	820	Larese et al. (1994)
Hum	Ab	Fl	Full	3.1	0.02	Ac	279.3		4	4	0.72	7.4	30	830	Larese et al. (1994)
Hum	Br	Fl	280	0.64	0.01	Me	93	5	24	24		7.5	0.59	5.5	Lockley et al. (2002)
Hum	Br	Fl	280	0.64	0.01		Neat	5	24	24		8.3	0.74	69	Lockley et al. (2002)
Hum	Br	Fl	500	0.64	0.2	H2O	3	4	24	24		5.1	43	13	Wilkinson & Williams (2002)
Hum	Br	Fl	500	0.64	0.1	H2O	3	5	24	24		14	*200*	*59*	Wilkinson & Williams (2002)
Hum	Br	Fl	500	0.64	0.2	H2O	6	6	24	24		18	160	98	Wilkinson & Williams (2002)
Hum	Br	Fl	500	0.64	0.2	H2O	3	4	24	24		11	*83*	25	Wilkinson & Williams (2002)
Hum	Br	Fl	500	0.64	0.2	H2O	3	5	24	24		13	*100*	31	Wilkinson & Williams (2002)
Hum	Br	Fl	500	0.64	0.2	H2O	3	5	24	24		12	*80*	24	Wilkinson & Williams (2002)
Hum	Br	Fl	500	0.64	0.01		Neat	5	24	24			*6.2*	580	Wilkinson & Williams (2002)
Hum	Br	Fl	500	0.64	0.2		Neat	4	24	24			*12*	1100	Wilkinson & Williams (2002)
Rat	Ba	Fl	330	0.64	0.01	Me	93	5	24	24		30	0.78	7.3	Lockley et al. (2002)
Rat	Ba	Fl	Full	0.64	0.01	Me	93	5	24	24		11	2.3	21	Lockley et al. (2002)
Rat	Ba	Fl	330	0.64	0.01		Neat	5	24	24		20	1.5	140	Lockley et al. (2002)
Rat	Ba	Fl	Full	0.64	0.01		Neat	5	24	24		11	0.75	70	Lockley et al. (2002)
Rat	Ba	Fl	330	0.64	0.01		Neat	5	24	24		22	4.7	440	Lockley et al. (2002)
In vivo															
Hum	Arm			1000		Vap	0.0037	5	0.75	100		58 mg	190000		Kezic et al. (1997)
Hum	Arm			27			Neat	5	0.25	100		5.2 mg	7.5	700	Kezic et al. (1997)
Rat	Ba			9.6	0.1		Neat	3	24	24		25	*1.1*	*100*	Lockley et al. (2002)
Rat	Ba			9.4	0.09	Ac	*0.00012* (120 µmol/rat)	4	72	72		27	*0.36*	*0.0000044*	Sabourin et al. (1992)
Rat	Ba			9.4	0.09	Ac	*0.00039* (390 µmol/rat)	4	72	72		17	*0.23*	*0.0000089*	Sabourin et al. (1992)
Rat	Ba			9.4	0.09	Ac	*0.00088* (880 µmol/rat)	4	72	72		20	*0.26*	*0.000023*	Sabourin et al. (1992)

Asessment

The studies using acetone or methanol as vehicle are excluded as they may affect skin permeation.

10^{-5}	10^{-4}	10^{-3}	10^{-2}	10^{-1}	10^{0}	10^{1}	10^{2}
	Neat	Aq. dilution				Vapour	

However, the Kp for vapour is an overestimate of the "true" Kp, since EGEE has an extremely high water:air partition coefficient of 23000 (Johanson et al. (1988b)) and is therefore concentrated on the skin

The preferred study is that of Kezic et al. (1997) were human skin in vivo is used, with a reported Kp value of neat EGEE is $8 \cdot 10^{-4}$ cm/h, which corresponds to "moderate" permeability.

It should be noted that the permeability of EGEE in aqueous solutions is one or two orders of magnitude higher.

Substance: Ethylene glycol monoethyl ether acetate (EGEEA)
CAS: 111-15-9
Scientific basis: Not available

Skin notation: Yes
Skin permeability: High

Molecular weight: 132.2
Density: 0.975 g/cm³
Melting point: -61.7°C
Boiling point: 156°C
Vapour pressure: 0.27 kPa (at 20°C)
Evaporation rate: 0.21
Log Kow: 0.59 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Dog	Br	St	Full	0.9		Neat	9	7	7	1.6		*23*	2200	Guest et al. (1984)
Hum		St	Epi	0.64/1.0		Neat	12	8	8	1-2		15	1400	Barber et al. (1992)
Hum	Ab	St	Epi	1.8	1-5	Neat	10	8	8	<1		8.1	800	Dugard et al. (1984)
Rat		St	Full	0.64/1.0		Neat	12	8	8	1-2		25	2400	Barber et al. (1992)
In vivo														
Dog	Br			56		Neat	5	0.5-1	24			*8.8*	860	Guest et al. (1984)

Asessment

Human, animal, in vitro and in vivo data show fairly consistent results in three different studies with Kp values between $8 \cdot 10^{-4}$ and $2 \cdot 10^{-3}$ cm/h.

These values suggest "high" permeability.

Substance: Ethylene glycol monoisopropyl ether (EGiPE)
CAS: 109-59-1
Scientific basis: AoH 1995:19

Skin notation: Yes
Skin permeability: No data

Molecular weight: 104.1
Density: 0.903 g/cm³
Melting point: -60°C
Boiling point: ~140°C
Vapour pressure: 0.69 kPa (at 25°C)
Evaporation rate: Not available
Log Kow: 0.05

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The Swedish consensus report (AoH 1995:19) states that based on analogy with other e.g. ethers, skin absorption may be high.

Substance: Ethylene glycol monoisopropyl ether acetate (EGiPEA)
CAS: 19234-20-9
Scientific basis: AoH 1995:19

Skin notation: Yes
Skin permeability: No data

Molecular weight: 146.2
Density: 0.95 g/cm³
Melting point: Not available
Boiling point: 164°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: 1.01 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The Swedish consensus report (AoH 1995:19) states that based on analogy with other e.g. ethers, skin absorption may be high.

Substance: Ethylene glycol monopropyl ether (EGPE)
CAS: 2807-30-9
Scientific basis: AoH 1994:30

Skin notation: Yes
Skin permeability: High

Molecular weight: 104.1
Density: 0.931 g/cm³
Melting point: -190°C
Boiling point: 149°C
Vapour pressure: 170-390 Pa (at 25°C)
Evaporation rate: 0.2
Log Kow: 0.08

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Hum		St	Epi	0.64/1.0		Neat	5	8	8	1-2		6.4	580	Barber et al. (1992)
Rat		St	Full	0.64/1.0		Neat	5	8	8	1-2		25	2300	Barber et al. (1992)
In vivo														
No data available														

Asessment

Quantitative uptake data on rat and human skin in vitro are available (Barber et al. (1992)). Human epidermis was prepared using hot (60°C) water, which may have affected the permeation properties. The preferred study is the one using intact rat skin.

The Kp value of $3 \cdot 10^{-3}$ cm/h corresponds to "high" permeability.

Substance: Ethylene oxide
CAS: 75-21-8
Scientific basis: AoH 1982:24

Skin notation: Yes
Skin permeability: Extremely high

Molecular weight: 44.1
Density: 0.882 g/cm³
Melting point: -111.3°C
Boiling point: 10.7°C
Vapour pressure: 150 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: -0.30

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum		St	500	1		Pol fab	*0.0033* (1800ppm)	2	24	24		1.3	*280*	*0.000092*	Wester et al. (1997)
Hum		St	500	1		Pol fab	*0.0033* (1800ppm)	2	24	24		46	*10000*	*0.0033*	Wester et al. (1997)
In vivo															
No data available															

Asessment

The skin notation by ACGIH (2001) is based on a case report (Sexton et al. (1949)) where three workers that were accidentally exposed to a 1% EO solution developed nausea and vomiting. It is however unclear to what extent inhalation exposure contributed.

In the first experiment of Wester et al. (1997), polyester fabric (Pol fab) was saturated with ethylene oxide. The skin piece was then exposed to the saturated fabric in an non-occluded fashion. Thus, most of the ethylene oxide evaporated into the air as seen in the low absorption percentage.

The second experiment was similar except that the polyester fabric was covered by a double-layer latex glove. The 46% absorption occurred within the first 4h suggesting high permeability of ethylene oxide.

The fluxes and Kp values in the table were calculated assuming a thickness of the fabric of 0.5 mm and, hence, an applied amount of 17 ng.

This highly uncertain exercise suggests a "very high" or even "extremely high" permeability of ethylene oxide.

Substance: Ethylenediamine
CAS: 107-15-3
Scientific basis: AoH 1983:36

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 60.1
Density: 0.899 g/cm³
Melting point: 8.5°C
Boiling point: 116.5°C
Vapour pressure: 1.4 kPa (at 20°C)
Evaporation rate: 0.91
Log Kow: -2.04

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
No data available															
In vivo															
Rat	Ba			49	0.2	H2O	25% (1000 µg/cm²)	4-6	24	24		55	*1*	*23*	Yang et al. (1987)
Rat	Ba			49	0.2	H2O	50% (2000 µg/cm²)	4-6	24	24		61	*1.2*	*52*	Yang et al. (1987)

Asessment

Only rat in vivo data were found. The Kp value of $1 \cdot 10^{-4}$ cm/h suggests "moderate" permeability.

Substance: Formaldehyde
CAS: 50-00-0
Scientific basis: AoH 1983:36

Skin notation: No
Skin permeability: Moderate

Molecular weight: 30.0
Density: 1.09 g/cm³
Melting point: -118°C
Boiling point: -19.5°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: 0.35

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Br		Full	0.35	0.035	H2O + MeOH (10-15%)	370	11	0.5	0.5		0.10 mg/cm²	*5.7*	*210*	Loden (1986a)
Hum	Br	Fl	Full	0.35		H2O + MeOH (1-1.5%)	37	5	21	21	*~1.4*		*4.6*	17	Loden (1986b)
Hum	Br	Fl	Full	0.35		H2O + MeOH (10-15%)	370	5	15	15	*~1.4*		*8.6*	320	Loden (1986b)
In vivo															
Rat	Ba			8	200 mg	Cream	0.10%	8	48	48		6.1	*0.32*	*0.032*	Bartnik et al. (1985)
Rat	Ba			8	200 mg	Cream	0.10%	4	48	48		9.2	*0.48*	*0.048*	Bartnik et al. (1985)
Rat	Ba			8	200 mg	Cream	0.10%	2	48	48		3.4	*0.18*	*0.018*	Bartnik et al. (1985)

Asessment

The in vivo study with rat skin Bartnik et al. (1985) used skin cream as vehicle, this may change the permeability properties significantly.
The preferred study is that of Loden (1986b), using human full thickness skin in vitro.

The Kp values range between $5 \cdot 10^{-4}$ and $9 \cdot 10^{-4}$ cm/h, corresponds to "moderate" permeability.

Substance: Formamide
CAS: 75-12-7
Scientific basis: AoH 1991:8

Skin notation: Yes
Skin permeability: No data

Molecular weight: 45.0
Density: 1.134 g/cm³
Melting point: 2.5°C
Boiling point: 210°C
Vapour pressure: 0.013 kPa (at 30°C)
Evaporation rate: 0.004
Log Kow: -1.51

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

No information regarding skin uptake is given in the Swedish consensus report (AoH 1991:8).
According to the ACGIH (2001) documentation, formamide is relatively non-toxic by skin application, with a dermal LD50 of 6 g/kg in rabbits. However, 3 months daily dermal treatment (5 d/wk) with 3 g/kg produced general systemic toxicity in rats.

According to theoretical calculations by Fiserova-Bergerova et al. (1990) the potential for dermal absorption and resulting toxicity is significant.

Substance: Furfural
CAS: 98-01-1
Scientific basis: AoH 1984:44

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 96.1
Density: 1.159 g/cm³
Melting point: -36.5°C
Boiling point: 167°C
Vapour pressure: 0.14 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 0.41

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
No data available															
In vivo															
Hum	Ha						Neat	6	0.25	20		27 mg	*1.6*	180	Flek et al. (1978)
Hum	WB					Vap	30 mg/m³	6	8	20			*180000*	*0.53*	Flek et al. (1978)

Asessment

The flux measurement is based on recovery of furfural metabolite in urine after dipping one hand in neat furfural.
This method measures the rate of penetration into skin, rather than the steady-state flux, and may thus be an overestimation.

This study gives a Kp value of $2 \cdot 10^{-4}$ cm/h, corresponding to "moderate" permeability.

Substance: Furfuryl alcohol
CAS: 98-00-0
Scientific basis: AoH 1985:32

Skin notation: Yes
Skin permeability: No data

Molecular weight: 98.1
Density: 1.128 g/cm³
Melting point: -20.2°C
Boiling point: 170°C
Vapour pressure: 0.69 kPa (at 25°C)
Evaporation rate: Not available
Log Kow: 0.28

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

Referring to an industry report, the Swedish consensus document (AoH 1985) states that the percutaneous uptake has been demonstrated in animals. ACGIH (2001) gives a similar statement with the additional information of dose-related mortality in animals.

Substance: Halothane
CAS: 151-67-7
Scientific basis: AoH 1985:32

Skin notation: No
Skin permeability: Very high

Molecular weight: 197.4
Density: 1.864 g/cm³
Melting point: -118°C
Boiling point: 50.2°C
Vapour pressure: 32 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 2.30

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
Rat	WB					Vap	50000ppm	4	4	4		0.2	450	18	McDougal et al. (1990)

Asessment

The only study found on halothane is that of McDougal et al. (1990) were rats were exposed to halothane vapour.

The reported Kp value of $5 \cdot 10^{-2}$ cm/h suggests a "very high" permeability

It should be noted that halothane is very volatile.

Substance: Heptane, n-
CAS: 142-82-5
Scientific basis: Not available

Skin notation: No
Skin permeability: Extremely low

Molecular weight: 100.2
Density: 0.684 g/cm³
Melting point: -90.6°C
Boiling point: 98.4°C
Vapour pressure: 4.2 kPa (at 20°C)
Evaporation rate: 4.3
Log Kow: 4.66

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Rat	Ab	St	Full	2.6	1	Neat	30	4-20	4-20		1-7 µg	*0.0021*	0.14	Tsuruta (1982)
In vivo														
No data available														

Asessment

The only found study on n-heptane is that of Tsuruta (1982) were rat skin was exposed to neat n-heptane in vitro.

The calculated Kp value of $2 \cdot 10^{-7}$ cm/h suggests an "extremely low" permeability.

It should be noted that heptane has very low solubility in water and Tsuruta (1982) used saline as receptor medium.
Hence, the Kp may be an underestimate.

Substance: Hexane, n-
CAS: 110-54-3
Scientific basis: AoH 1986:20

Skin notation: No
Skin permeability: Very low

Molecular weight: 86.2
Density: 0.655 g/cm³
Melting point: -95°C
Boiling point: 69°C
Vapour pressure: 14 kPa (at 20°C)
Evaporation rate: 9
Log Kow: 3.90

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Br	Fl	Full				Neat	5	12	12	*~5.2*		*0.01*	0.83	Loden (1986b)
Rat	Ab	St	Full	2.6	1		Neat	51	2-22	2-22		0.4-3 µg	*0.00092*	0.061	Tsuruta (1982)
In vivo															
Hum	Arm/Ha			1000		Vap	1.3 mmol/l	5	0.5	6			130	*1.5*	Kezic et al. (2000)
Rat	WB					Vap	60000ppm	5	4	4		0.1	310	6.5	McDougal et al. (1990)

Asessment

There is a huge difference in Kp values between experiments in vivo and in vitro.

Tsuruta (1982) used saline as receptor medium, this is likely to give a severe under estimate of the flux and Kp due to the low solubility of n-hexane.

The preferred study is that by Loden (1986b) were human skin was exposed to neat n-hexane.

The calculated Kp value of $1 \cdot 10^{-6}$ cm/h suggesting a "very low" permeability.

Substance: Hexanone, 2-; methyl n-butyl ketone
CAS: 591-78-6
Scientific basis: Not available

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 100.2
Density: 0.811 g/cm³
Melting point: -57°C
Boiling point: 127°C
Vapour pressure: 0.33 kPa (at 20°C)
Evaporation rate: 1.2
Log Kow: 1.38

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
Hum	Arm			56	15	Neat	4	1	12		19 mg	*4.2*	340	DiVincenzo et al. (1978)

Asessment

The only found study is that of DiVincenzo et al. (1978) which was an in vivo study were human skin was exposed to neat 2-hexanone.

The calculated Kp value corresponds to "moderate" permeability.

Substance: Hydrogen cyanide
CAS: 74-90-8
Scientific basis: AoH 2001:19

Skin notation: Yes
Skin permeability: Very high

Molecular weight: 27.1
Density: 0.69 g/cm³
Melting point: -13.4°C
Boiling point: 25.6°C
Vapour pressure: 84 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: -0.25

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Hum	Ab	St	40	1.8		Vap	*1.3* (Saturated)				0.1		100	13	Dugard (1987)
In vivo															
No data available															

Asessment

The single study found on hydrogen cyanide was that of Dugard (1987) were human skin was exposed to saturated cyanide vapour (concentration not given, but could be calculated from flux and Kp).

The reported Kp value of $1 \cdot 10^{-2}$ corresponds to "very high" permeability.

It should be noted that the permeability of sodium cyanide is two orders of magnitude lower.

Substance: Hydroquinone
CAS: 123-31-9
Scientific basis: AoH 1991:8

Skin notation: No
Skin permeability: Very low

Molecular weight: 110.1
Density: 1.332 g/cm³
Melting point: 170°C
Boiling point: 285°C
Vapour pressure: 0.0024 Pa (at 20°C)
Evaporation rate: Negligible
Log Kow: 0.59

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
HGP		Fl	250-300	*1.1*		OiW	*0.08%* (2.5 µg/cm²)	9	24	24		4.3	*0.036*	*0.004*	Hood et al. (1999)
Hum	Ab	St	Epi		Inf	H2O	56	9	8	8			0.093	0.52	Barber et al. (1995)
Hum	Ab	Fl	500	1	0.01	Cream	2%	6	24	24		34	*1.1*	2.9	Wester et al. (1998c)
Rat	Ab	St	Full		Inf	H2O	49	9	8	8			0.23	1.1	Barber et al. (1995)
Rat	Ab	St	320	0.95		Cream	50 (5%)	5	7	7	0	14 mg	38	*200*	Matsubayashi et al. (2003)
In vivo															
Hum	FH			25		Cream	2% (2.5 mg)	6	24	96		37	*0.71*	1.9	Wester et al. (1998c)
Hum	Arm			25		Cream	2% (2.5 mg)	6	8	8		45	*0.38*	1	Wester et al. (1998c)

Asessment

The study by Matsubayashi et al. (2003) seems unrealistic in that no lag time was observed.
The other in vitro studies are in accordance with the in vivo studies.

The in vitro study using human skin and water as vehicle (Barber et al. (1995)) is preferred.

The Kp value of $9 \cdot 10^{-6}$ cm/h corresponds to "very low" permeability

It should be noted that Kp values calculated for aqueous solutions are generally much higher than those obtained for neat substances.

Substance: Hydroxyethylacrylate, 2-; propenoic acid, 2-
CAS: 818-61-1
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No data

Molecular weight: 116.1
Density: 1.101 g/cm³
Melting point: -60.2°C
Boiling point: 210°C
Vapour pressure: 7 Pa (at 25°C)
Evaporation rate: Not available
Log Kow: -0.21

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux Reference (µg/cm^2/h)
In vitro													
No data available													
In vivo													
No data available													

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

No documentation was found from the Swedish criteria group or the ACGIH-TLV committee.

OECD (2005) reports the following LD50 values (mg/kg bw):

oral rat/mouse	601, 1070, 1040, 810, 540, 650, 548
dermal rabbit	250, 298, 154, >63, 1100, 3000
dermal rat	>1000

The dermal and oral LD50 values are in the same range, suggesting that skin absorption may be significant.

Also a study cited in OECD (2005) showed that two thirds (66%) of dermally applied radiolabelled 2-hydroxyethylacrylate (4 male rats, clipped fur, 12.5 mg/kg bw, exposed area not given) was recovered within 48h. This suggests extensive skin penetration.

Substance: Isoflurane
CAS: 26675-46-7
Scientific basis: Not available

Skin notation: No
Skin permeability: Very high

Molecular weight: 184.5
Density: 1.45 g/cm³
Melting point: ~-103°C
Boiling point: 48.5°C
Vapour pressure: 32 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 2.06

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
Rat	WB					Vap	50000ppm	6	4	4		0.1	250	9.6	McDougal et al. (1990)

Asessment

The only found study on isoflurane is that of McDougal et al. (1990).

The reported Kp value of $3 \cdot 10^{-2}$ cm/h suggests a "very high" permeability.

It should be noted that vapour exposure usually yield for higher Kp values than does liquid exposure.

Substance: Isopropanol
CAS: 67-63-0
Scientific basis: AoH 1982:24

Skin notation: No
Skin permeability: Moderate

Molecular weight: 60.1
Density: 0.785 g/cm³
Melting point: -88.5°C
Boiling point: 82.4°C
Vapour pressure: 3.9 kPa (at 20°C)
Evaporation rate: 2.9
Log Kow: 0.05

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum		St	900	0.64	0.13	H2O	10%		8	8	1	*26 µg (4h)*	*1.7*	*13*	Korinth et al. (2003)
Hum		St	900	0.64	0.13	H2O	50%		8	8	1	*430 µg*	*2.4*	*96*	Korinth et al. (2003)
In vivo															
Rat	Ba			4.3		H2O	70%		4	48			14-15	780-850	Boatman et al. (1998)

Asessment

The human in vitro and rat in vivo give concordant results.

The human data yield a Kp value of $2 \cdot 10^{-4}$ cm/h suggesting "moderate" permeability.

Substance: Isopropylbenzene; cumene
CAS: 98-82-8
Scientific basis: AoH 1982:24

Skin notation: Yes
Skin permeability: No data

Molecular weight: 120.2
Density: 0.862 g/cm³
Melting point: -96°C
Boiling point: 151°C
Vapour pressure: 610 Pa (at 25°C)
Evaporation rate: 0.43
Log Kow: 3.66

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

According to the Swedish consensus report (AoH 1982), there are indications that it is absorbed by the skin. According to ACGIH (2001) the cited study (Valette et al. (1954)) did not directly demonstrate skin absorption of isopropylbenzene.

Substance: Mercury bichloride; dichloromercury
CAS: 7487-94-7
Scientific basis: AoH 1984:44

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 271.5
Density: 5.44 g/cm³
Melting point: 277°C
Boiling point: 302°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: -0.22

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
GP	Ba	Fl	Full	3.1		H2O	*1-48* (0.005-0.24M)	30	48	48			*17-20*	2-81	Wahlberg (1965)
Hum	Ab	Fl	Full	3.1		H2O	1 (0.005M)	10	48	48			*8*	0.8	Wahlberg (1965)
Hum	Ab	Fl	Full	3.1		H2O	*16* (0.080M)	10	48	48			*4.5*	7.2	Wahlberg (1965)
Hum	Br	Fl	Full	3.1		H2O	*16* (0.080M)	10	48	48			*9.4*	15	Wahlberg (1965)
Hum	Ab	Fl	Full	3.1		H2O	*48* (0.24M)	10	48	48			*6.3*	30	Wahlberg (1965)
Hum		St	250	*1*	1.5	H2O	*50* (5%)	10	17.5	17.5		92 µg	*1.1*	*5.3*	Pilgram et al. (2000)
Hum	Ab	Fl	300-600	0.95	40 mg	Soil	0.0088 nmol/cm³	5	72	72			140	*0.000032*	Sartorelli et al. (2003)
Hum	Ab	Fl	300-600	0.95	40 mg	Soil	0.061 nmol/cm³	4	72	72			30	*0.000049*	Sartorelli et al. (2003)
Pig	Ab	Fl	200	0.64	0.005	Et	*0.032* (160 ng)		16	16		*0.13 (1h)*	*0.14*	*0.00046*	Skowronski et al. (2000)
In vivo															
Hum	Arm			22	0.3	H2O	*27* (0.1M)	3	0.08	1		1.0 mg	*210*	560	Baranowska-Dutkiewicz (1982a)
Hum	Arm			22	0.3	H2O	*27* (0.1M)	3	0.17	1		1.5 mg	*150*	400	Baranowska-Dutkiewicz (1982a)
Hum	Arm			22	0.3	H2O	*27* (0.1M)	3	0.25	1		1.9 mg	*130*	340	Baranowska-Dutkiewicz (1982a)
Hum	Arm			22	0.3	H2O	*27* (0.1M)	4	0.5	1		3.0 mg	*100*	280	Baranowska-Dutkiewicz (1982a)
Hum	Arm			22	0.3	H2O	*27* (0.1M)	3	1	1		3.2 mg	*56*	150	Baranowska-Dutkiewicz (1982a)

Asessment

The studies found on mercury bichloride exposing human skin to aqueous solutions are not consistent.
The range for the calculated Kp values is $1 \cdot 10^{-4}$ to $1 \cdot 10^{-2}$ cm/h, i.e. two orders of magnitude.
The preferred study is that of Wahlberg (1965) with calculated Kp values ranging between $5 \cdot 10^{-4}$ and $9 \cdot 10^{-4}$ cm/h, suggesting "moderate" permeability.
The in vivo study by Baranowska-Dutkiewicz (1982a) show that the penetration into skin is approximately 20 times higher. This suggests that a depot of dichloromercury is created in the skin that may later become systemically available.

Substance: Mercury chloride; dimercury dichloride
CAS: 10112-91-1
Scientific basis: AoH 1984:44

Skin notation: Yes
Skin permeability: Very high

Molecular weight: 472.1
Density: 7.15 g/cm³
Melting point: 400 to 500 °C
Boiling point: Not available
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: -0.55 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Hum	Ab	St	Full	0.64		Cream	290 µg/l	10	24	24			270	*0.0078*	Palmer et al. (2000)
Hum	Ab	St	Full	0.64		H2O	290 µg/l	10	24	24			150	*0.0044*	Palmer et al. (2000)
In vivo															
No data available															

Asessment
The only study found on mercury chloride was that of Palmer et al. (2000).

The preferred experiment is the one using water as vehicle. The reported Kp value of $2 \cdot 10^{-2}$ cm/h suggests a "very high" permeability.

Substance: Mercury, dimethyl
CAS: 593-74-8
Scientific basis: AoH 1984:44

Skin notation: Yes
Skin permeability: No data

Molecular weight: 230.7
Density: 2.96 g/cm³
Melting point: -43°C
Boiling point: 93 to 94°C
Vapour pressure: 6.7-10.9 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 2.59

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

The Swedish skin notation applies to organic mercury compounds in general (including dimethyl mercury).

No quantitative experimental data on dermal uptake were found in the literature.

A case report (Nierenberg et al. (1998)) describes the death of a chemist 10 months after spilling dimethyl mercury on the dorsum of her gloved hand. The estimated dose was 1344 mg corresponding to 0.44 ml neat dimethyl mercury. Although additional exposure(s) cannot be excluded, this case strongly supports high potential for dermal toxicity.

Substance: Mercury, metal
CAS: 7439-97-6
Scientific basis: AoH 1984:44

Skin notation: Yes
Skin permeability: Extremely high

Molecular weight: 200.6
Density: 13.53 g/cm³
Melting point: -38.9°C
Boiling point: 356.5°C
Vapour pressure: 0.16 Pa (at 20°C)
Evaporation rate: 4
Log Kow: 0.62

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
Hum	Arm			360-430	Inf Vap	0.88-2.1 ng/ml	5	0.45-0.72	60 d		220-850 ng	*6100-24000*	*0.001-0.005*	Hursh et al. (1989)

Asessment

The only found study on metal mercury was that of Hursh et al. (1989) were a human arm was exposed to mercury vapour.

The reported range of Kp values suggests an "extremely high" permeability.

It should be noted that studies on vapour exposure tend to overestimate the Kp value.

Substance: Methanol
CAS: 67-56-1
Scientific basis: AoH 1985:32

Skin notation: Yes
Skin permeability: Very high

Molecular weight: 32.0
Density: 0.791 g/cm³
Melting point: -98°C
Boiling point: 64.6°C
Vapour pressure: 13 kPa (at 20°C)
Evaporation rate: 4.6
Log Kow: -0.77

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
GP	Ba	Fl	Full	5	0.1		Neat	9	19	19		44	*4.7*	*368*	Gummer & Maibach (1986)
Hum	Ab	St	27	2.5		*H2O*	*7.4*	10					5	*1.6*	Scheuplein & Blank (1973)
Hum	Ab	St	2500	2.5		*H2O*	*7.4*	3					530	*170*	Scheuplein & Blank (1973)
Hum	Ab	St	27	2.5			Neat	7					100	*8300*	Scheuplein & Blank (1973)
Hum	Ab	St	2500	2.5			Neat	2					230	*18000*	Scheuplein & Blank (1973)
Hum	Ab	St	Epi		10	H2O	10	8	6	6	0.37		16	*1300*	Southwell et al. (1984)
Hum	Ab	St	40		10	H2O	*3.2* (0.1M)	2	5-7	5-7			12-21	3.8-6.3	Southwell et al. (1983)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	0.3	0.3			18	*0.0059*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	5.8	5.8			16	*0.0051*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	9.8	9.8			17	*0.0054*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	13.8	13.8			19	*0.0061*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	17.8	17.8			18	*0.0059*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	26.3	26.3			18	*0.0059*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	0.3	0.3			29	*0.0093*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	4.3	4.3			26	*0.0083*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	7.8	7.8			23	*0.0074*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	11.3	11.3			28	*0.009*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	14.3	14.3			25	*0.008*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	1	26.3	26.3			24	*0.0077*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	0.3	0.3			17	*0.0054*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	5.8	5.8			16	*0.0051*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	9.8	9.8			15	*0.0048*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	13.8	13.8			15	*0.0048*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	17.8	17.8			14	*0.0045*	Behl et al. (1980)

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	26.3	26.3			15	*0.0048*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	8	0.5	0.5			21	*0.0067*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	8	5	5			18	*0.0059*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	8	10	10			19	*0.0061*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	8	15	15			19	*0.0061*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	8	20	20			19	*0.0061*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	8	28	28			20	*0.0064*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	0.5	0.5			61	*0.02*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	5	5			57	*0.018*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	10	10			52	*0.017*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	15	15			60	*0.019*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	20	20			63	*0.02*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	25	25			62	*0.02*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	4	30	30			58	*0.019*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	8	0.8	0.8			23	*0.0074*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	8	6.2	6.2			22	*0.007*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	8	10	10			22	*0.007*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	8	15	15			23	*0.0074*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	8	22	22			25	*0.008*	Behl et al. (1980)
Mou	Ab/Ba	St	Full	0.6	1.4	NaCl	*0.0032* (0.0001M)	8	27	27			26	*0.0083*	Behl et al. (1980)
Mou	Ab	St	Full	0.6	0.2	NaCl		3	2	2			10		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		2	2	2			12		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		4	2	2			26		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		5	2	2			34		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		5	2	2			13		Behl et al. (1984)
Mou	Ab	St	Full	0.6	0.2	NaCl		5	2	2			8		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		4	2	2			27		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		2	2	2			35		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		4	2	2			43		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		5	2	2			68		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		5	2	2			11		Behl et al. (1984)
Mou	Ba	St	Full	0.6	0.2	NaCl		5	2	2			10		Behl et al. (1984)
Mou	Ab	St	Full	0.6		NaCl	*0.0032* (0.0001M)	5	2	2			54		Behl & Barrett (1981)

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
Mou	Ba	St	Full	0.6		Ph/NaCl	*4.0* (0.5%)	6	2.5	2.5			26	*10*	Behl et al. (1983)
Mou	Ba	St	Full	0.6		Ph/NaCl	*7.9* (1.0%)	6	2.5	2.5			39	*31*	Behl et al. (1983)
Mou	Ba	St	Full	0.6		Ph/NaCl	*16* (2.0%)	6	2.5	2.5			69	*110*	Behl et al. (1983)
Mou	Ba	St	Full	0.6		Ph/NaCl	*32* (4.0%)	6	2.5	2.5			850	*2700*	Behl et al. (1983)
Mou	Ba	St	Full	0.6		Ph/NaCl	*47* (6.0%)	6	2.5	2.5			1700	*8000*	Behl et al. (1983)
Mou	Ab	St	Full	0.79		NaCl	≤10-4M		2	2			4.1		Durrheim et al. (1980)
Mou	Ab	St	Full	0.79		NaCl	≤10-4M		2	2			9.3		Durrheim et al. (1980)
Mou	Ab	St	Full	0.79		NaCl	≤10-4M		2	2			26		Durrheim et al. (1980)
In vivo															
Hum	Ha			480	Inf		Neat	65	0.03-0.27	7	0.5	1200 mg	*100*	8100	Batterman et al. (1997)
Hum	Arm			11	0.2		Neat	3	0.25	8		22-27 mg	*110*	8800	Dutkiewicz et al. (1980)
Hum	Arm			11	0.2		Neat	3	0.33	8		38-41 mg	*140*	11000	Dutkiewicz et al. (1980)
Hum	Arm			11	0.2		Neat	6	0.5	8		65-81 mg	*180*	14000	Dutkiewicz et al. (1980)
Hum	Arm			11	0.2		Neat	3	0.58	8		81-92 mg	*160*	13000	Dutkiewicz et al. (1980)
Hum	Arm			11	0.2		Neat	3	0.75	8		92-110 mg	*150*	12000	Dutkiewicz et al. (1980)
Hum	Arm			11	0.2		Neat	4	1	8		120-130 mg	*140*	11000	Dutkiewicz et al. (1980)

Asessment

The data on methanol are abundant.

The study by Scheuplein & Blank (1973) is disregarded since heat-separated (60°C) epidermis was used.

The study by Behl et al. (1983) is also disregarded as phenol was used as a vehicle.

The remaining studies show a consistent pattern with Kp values ranging between $1 \cdot 10^{-3}$ and $7 \cdot 10^{-3}$ cm/h for mouse and human skin and aqueous solutions of methanol.

The preferred studies are those of Batterman et al. (1997) and Dutkiewicz et al. (1980), since they used human skin in vivo exposed to neat methanol reporting higher Kp values of $1 \cdot 10^{-2}$ to $2 \cdot 10^{-2}$ cm/h, suggesting "very high" permeability.

Substance: Methyl acrylate
CAS: 96-33-3
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No data

Molecular weight: 86.1
Density: 0.956 g/cm³
Melting point: -76.5°C
Boiling point: 80.5°C
Vapour pressure: 9.1 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 0.80

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

No document from the Swedish Criteria Group was found on methyl acrylate.

The dermal LD50 values for rats and rabbits are 4-6 times higher than the corresponding oral LD50 values, this forms the basis for a skin notation by ACGIH (2001).

Substance: Methyl bromide
CAS: 74-83-9
Scientific basis: AoH 1988:32

Skin notation: Yes
Skin permeability: No data

Molecular weight: 94.9
Density: 1.732 g/cm³
Melting point: -93.7°C
Boiling point: 3.6°C
Vapour pressure: 200 kPa (at 23.3°C)
Evaporation rate: Not available
Log Kow: 1.19

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

Toxic amounts can be absorbed by the skin, both with direct contact and with exposure to high air concentrations (Jordi (1953)).

A case report (Longley et al. (1965)) is also sited in ACGIH (2001).

Substance: Methyl ethyl ketone (MEK); 2-butanone
CAS: 78-93-3
Scientific basis: AoH 1985:32

Skin notation: No
Skin permeability: Low

Molecular weight: 72.1
Density: 0.805 g/cm³
Melting point: -86.3°C
Boiling point: 79.6°C
Vapour pressure: 11 kPa (at 20°C)
Evaporation rate: 5.7
Log Kow: 0.29

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro														
Hum	Br	St	300-600	0.64		Neat	3	6	6			*66*	5800	Ursin et al. (1995)
Hum	Br	Fl	280	0.64	0.2	Neat	5	24	24	0.33	0.13	0.41	33	Wilkinson & Williams (2001)
Hum	Br	Fl	280	0.64	0.2 H2O	3	5	24	24	0.35	0.77	28	8.4	Wilkinson & Williams (2001)
In vivo														
No data available														

Asessment

Ursin et al. (1995) stretched the skin when mounting it in the diffusion cell, reaching a final thickness of about one-third of the original thickness. This procedure may give overestimates of the flux and Kp values.

The preferred experiment is the one using neat MEK (Wilkinson & Williams (2001), data only presented at a conference), with a reported Kp value $4 \cdot 10^{-5}$ cm/h, suggesting "low" permeability.

Substance: Methyl iodide
CAS: 74-88-4
Scientific basis: AoH 1981:21

Skin notation: Yes
Skin permeability: No data

Molecular weight: 141.9
Density: 2.279 g/cm³
Melting point: -66.5°C
Boiling point: 42.4°C
Vapour pressure: 50 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 1.51

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The Swedish consensus report (AoH 1981:21) states that methyl iodine can be absorbed via skin, with no additional data.

In ACGIH (2001), no direct studies or case reports on dermal absorption and resultant systemic toxicity are given.

The skin notation is based on two case reports of fatal and acute, permanent CNS damage following accidental exposure to methyl iodine with unknown air concentrations (Garland et al. (1945), Appel et al. (1975)).

According to theoretical calculations by Fiserova-Bergerova et al. (1990) the potential for dermal absorption and resulting toxicity is significant.

Substance: Methyl isobutyl ketone (MiBK)
CAS: 108-10-1
Scientific basis: Not available

Skin notation: No
Skin permeability: High

Molecular weight: 100.2
Density: 0.798 g/cm³
Melting point: -80°C
Boiling point: 117.4°C
Vapour pressure: 0.63 kPa (at 20°C)
Evaporation rate: 1.6
Log Kow: 1.31

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
GP	Ba			3.1		Neat	8	2.5	2.5			*83*	6600	Hjelm et al. (1991)

Asessment
The only available study is that of Hjelm et al. (1991) were guinea pig was exposed in vivo to neat MiBK.

The reported Kp value of $8 \cdot 10^{-3}$ cm/h, corresponds to "high" permeability.

Substance: Methyl metacrylate
CAS: 80-62-6
Scientific basis: AoH 1993:37

Skin notation: Yes
Skin permeability: Very high

Molecular weight: 100.1
Density: 0.943 g/cm³
Melting point: -48°C
Boiling point: 100°C
Vapour pressure: 3.6 kPa (at 20°C)
Evaporation rate: 3.1
Log Kow: 1.38

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Hum[1]	Ab	St	Epi	2.54	2.5	Neat	6	1	1	0.17	0.48	*110*	110	Betts et al. (2006)
Hum[1]	Ab	St	Epi	2.54	2.5	Neat	6	10	10	0.17	0.56	*3.7*	3.5	Betts et al. (2006)
Hum[2]	Ab	St	Epi	2.54	2.5	Neat	6	1	1	0.17	2.4	*290*	270	Betts et al. (2006)
Hum[2]	Ab	St	Epi	2.54	2.5	Neat	6	10	10	0.17	15	*160*	150	Betts et al. (2006)
In vivo														
No data available														

Asessment

[1]Non occluded [2]Occluded

The only study found on methyl metacrylate was that by Betts et al. (2006) where human skin was exposed to neat MMA.

The 1h occluded exposure is preferred and the calculated Kp value of $3 \cdot 10^{-2}$ cm/h corresponds to "very high" permeability.

Substance: Methyl morpholine, N-
CAS: 109-02-4
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No data

Molecular weight: 101.1
Density: 0.92 g/cm³
Melting point: -66°C
Boiling point: 115°C
Vapour pressure: 2.3 kPa (at 20°C)
Evaporation rate: 1.8
Log Kow: -0.33

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux ($\mu g/cm^2/h$)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

No Swedish consensus or ACGIH report was found on n-methyl morpholin.

The Swedish skin notation is likely based on analogy with the closely related substance morpholine.

Substance: Methyl tert-butyl ether (MTBE)
CAS: 1634-04-4
Scientific basis: AoH 1999:25

Skin notation: No
Skin permeability: Very high

Molecular weight: 88.1
Density: 0.741 g/cm³
Melting point: -109°C
Boiling point: 55.2°C
Vapour pressure: 33 kPa (at 25°C)
Evaporation rate: 8.1
Log Kow: 0.94

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
No data available															
In vivo															
Hum	Ha				Inf	H2O	0.051	14	1	24			280	*1400*	Prah et al. (2004)
Rat	Ba			*2-5*	*10 ml/kgBW*	NaCl	*4* (40 mg/kb BW)	120	6	45		16	*110-280*	*43-110*	Miller et al. (1997)
Rat	Ba			*2-5*	*10 ml/kgBW*	NaCl	*40* (400 mg/kb BW)	120	6	45		34	*230-580*	*910-2300*	Miller et al. (1997)

Asessment

The exposed skin area was not given by Miller et al. (1997). The values in the table were therefore calculated using an area of 2-5 cm² and assuming a bodyweight of 200 g. The Kp values thus obtained agree well with that reported for human skin.

The preferred study is that of Prah et al. (2004) were human skin in vivo was used, and the reported Kp value of $3 \cdot 10^{-2}$ cm/h corresponds to "very high" permeability.

It should be noted that the experiment used MTBE diluted in water. This procedure tends to give much higher Kp values than that obtained using neat substance.

Substance: Methyl-2-pentanol, 4-
CAS: 108-11-2
Scientific basis: AoH 1993:37

Skin notation: Yes
Skin permeability: No data

Molecular weight: 102.2
Density: 0.807 g/cm³
Melting point: -90°C
Boiling point: 132°C
Vapour pressure: 0.54 kPa (at 20°C)
Evaporation rate: 0.3
Log Kow: 1.68 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
No data available															

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

No data was found in the Swedish consensus report (AoH 1993:37).

The ACGIH (2001) report states that the skin notation is based on data from Smyth et al. (1951), suggesting similar dermal (3.6 g/kg bw in rabbits) and oral (2.6 g/kg bw in rats) LD50 values.

Substance: Methyl-2-pyrrolidone, n- (NMP)
CAS: 872-50-4
Scientific basis: AoH 1987:39

Skin notation: No
Skin permeability: Very high

Molecular weight: 99.1
Density: 1.033 g/cm³
Melting point: -24°C
Boiling point: 202°C
Vapour pressure: 66 Pa (at 25°C)
Evaporation rate: 0.06
Log Kow: -0.38

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum			200-400	0.64	Inf		Neat		4-6.5	4-6.5			98	10000	Dick et al. (2001)
Hum			200-400	0.64	Inf	H2O	30%		2-8	2-8			4.1	110	Dick et al. (2001)
Hum			200-400	0.64	0.006		Neat		3	3			*16*	1700	Dick et al. (2001)
Hum			200-400	0.64	0.006	H2O	30%		3	3			*19*	580	Dick et al. (2001)
Hum	Br	St	300-600	0.64			Neat	6	6	6			*160*	19200	Ursin et al. (1995)
Rat			200-400	0.64	0.006		Neat		3	3			*30*	3100	Dick et al. (2001)
Rat			200-400	0.64	0.006	H2O	30%		3	3			*30*	910	Dick et al. (2001)
Rat	Ba	St	Full	1.8	0.045/0.72		Neat	26	24	24			*51-54*	*5300-5600*	Payan et al. (2003)
Rat	Fk	St	Full	1.8	0.045/0.72		Neat	26	24	24			*58-65*	*6000-6700*	Payan et al. (2003)
Rat	Ba/Fk	St	Full	1.8	0.045		Neat	6	24	24		91	*20*	2100	Payan et al. (2003)
Rat	Ba/Fk	St	Full	1.8	0.09		Neat	6	24	24		89	*33*	3400	Payan et al. (2003)
Rat	Ba/Fk	St	Full	1.8	0.18		Neat	4	24	24			*51*	5300	Payan et al. (2003)
Rat	Ba/Fk	St	Full	1.8	0.36		Neat	7	24	24		68	*62*	6400	Payan et al. (2003)
Rat	Ba/Fk	St	Full	1.8	0.72		Neat	16	24	24		53	*73*	7500	Payan et al. (2003)
Rat	Ba/Fk	St	Full	1.8	0.045	H2O	50%	6	24	24			23		Payan et al. (2003)
Rat	Ba/Fk	St	Full	1.8	0.18	H2O	50%	4	24	24			50		Payan et al. (2003)
Rat	Ba/Fk	St	Full	1.8	0.36	H2O	50%	7	24	24			43-53		Payan et al. (2003)
Rat	Ba/Fk	St	Full	1.8	0.72	H2O	50%	7	24	24			51-53		Payan et al. (2003)
Rat	Ba/Fk	St	Full	1.8	1.4	H2O	50%	4	24	24			47		Payan et al. (2003)
Rat	Ba/Fk	St	Full	1.8	0.18	H2O	13%	3	24	24			51		Payan et al. (2003)
Rat	Ba/Fk	St	Full	1.8	0.72	H2O	13%	3	24	24			76		Payan et al. (2003)
Rat	Ba/Fk	St	Full	1.8	0.72	H2O	6.30%	3	24	24			57		Payan et al. (2003)
Rat	Ba/Fk	St	Full	1.8	0.72	H2O	3.20%	3	24	24			47		Payan et al. (2003)

Sp	Loc	Cell	L (µm)	A (cm²)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vivo														
Hum	Ha			*~500*	Inf H2O	5%	1	0.17	48		*5.0 mg*	*12*	*60*	Akrill et al. (2002)
Hum	Ha			*~500*	Inf H2O	5%	2	0.25	48		*6.4 mg*	*10*	*52*	Akrill et al. (2002)
Hum	Ha			*~500*	Inf H2O	10%	2	0.25	48		*14 mg*	*11*	*110*	Akrill et al. (2002)
Hum	Ha			*~500*	Inf H2O	15%	2	0.25	48		*32 mg*	*17*	*260*	Akrill et al. (2002)
Hum	Ha			*~500*	Inf H2O	20%	2	0.25	48		*32 mg*	*13*	*260*	Akrill et al. (2002)
Hum	Ha			*~500*	Inf H2O	25%	2	0.25	48		*52 mg*	*17*	*420*	Akrill et al. (2002)
Rat	Ba			10	0.2	Neat (20 µl/cm²)	4	0.25	0.25		6	*48*	5000	Payan et al. (2003)
Rat	Ba			10	0.2	Neat (20 µl/cm²)	4	0.5	0.5		18	*72*	7400	Payan et al. (2003)
Rat	Ba			10	0.2	Neat (20 µl/cm²)	4	0.75	0.75		29	*76*	7900	Payan et al. (2003)
Rat	Ba			10	0.2	Neat (20 µl/cm²)	4	1	1		36	*73*	7500	Payan et al. (2003)
Rat	Ba			10	0.2	Neat (20 µl/cm²)	4	2	2		60	*60*	6200	Payan et al. (2003)

Asessment

The in vivo and in vitro data show a consistent pattern for both neat and water-diluted NMP, with nearly all Kp values between $2{\cdot}10^{-3}$ and $1{\cdot}10^{-2}$ cm/h.

Most experiments by Dick et al. (2001) and Akrill et al. (2002) with human skin also show a consistent pattern with Kp values between $1{\cdot}10^{-3}$ and $3{\cdot}10^{-3}$ cm/h.

The preferred experiment is that of Dick et al. (2001) using human skin in vitro.

The Kp value of $1{\cdot}10^{-2}$ cm/h corresponds to "very high" permeability.

Substance: Methylamine
CAS: 74-89-5
Scientific basis: AoH 1983:36

Skin notation: Yes
Skin permeability: No data

Molecular weight: 31.1
Density: 0.902 g/cm³
Melting point: -38°C
Boiling point: 48°C
Vapour pressure: 31 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: -0.57

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The Swedish consensus report (AoH 1983:36) states that; "With massive exposure, amines can be absorbed via the skin. However we found no uptake via intact skin."

According to ACGIH (2001), there is insufficient data to assign a skin notation, and no accounts of systemic reactions have been reported in the literature.

Theoretical calculations by Fiserova-Bergerova et al. (1990) showed that the potential for dermal absorption and resulting toxicity is significant.

Substance: Methylene chloride; dichloromethane
CAS: 75-09-2
Scientific basis: AoH 1981:21

Skin notation: Yes
Skin permeability: High

Molecular weight: 84.9
Density: 1.326 g/cm³
Melting point: -96.7°C
Boiling point: 39.8°C
Vapour pressure: 47 kPa (at 20°C)
Evaporation rate: 28
Log Kow: 1.25

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro														
Hum	Br	St	300-600	0.64		Neat	3	6	6			*18*	2700	Ursin et al. (1995)
Rat	Ab	St	Full	3.7	1	Neat	25	0.5-3	0.5-3	0.5	5-55 mg	*44*	5800	Tsuruta (1977)
In vivo														
Mou	Ab			2.9	0.5	Neat		0.25				*50*	6600	Tsuruta (1975)

Asessment

Ursin et al. (1995) stretched the skin when mounting it in the diffusion cell, reaching a final thickness of about one-third of the original thickness. This procedure may give overestimates of the flux and Kp values.

The three studies report fairly similar Kp values, ranging between $2 \cdot 10^{-3}$ to $5 \cdot 10^{-3}$ cm/h.

The preferred study is that of Ursin et al. (1995), were human skin was used in vitro.

The reported Kp value of $2 \cdot 10^{-3}$ cm/h corresponds to "high" permeability.

Substance: Methylpentane, 2-
CAS: 107-83-5
Scientific basis: Not available

Skin notation: No
Skin permeability: Extremely low

Molecular weight: 86.2
Density: 0.653 g/cm³
Melting point: -154°C
Boiling point: 62°C
Vapour pressure: 21 kPa (at 20°C)
Evaporation rate: 8.3
Log Kow: 3.21 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro														
Rat	Ab	St	Full	2.6	1	Neat	15	4-22	4-22		1-6 µg	*0.0017*	0.11	Tsuruta (1982)
In vivo														
No data available														

Asessment

The only study found suggest a Kp value of $2 \cdot 10^{-7}$ cm/h in rat skin, corresponding to "extremely low" permeability.

It should be noted that Tsuruta (1982) used physiological saline as receptor medium, resulting in low solubility for lipophilic substances. This may lead to underestimated permeability.

Substance: Monochloroacetic acid
CAS: 79-11-8
Scientific basis: AoH 1992:6

Skin notation: Yes
Skin permeability: Very high

Molecular weight: 94.5
Density: 1.58 g/cm³
Melting point: 61 to 62°C
Boiling point: 188°C
Vapour pressure: 0.1 kPa (at 23°C)
Evaporation rate: 1
Log Kow: 0.22

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)		C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
Rat	Ba			0.79	*0.5 ml/kgBW*	Ac	250 (130 mg/kg BW)	4		32		76	*480*	*12000*	Saghir et al. (2003)

Asessment

The only available study is on monochloroacetic acid is on rat skin in vivo with acetone as vehicle.

The calculated Kp value suggests "very high" permeability.

It should be noted that acetone may damage the skin causing increased penetration.

Substance: Morpholine
CAS: 110-91-8
Scientific basis: AoH 1996:25

Skin notation: Yes
Skin permeability: No data

Molecular weight: 87.1
Density: 0.994 g/cm³
Melting point: -4.9°C
Boiling point: 128.9°C
Vapour pressure: 1.1 kPa (at 20°C)
Evaporation rate: 0.66
Log Kow: -0.86

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
No data available															

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

Morpholine is well absorbed via intact skin, whereas neutralized morpholine is not (AoH 1996:25, 1982:32).
The skin notation by ACGIH (2001) is based on the lower dermal (0.5 g/kg bw) compared to oral (1.05 g/kg bw) LD50 value in rats.
There is also a report of human dermal penetration (ACGIH (2001)).

According to theoretical calculations by Fiserova-Bergerova et al. (1990) the potential for dermal absorption and resulting toxicity is significant.

Substance: Naphtalenes, chlorinated
CAS: 1321-65-9
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No data

Molecular weight: 231.5
Density: 1.58 g/cm³
Melting point: 93°C
Boiling point: 304 to 354°C
Vapour pressure: <0.1 Pa (at 20°C)
Evaporation rate: Not available
Log Kow: 5.10 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
No data available															

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The WHO document on chloro-naphtalenes (WHO (2001)) states that: "Dermal and inhalation absorption of PCNs can be concluded from systemic effects in animals and humans. A quantification is not possible."

The Dutch committee on updating of OELs found no data regarding dermal uptake of trichloronaphtalene.

Substance: Naphthalene
CAS: 91-20-3
Scientific basis: AoH 1998:25

Skin notation: No
Skin permeability: Moderate

Molecular weight: 128.2
Density: 0.997 g/cm³
Melting point: 80.6°C
Boiling point: 218°C
Vapour pressure: 11 Pa (at 25°C)
Evaporation rate: <<1
Log Kow: 3.30

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum		St	500	1.1		JP-8			24	24			2.2	0.45	Kanikkannan et al. (2001)
Mon	Ab	St	Full	1.8	0.03	Ac	150 nmol/cm²	9?	72	72	2.17		*51*	5.7	Sartorelli et al. (1998)
MP	Ear	St	500	1.1		JP-8			24	24			1.8	0.38	Kanikkannan et al. (2001)
Pig	Ba	Fl	200-300	0.32		JP-8	1.20%	4	5	5	2.5-3		1.4	0.19	Baynes et al. (2000)
Pig	Ba	Fl	200-300	0.32		JP-8	1.20%	4	5	5	2.5-3		1.4	0.19	Baynes et al. (2001)
Pig		Fl	450-550	0.64	0.02	JP-8	*11* (340 µg/cm²)	5	5	5			2.1	2.2	Muhammad et al. (2004)
Rat	Ba	St	560	4.9	2	JP-8	0.26%	8	4	4	0.5		5.1	1	McDougal et al. (2000)
In vivo															
No data available															

Asessment

The reported Kp values are fairly consistent, even between different species.

The preferred studies are those using jet fuel, rather that acetone, as vehicle. Jet fuel may also affect skin permeation, although probably to a lesser extent than acetone.

Human skin was used in one experiment by Kanikkannan et al. (2001).

The reported Kp value of $2 \cdot 10^{-4}$ cm/h suggests a "moderate" permeability.

Substance: Nicotine
CAS: 54-11-5
Scientific basis: AoH 2004:16

Skin notation: Yes
Skin permeability: High

Molecular weight: 162.2
Density: 1.01 g/cm^3
Melting point: -7.9°C
Boiling point: 247°C
Vapour pressure: 5.7 Pa (at 20°C)
Evaporation rate: Not available
Log Kow: 1.17

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_p (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Hum	Ab	St	Full	1	1.5	H2O		3	72	72			33		Degim et al. (1998)
Hum	Ab/Br	St	410	1.8		PB	20 (0.05 M)	9	28	28			100	210	Qvist et al. (2000)
Hum	Ab/Br	St	410	1.8	0.36	H2O	10%	6	1.5	1.5	0.13		84	880	Zorin et al. (1999)
Hum	Ab/Br	St	410	1.8	0.36	H2O	20%	6	1.5	1.5	0.15		43	880	Zorin et al. (1999)
Hum	Ab/Br	St	410	1.8	0.36	H2O	50%	6	1.5	1.5	0.16		27	1300	Zorin et al. (1999)
Hum	Ab/Br	St	410	1.8	0.1		Neat	6	1.5	1.5	0.22		0.8	82	Zorin et al. (1999)
Hum	Ab		Epi	0.79	1	PB	1%	6	12	12	2.1		5.9	5.9	Pongjanyakul et al. (2002)
MP	Ba	St	770	1.8		PB	20 (0.05 M)	9	28	28			87	170	Qvist et al. (2000)
MP	Ba	St	770	1.8		PB	20 (0.05 M)	9	28	28			100	210	Qvist et al. (2000)
MP	Ba	St	770	1.8		PB	20 (0.05 M)	9	28	28			100	200	Qvist et al. (2000)
Pig	Ba	St	770	1.8		PB	20 (0.05 M)	9	28	28			110	220	Qvist et al. (2000)
Pig	Th		1.1	0.64	3.3	PB	50		30	30			*110*	560	Nair et al. (1997)
Pig	Th		1.1	0.64	3.3	PB	50		30	30			*36*	180	Nair et al. (1997)
Pig	Ear		0.9	0.64	3.3	PB	50		30	30			*120*	610	Nair et al. (1997)
Pig	Ba		1.8	0.64	3.3	PB	50		30	30			*34*	150	Nair et al. (1997)
Pig	Ab		1.2	0.64	3.3	PB	50		30	30			*170*	850	Nair et al. (1997)
Sn			SC	0.79	1	PB	1%	15	12	12	0.55		3.5	3.5	Pongjanyakul et al. (2002)
Sn			SC	0.79	1	PB	1%	15	12	12	0.74		4.2	4.2	Pongjanyakul et al. (2002)

Sp	Loc	Cell	L (µm)	A (cm²)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_p (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vivo															
Rat	Ba			2.8	0.1	Ac	0.084	3	72	72		44	*2.2*	*0.018*	Shah et al. (1987)
Rat	Ba			5.6	0.2	Ac	0.065	3	72	72		67	*3.3*	*0.022*	Shah et al. (1987)
Rat	Ba			2.8	0.1	Ac	3	3	72	72		12	*0.6*	*0.18*	Shah et al. (1987)
Rat	Ba			5.6	0.2	Ac	2.4	3	72	72		74	*3.7*	*0.88*	Shah et al. (1987)
Rat	Ba			2.8	0.1	Ac	12	3	72	72		76	*3.8*	*4.5*	Shah et al. (1987)
Rat	Ba			5.6	0.2	Ac	12	3	72	72		55	*2.7*	*3.3*	Shah et al. (1987)

Asessment

The only experiment found on neat nicotine was that of Zorin et al. (1999), which reported a Kp value of $8 \cdot 10^{-5}$ cm/h, corresponding to "low" permeability.

The other in vitro experiments using human skin have diluted solutions. The reported Kp values range between $6 \cdot 10^{-4}$ and $1 \cdot 10^{-2}$ cm/h, suggesting "moderate-very high" permeability.

The preferred experiments are those by Zorin et al. (1999) when human skin is exposed to diluted nicotine (10-50%), reporting Kp values between $3 \cdot 10^{-3}$ and $8 \cdot 10^{-3}$ cm/h, which corresponds to "high" permeability.

Substance: Nitrobenzene
CAS: 98-95-3
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No conclusion

Molecular weight: 123.1
Density: 1.196 g/cm³
Melting point: 5.7°C
Boiling point: 210.8°C
Vapour pressure: 20 Pa (at 20°C)
Evaporation rate: 0.029
Log Kow: 1.85

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Hum	Ab	St	350	1.1	Ac	*Neat* (4 µg/cm^2)	6	24	24		7.8	*0.00011*	*0.013*	Bronaugh et al. (1985a)
Hum	Ab	St	350	1.1	Ac	*Neat* (4 µg/cm^2)	3	24	24		41	*0.00056*	*0.067*	Bronaugh et al. (1985a)
Hum		Fl	350	0.64	Ac	*Neat* (4 µg/cm^2)	6	12	12		100 ng (2h)	*0.00067*	0.08	Bronaugh et al. (1985a)
Mon	Ab	St	350	1.1	Ac	*Neat* (4 µg/cm^2)	6	24	24		6.2	*0.000083*	*0.01*	Bronaugh et al. (1985a)
In vivo														
Hum	Arm			13	Ac	*Neat* (4 µg/cm^2)	6	24	120		1.5	*0.000021*	*0.0025*	Feldmann et al. (1970)
Hum	WB			*20000*	Vap	5-30 ng/ml	12	6	24		4-80 mg	*17000-20000*	*0.1-0.5*	Piotrowski (1967)
Mon	Ab			13	Ac	*Neat* (4 µg/cm^2)	4	24	120		4.2	*0.000058*	*0.007*	Bronaugh et al. (1985a)

Asessment

The Kp value obtained using nitrobenzene vapour differ by 8-9 orders of magnitude from those obtained using nitrobenzene dissolved in acetone.
Further, the Kp values in acetone are about 4 orders of magnitude lower than for di- and trinitrotoluene.

Thus, the Kp values for nitrobenzene seems unrealistic.

Substance: Nitroglycerin
CAS: 55-63-0
Scientific basis: AoH 1985:32

Skin notation: Yes
Skin permeability: Low

Molecular weight: 227.1
Density: 1.6 g/cm³
Melting point: 13°C
Boiling point: 218°C
Vapour pressure: 0.035 Pa (at 20°C)
Evaporation rate: Not available
Log Kow: 1.62

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
HM	Ba	Fl	Full	0.95		H2O	0.1	5	10	10	~1		200	*2*	Kikkoji et al. (1991)
HM		St	Full	0.64			*Neat?*	5	24	24			0.19	31	Minghetti et al. (1999)
HM	Ba	Fl	Full	0.95	1	H2O	0.1	6	6	6			*45-160*	*0.45-1.6*	Higo et al. (1992a)
HM	Ba	Fl	Full	0.95	1	H2O	0.1	8	10	10			*45-190*	*0.45-1.9*	Higo et al. (1992b)
Hum	Ab	St	Epi	3.1		H2O	2	31	48	48			*85*	17	Langguth et al. (1986a)
Hum	Th	St	200	0.64			*Neat?*	5	24	24			0.14	22	Minghetti et al. (1999)
Hum	Th	St	200	0.64			*Neat?*	5	24	24			0.21	33	Minghetti et al. (1999)
Hum	Th	St	Epi	0.64			*Neat?*	5	24	24			0.14	23	Minghetti et al. (1999)
Hum	Ab	Fl	Full	0.34		Patch		6	24	24				15	Roberts et al. (1990)
Hum	Br	St	300	0.79	1	Et (5%) + H2O	0.05%	3	10	10			*47*	*3.5*	Ponec et al. (1990)
Hum	Br	St	SC	0.79	1	Et (5%) + H2O	0.05%	6	10	10			*41*	*3.1*	Ponec et al. (1990)
Hum	Ba	St	SC	0.5		Et (40-80%) + H2O	10%	6					*2-10*	30-150	Berner et al. (1989)
Hum	Ab	St	Epi	3.1	11	H2O	2	25	48	48			*85*	17	Langguth et al. (1986b)
Hum								8	24	24				6-20	Noonan et al. (1989-1990)
Mou		St	Full				Neat		24	24	<1		*0.27*	41	Chien et al. (1984)
In vivo															
No data available															

Asessment

The experiments using ethanol as vehicle are disregarded as it may affect skin permeability.
There seems to be a vehicle effect for nitroglycerin. The reported Kp values for neat nitroglycerin range between $1 \cdot 10^{-5}$ and $3 \cdot 10^{-5}$ cm/h, corresponding to "low" permeability.

It should be noted that for diluted nitroglycerin the reported Kp values range between $5 \cdot 10^{-3}$ and $2 \cdot 10^{-2}$ cm/h, corresponding to "high/very high" permeability.

Substance: Nitrotoluene
CAS: 1321-12-6
Scientific basis: AoH 1992:6

Skin notation: Yes
Skin permeability: No data

Molecular weight: 137.1
Density: 1.16 to 1.25 g/cm³
Melting point: -10 to 54°C
Boiling point: 222 to 238°C
Vapour pressure: 16-20 Pa (at 20°C)
Evaporation rate: Not available
Log Kow: 2.30

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
No data available															

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The Swedish consensus report (AoH 1992:6) refers to Sax (1984), stating that nitrotoluene can be taken up by skin in toxic amounts.

According to ACGIH (2001) no quantitative data on nitrotoluene were found. The skin notation is based on analogy with aniline and nitrobenzene.

OECD SIDS, judge nitrotoluene to be rapidly absorbed via all routes.

Theoretical calculations by Fiserova-Bergerova et al. (1990) show that the potential for dermal absorption and resulting toxicity is significant.

Substance: Octanes
CAS: 111-65-9
Scientific basis: Not available

Skin notation: No
Skin permeability: Extremely low

Molecular weight: 114.2
Density: 0.703 g/cm³
Melting point: -56.8°C
Boiling point: 126°C
Vapour pressure: 1.9 kPa (at 25°C)
Evaporation rate: 1.4
Log Kow: 5.18

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Rat	Ab	St	Full	2.6	1	Neat	14	23-51	23-51			*0.000008*	0.0006	Tsuruta (1982)
In vivo														
No data available														

Asessment

The only available study suggests a Kp value of 10^{-9} cm/h, corresponding to "extremely low" permeability.

It should be noted that Tsuruta (1982) used physiological saline as receptor medium,
resulting in lower solubility for lipophilic substances. This may have led to a underestimated Kp value.

Substance: Pentachlorophenol
CAS: 87-86-5
Scientific basis: Not available

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 266.3
Density: 1.979 g/cm³
Melting point: 174°C
Boiling point: 310°C
Vapour pressure: 0.01 Pa (at 25°C)
Evaporation rate: Not available
Log Kow: 5.12

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Pig		Fl		5	0.1	Et	*0.4* (40 µg/cm²)	4	8	8		1.1	*7*	*0.28*	Riviere et al. (2001)
Pig		Fl		5	0.1	Et (40%) + H2O (60%)	*0.4* (40 µg/cm²)	4	8	8		6.9	*43*	*1.7*	Riviere et al. (2001)
Pig	Ab			5	0.07	Et	3	3	8	8		1.1	*0.4*	*0.12*	Qiao et al. (2002)
Hum		Fl	500	1		Soil	17ppm (0.7 µg/cm²)	6	15	15		0.01-0.07	*0.0028-0.019*	*0.0000047-0.000033*	Wester et al. (1993b)
Hum		Fl	500	1		Ac	17ppm (0.8 µg/cm²)	6	15	15		0.6-1.5	*0.19-0.47*	*0.00032-0.0008*	Wester et al. (1993b)
Hum	Ab	St	Full?	1	0.01	H2O + TCP	4.4	9	24	24		0.8	*0.033*	*0.015*	Horstman et al. (1989)
Hum	Ab	St	Full?	1	0.01	Diesel + TCP	150	9	24	24		0.14	*0.0058*	*0.088*	Horstman et al. (1989)
Pig	Ba	Fl	200-300	0.64		H2O	4 µg/cm²	4	8	8		0.13 µg	1.7	0.031	Baynes et al. (2002)
Pig	Ba	Fl	200-300	0.64		H2O	40 µg/cm²	4	8	8	2.2	2.2 µg	3.7	0.92	Baynes et al. (2002)
Pig	Ba	Fl	200-300	0.64		Et	4 µg/cm²	4	8	8		0.05 µg	0.5	0.014	Baynes et al. (2002)
Pig	Ba	Fl	200-300	0.64		Et	40 µg/cm²	4	8	8	1.8	0.39 µg	0.6	0.14	Baynes et al. (2002)
Pig	Ab		500	0.33		Et	3 (40 µg/cm²)	3	8	8		0.2	*0.04*	*0.012*	Qiao et al. (2002)
In vivo															
Mon	Ab			12		Soil	*17ppm* (0.7 µg/cm²)	4	24	336		24	*4.2*	*0.0071*	Wester et al. (1993b)
Mon	Ab			12		Ac	*17ppm* (0.8 µg/cm²)	4	24	336		29	*5.7*	*0.0097*	Wester et al. (1993b)
Pig	Ab			7.5	100 mg	Soil	40 µg/cm² (300µg)	3	408	408		29	*70*	*0.21*	Qiao et al. (1997)
Pig	Ab			7.5	0.1	Et	3	3	264	264		50	*0.25*	*0.076*	Qiao et al. (2002)

Asessment

The experiments with acetone, ethanol, diesel or tetrachlorophenol as vehicles are disregarded as the skin permeation could be affected.
The preferred study is that on pig skin in vitro with water as vehicle (Baynes et al. (2002)).

The reported Kp value of $4 \cdot 10^{-4}$ cm/h suggests a "moderate" permeability.

Substance: Pentane
CAS: 109-66-0
Scientific basis: Not available

Skin notation: No
Skin permeability: Extremely low

Molecular weight: 72.1
Density: 0.626 g/cm³
Melting point: -129.7°C
Boiling point: 36.1°C
Vapour pressure: 48 kPa (at 20°C)
Evaporation rate: 29
Log Kow: 3.39

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux ($\mu g/cm^2/h$)	Reference
In vitro														
Rat	Ab	St	Full	2.6	1	Neat	39	2.5-18.5	2.5-18.5	3.11	5-89 µg	*0.0006*	0.04	Tsuruta (1982)
In vivo														
No data available														

Asessment

The only available study suggests a Kp value of 10^{-8} cm/h, corresponding to "extremely low" permeability.

It should be noted that Tsuruta (1982) used physiological saline as receptor medium, resulting in lower solubility for lipophilic substances. This may have led to a underestimated Kp value.

Substance: Phenol
CAS: 108-95-2
Scientific basis: AoH 1985:32

Skin notation: Yes
Skin permeability: High

Molecular weight: 94.1
Density: 1.07 g/cm³
Melting point: 40.5°C
Boiling point: 181.7°C
Vapour pressure: 47 Pa (at 29°C)
Evaporation rate: <0.01
Log Kow: 1.46

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Pig			Full	7.5	0.08-0.1	Et	*0.3* (4 µg/cm²)	2	8	8		5.5	*2.4*	*0.072*	Brooks et al. (1996)
Pig			Full	7.5	0.08-0.1	Et	*0.3* (4 µg/cm²)	2	8	8		7.3	*3.3*	*1*	Brooks et al. (1996)
Pig			Full	7.5	0.08-0.1	Et	*0.3* (4 µg/cm²)	4	8	8		9.2	*6*	*0.18*	Brooks et al. (1996)
Pig			Full	7.5	0.08-0.1	Et	*3* (40 µg/cm²)	4	8	8		7.4	*3.7*	*1.1*	Brooks et al. (1996)
Pig			Full	7.5	0.08-0.1	Ac	*0.3* (4 µg/cm²)	2	8	8		2.9	*1.3*	*0.038*	Brooks et al. (1996)
Pig			Full	7.5	0.08-0.1	Ac	*3* (40 µg/cm²)	2	8	8		2	*0.47*	*0.14*	Brooks et al. (1996)
Pig			Full	7.5	0.08-0.1	Ac	*0.3* (4 µg/cm²)	4	8	8		15	*5*	*0.15*	Brooks et al. (1996)
Pig			Full	7.5	0.08-0.1	Ac	*3* (40 µg/cm²)	4	8	8		11	*5*	*1.5*	Brooks et al. (1996)
Hum	Ab	Fl	350	0.32		VIC	4 µg/cm²	7	24	72		26		*0.13*	Bronaugh et al. (1985b)
Hum	Ab	St	Full	1	0.01	Ac	*Neat* (4 µg/cm²)	7	48	48		11	*0.000085*	*0.0091*	Franz (1975)
Hum	Br	Fl	Full	0.32	0.005-0.01	Et	*0.27* (2.7 µg/cm²)	6	72	72		19-20	*0.81-0.89*	*0.022-0.024*	Hotchkiss et al. (1992)
Hum	Br	Fl	Full	0.32	0.005-0.01	Et	*0.27* (2.7 µg/cm²)	3	72	72		47	*2*	*0.055*	Hotchkiss et al. (1992)
Hum	Ab	St	Epi	2.5	Inf	H2O	4	2	8	8	0.25		82	*33*	Roberts et al. (1977)
Hum	Ab	St	SC		1	H2O	10	33	10	10	0.55		*1.5*	1.5	Southwell et al. (1984)
Hum	Ab	St	SC		1	H2O	10	1	10	10	0.35		*2.6*	2.6	Southwell et al. (1984)
Hum	Ab	St	SC		1	H2O	10	2	10	10	0.72		*1.7*	1.7	Southwell et al. (1984)
Hum	Ab	St	SC		1	H2O	10	1	10	10	0.25		*1.6*	1.6	Southwell et al. (1984)
Hum	Ab	St	SC		1	H2O	10	2	10	10	0.4		*1.4*	1.4	Southwell et al. (1984)
Hum	Ab	St	SC		1	H2O	10	2	10	10	0.43		*0.98*	0.98	Southwell et al. (1984)
Hum	Ab	St	SC		1	H2O	10	9	10	10	0.93		*2.2*	2.2	Southwell et al. (1984)
Hum	Ab	St	SC		1	H2O	10	3	10	10	0.57		*1.1*	1.1	Southwell et al. (1984)
Hum	Ab	St	SC		1	H2O	10	4	10	10	0.85		*0.89*	0.89	Southwell et al. (1984)
Hum	Ab	St	SC		1	H2O	10	4	10	10	0.6		*1.8*	1.8	Southwell et al. (1984)
Hum	Ab	St	SC		1	H2O	10	3	10	10	0.37		*0.59*	0.59	Southwell et al. (1984)
Hum	Ab	St	Epi		Inf	H2O	1%	33	7-10	7-10	0.55		*1.5*	1.5	Southwell et al. (1984)

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
Mou	Ba	St	Full	0.6		NaCl	0.50%	6	2.5	2.5			230	*120*	Behl et al. (1983)
Mou	Ba	St	Full	0.6		NaCl	1.00%	6	2.5	2.5			310	*330*	Behl et al. (1983)
Mou	Ba	St	Full	0.6		NaCl	2.00%	6	2.5	2.5			470	*1000*	Behl et al. (1983)
Mou	Ba	St	Full	0.6		NaCl	4.00%	6	2.5	2.5			170	*710*	Behl et al. (1983)
Mou	Ba	St	Full	0.6		NaCl	6.00%	6	2.5	2.5			2000	*13000*	Behl et al. (1983)
Mou		St	Full	0.79			33				0.17		1700	*5600*	Huq et al. (1986)
Mou		St	Full	0.79			Trace				0.17		190		Huq et al. (1986)
Pig	Ab	Fl	200	0.64	0.01	Et	*Neat* (5.5 µg/cm^2)	6	16	16	*~0.5*	56	*0.0018*	*0.19*	Skowronski et al. (1994)
Rat	Ba	Fl	350	0.32		VIC	4 µg/cm^2	6	24	72		16			Bronaugh et al. (1985b)
Rat	Ba	Fl	Full	0.32	0.005-0.01	Et	*0.13* (1.3 µg/cm^2)	6	72	72		36	*0.5-0.51*	*0.0065-0.0066*	Hotchkiss et al. (1992)
Rat	Ba	Fl	Full	0.32	0.005-0.01	Et	*0.14* (1.4 µg/cm^2)	6	72	72		25-27	*0.34-0.37*	*0.0048-0.0052*	Hotchkiss et al. (1992)
Rat	Ba	St	350	0.64	0.005-0.01	Et	*0.4* (4 µg/cm^2)	7	72	72		98	*1.4*	*0.054*	Hughes et al. (1993)
Rat	Ba	Fl	350	0.32	0.005-0.01	Et	*0.4* (4 µg/cm^2)	10	72	72		95	*1.3*	*0.053*	Hughes et al. (1993)
Sn	Ba	St	Full	1.8		PBS	1-3	4	6	6			52	*5.2-16*	Itoh et al. (1990)
In vivo															
Hum	Arm			2.5	0.02	H2O+Et	5%	5	24	168		34	*23*	*120*	Bucks et al. (1989-1990)
Hum	Arm			2.5	0.02	H2O+Et	5%	5	24	168		24	*16*	*86*	Bucks et al. (1989-1990)
Hum	Arm			13		Ac	*Neat* (4 µg/cm^2)	3	24	120		4.4	*0.00009*	*0.01*	Feldmann & Maibach (1970)
Hum	WB					Vap	5-25 mg/m^3	12	6	24		5-65 mg	*20*	*0.1-0.5*	Piotrowski (1971)
Rat	Ba			2.54	0.02	Et	*Neat* (2.4 µg/cm^2)	4	72	72		67	*0.0015*	*0.16*	Hughes et al. (1995)

Asessment

The experiments using ethanol, acetone and Vaseline are disregarded as these substances may affect skin permeability.
The experiments using neat phenol cannot be used, since the substance appears as solid crystals at skin temperature (m.p. ~40°C).

The preferred study is that of Bucks et al. (1989-1990) using 5% phenol in water.

The Kp value of $2 \cdot 10^{-3}$ cm/h is consistent with the full thickness skin in vitro mouse study by (Behl et al. (1983)) and suggest "high" permeability.

Substance: Propanol, n-
CAS: 71-23-8
Scientific basis: Not available

Skin notation: No
Skin permeability: High

Molecular weight: 60.1
Density: 0.803 g/cm³
Melting point: -126°C
Boiling point: 97.2°C
Vapour pressure: 0.53 kPa (at 20°C)
Evaporation rate: 1.3
Log Kow: 0.25

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Ab	St	27	2.5		*H2O*	*7.4*	21					12	*7.2*	Scheuplein & Blank (1973)
Hum	Ab	St	2500	2.5		*H2O*	*7.4*	9					310	*190*	Scheuplein & Blank (1973)
Hum	Ab	St	27	2.5			Neat	20					1.6	*130*	Scheuplein & Blank (1973)
Hum	Ab	St	2500	2.5			Neat	7					18	*1400*	Scheuplein & Blank (1973)
Mou	Ab	St	Full	0.79		NaCl	≤10-4M		2	2			54		Durrheim et al. (1980)
In vivo															
No data available															

Asessment

The only found study is that of Scheuplein & Blank (1973), were human skin was exposed to neat and diluted n-propanol. The preferred experiment is the one using full thickness skin.

The Kp value of $2 \cdot 10^{-3}$ cm/h, suggests "high" permeability.

Substance: Propionic acid
CAS: 79-09-4
Scientific basis: AoH 1988:32

Skin notation: No
Skin permeability: Very high

Molecular weight: 74.1
Density: 0.993 g/cm³
Melting point: -21.5°C
Boiling point: 140.7°C
Vapour pressure: 390 Pa (at 20°C)
Evaporation rate: 0.24
Log Kow: 0.33

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
MP	Ba	Fl	Full	1	Hep	74	4	2	2	0.07		4000	*30000*	Liron et al. (1984a)
MP	Ba	Fl	Full	1	Hep	74	4	4	4	0.13		1800	*8000*	Liron et al. (1984a)
MP	Ba	Fl	Full	1	Hep	74	4	8	8	0.17		980	*7300*	Liron et al. (1984a)
MP	Ba	Fl	Full	1	Hep	74	3	7	7	0.33		750	*5600*	Liron et al. (1984a)
MP	Ba	Fl	Full	1	Hep	74	3	7	7	0.67		490	*3600*	Liron et al. (1984a)
MP	Ba	Fl	Full	1		Neat		5	5	*~0.5*		160	3.3	Liron et al. (1984b)
In vivo														
No data available														

Asessment

The experiments using n-heptane as vehicle are disregarded, as the skin permeation could be affected.
The only remaining study is that of Liron et al. (1984b).

The reported Kp value of $2 \cdot 10^{-2}$ cm/h suggests a "very high" permeability.

Substance: Propylene glycol dinitrate
CAS: 6423-43-4
Scientific basis: AoH 1983:36

Skin notation: Yes
Skin permeability: High

Molecular weight: 166.1
Density: 1.2 g/cm³
Melting point: -8°C
Boiling point: 121°C
Vapour pressure: 9 Pa (at 20°C)
Evaporation rate: Not available
Log Kow: 1.59 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
Rat	Ba			4		Corn oil	10% (50 mg/kg bw)		0.5	0.5		10	*53*	*630*	Clark & Litchfield (1969)

Asessment

Only one study was found on propylene glycol dinitrate. In Clark & Litchfield (1969), rats were exposed to a 10% solution of propylene glycol dinitrate in corn oil.

The calculated Kp value of $5 \cdot 10^{-3}$ cm/h suggests a "high" permeability.

Substance: Propylene glycol monomethyl ether (PGME); 1-methoxy-2-propanol
CAS: 107-98-2
Scientific basis: AoH 1987:39

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 90.1
Density: 0.924 g/cm³
Melting point: -97°C
Boiling point: 119.6°C
Vapour pressure: 1.2 kPa (at 20°C)
Evaporation rate: 0.71
Log Kow: -0.49 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Hum	Ab	St	Epi	1.8	5		Neat		8	8			13	1200	Dugard et al. (1984)
Hum	Ab	St	Epi	1.8	1-5		Neat	11	8	8	<1		13	1200	Dugard et al. (1984)
Hum	Ab	St	Full	3.1			Neat	8	4	4	0.5		5.1	470	Larese Filon et al. (1999)
Hum	Br	Fl	500	0.64	0.2	H2O	3	5	24	24		2.3	*14*	4.3	Wilkinson & Williams (2002)
Hum	Br	Fl	500	0.64	0.01		Neat	4	24	24			*0.65*	60	Wilkinson & Williams (2002)
Hum	Br	Fl	500	0.64	0.2		Neat	5	24	24			*6.5*	600	Wilkinson & Williams (2002)

In vivo

No data available

Asessment

The experiment with a applied amount of 0.011 ml (Wilkinson & Williams (2002)) is disregarded since depletion of PGME occurred.

The remaining studies show consistent results with Kp values ranging between $5 \cdot 10^{-4}$ to $1 \cdot 10^{-3}$ cm/h.

The preferred studies of Wilkinson & Williams (2002) and Larese Filon et al. (1999) with human skin exposed to neat PGME in vitro, reports Kp values corresponding to "moderate" permeability.

Substance: Propylene glycol monomethyl ether acetate (PGMEA)
CAS: 108-65-6
Scientific basis: AoH 1987:39

Skin notation: Yes
Skin permeability: No data

Molecular weight: 132.2
Density: 0.969 g/cm³
Melting point: -10°C
Boiling point: 145.8°C
Vapour pressure: 0.5 kPa (at 20°C)
Evaporation rate: 0.3
Log Kow: 0.56

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
No data available															

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

There is no mention regarding skin uptake of PGMEA in the Swedish consensus document (AoH 1987:39).

No documentation has been produced by ACGIH.

Substance: Resorcinol
CAS: 108-46-3
Scientific basis: AoH 1992:47

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 110.1
Density: 1.27 g/cm³
Melting point: 110°C
Boiling point: 281°C
Vapour pressure: 7.1 kPa (at 190°C)
Evaporation rate: Not available
Log Kow: 0.80

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Hum	Ab	St	Epi	2.5	Inf H2O	100	2	8	8	1.33		2.4	*24*	Roberts et al. (1977)
In vivo														
No data available														

Asessment

Only one study was found on resorcinol. Roberts et al. (1977) exposed human abdominal skin to an aqueous solution of resorcinol.

The reported Kp value of $2 \cdot 10^{-4}$ cm/h, suggests a "moderate" permeability.

It should be noted that in the experiments by Roberts et al. (1977), epidermal sheets were separated by exposing skin to ammonia vapour for 30 min. Ammonia is well known to cause severe skin damage Amshel et al. (2000). The alkaline nature of ammonia quickly saponifies the epidermal fats, thus destroying the protective structure of the epidermis. Therefore, the method used by Roberts et al. (1977) is likely to result in severe overestimates of the flux and Kp value of undamaged skin.

Substance: Sodium cyanide
CAS: 143-33-9
Scientific basis: AoH 2001:19

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 49.0
Density: 1.6 g/cm³
Melting point: 563.7°C
Boiling point: 1496°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: -1.69 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Hum	Ab	St	40	1.8	H2O	0.0012 (0.00025%)	6			1.5		3.7	0.00045	Dugard (1987)
Hum	Ab	St	40	1.8	H2O	5.3 (1%)	5			1.5		4.3	2.3	Dugard (1987)
Hum	Ab	St	40	1.8	H2O	53 (10%)	11			1.5		11	58	Dugard (1987)
Hum	Ab	St	40	1.8	H2O	210 (40%)	9			1.5		2.9	62	Dugard (1987)
In vivo														
No data available														

Asessment

Several in vitro experiments with human skin exposed to aqueous solutions of sodium cyanide are reported (Dugard (1987)).

The Kp value of $3 \cdot 10^{-4}$ cm/h, corresponds to "moderate" permeability.

It should be noted that the permeability of hydrogen cyanide is two orders of magnitude higher.

Substance: Styrene
CAS: 100-42-5
Scientific basis: AoH 1991:8

Skin notation: Yes
Skin permeability: Low

Molecular weight: 104.2
Density: 0.905 g/cm³
Melting point: -30.6°C
Boiling point: 145.2°C
Vapour pressure: 0.86 kPa (at 20°C)
Evaporation rate: 0.54
Log Kow: 2.95

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Rat	Ab	St	Full	2.5	1		Neat	28	2.5-6	2.5-6	1.67	43-330 µg	*0.33*	30	Tsuruta (1982)
In vivo															
Hum	Ha			500	Inf		Neat	9	0.17-0.5	2		15 mg	*0.67*	60	Berode et al. (1985)
Hum	Arm/Ha						Neat	10	<0.1				*99-170*	9000-15000	Dutkiewicz et al. (1968b)
Hum	Arm/Ha					H2O	0.067-0.27	10	1				*6000-6700*	40-180	Dutkiewicz et al. (1968b)
Hum	WB			19000		Vap	*0.0026* (600ppm)	2	3.5	24		60 mg	*3500*	0.9	Riihimaki et al. (1978)
Rat	WB					Vap	*0.013* (3000ppm)	5	4	4			18000	21	McDougal et al. (1990)

Asessment

Tsuruta (1982) used physiological saline as receptor medium, resulting in lower solubility for lipophilic substances, thus probably underestimating the permeability.
The vapour studies are also disregarded.
The studies by Dutkiewicz et al. (1968b) are only described very briefly and appear to give unrealistic Kp values.

The preferred study is the human skin in vivo study with neat styrene of (Berode et al. (1985)).

The Kp value of $7 \cdot 10^{-5}$ cm/h suggests "low" permeability.

Substance: Tetrachloroethylene
CAS: 127-18-4
Scientific basis: AoH 1981:21

Skin notation: No
Skin permeability: Moderate

Molecular weight: 165.8
Density: 1.623 g/cm³
Melting point: -22.3°C
Boiling point: 121.1°C
Vapour pressure: 1.9 kPa (at 20°C)
Evaporation rate: 2.8
Log Kow: 3.40

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Ab	Fl	200-400	0.2	Inf	H2O	0.13-0.31 µg/ml	35	6	6			160-580	*0.0021-0.018*	Nakai et al. (1999)
Hum	Ab	Fl	200-400	0.2	Inf	H2O	0.12-0.29 µg/ml	29	6	6			110-610	*0.0013-0.018*	Nakai et al. (1999)
Rat	Ab	St	Full	3.7	1		Neat	49	2-6	2-6	2.46	5-74 µg	*0.03*	5	Tsuruta (1977)
In vivo															
HGP	WB			~300	Inf	H2O	*0.044-0.10 µg/ml* (27-64 ppb)	5	1.2	2-4w			3700	*0.016-0.037*	Bogen et al. (1992)
HM	WB					Vap	*0.0069* (1000ppm)	6	2-6	2-6			*10000*	6.9	Tsuruta (1989)
HM	WB					Vap	*0.021* (3000ppm)	6	2-6	2-6			*9500*	20	Tsuruta (1989)
HM	WB					Vap	*0.0014* (200ppm)	6	2-6	2-6			*7900*	1.1	Tsuruta (1989)
Hum	Arm/Ha			1000		Vap	*1.1* (6.7 mmol/l)	5	0.33	6			540	*60*	Kezic et al. (2000)
Hum	WB			19000		Vap	*0.0042* (600ppm)	3	3.5	24		48 mg	*1700*	0.72	Riihimaki & Pfaffli (1978)
Hum	Ha				4 kg	Soil	30 g/kg soil	3	2	2	0.38	20 mg	9		Poet et al. (2002)
Mou	Ab			2.9	0.5		Neat	3	0.25			180 µg	*1.5*	240	Tsuruta (1975)
Rat	WB					Vap	*0.086* (12500ppm)	4	4	4			6700	54	McDougal et al. (1990)
Rat	Ba			8	0.5 g	Soil	4.6 g/kg soil	3	5	5		57	900		Poet et al. (2002)
Rat	Ba			8	0.5 g	Soil	15 g/kg soil	3	5	5		55	880		Poet et al. (2002)
Rat	Ba			8	0.5 g	Soil	51 g/kg soil	3	5	5		51	860		Poet et al. (2002)
Rat	Ba			5	5 g	Soil	16 g/kg soil	3	5	5		11	1100		Poet et al. (2002)
Rat	Ba			5	5 g	Soil	53 g/kg soil	3	5	5		8.7	1100		Poet et al. (2002)
Rat	Ba			5	5 g	Soil	16 g/kg soil	5	5	5		49	1100		Poet et al. (2002)
Rat	Ba			5	5 g	Soil	50 g/kg soil	5	5	5		53	1100		Poet et al. (2002)

Asessment

The in vitro study of Tsuruta (1977) used physiological saline as the receptor medium, this may lead to a severe underestimate of flux and Kp for highly lipophilic substances.
Bogen et al. (1992) and Nakai et al. (1999) used dilute aqueous solution of tetrachloroethylene.
The studies with human skin used aqueous solutions, vapour or soil, leading to very high Kp values.

The preferred study is that of Tsuruta (1975) using neat tetrachloroethylene and mouse skin.

The Kp value of $2 \cdot 10^{-4}$ cm/h suggests "moderate" permeability

Substance: Tetrachlorophenol
CAS: 25167-83-3
Scientific basis: AoH 1986:35

Skin notation: Yes
Skin permeability: Low

Molecular weight: 231.9
Density: 1.8 g/cm³
Melting point: ~70°C
Boiling point: 150 to 200°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: 4.45

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Ab	St	Full?	1	0.01	H2O + PCP	16	9	24	24		3	*0.13*	*0.2*	Horstman et al. (1989)
Hum	Ab	St	Full?	1	0.01	Diesel + PCP	9.4	9	24	24		0.5	*0.021*	*0.02*	Horstman et al. (1989)
In vivo															
No data available															

Asessment

The only study that was found on tetrachlorophenol was Horstman et al. (1989),
were diesel and/or pentachlorophenol as used as vehicle.

The preferred experiment gives a Kp value of 10^{-5} cm/h, suggesting "low" permeability.

Substance: Tetraethyl lead
CAS: 78-00-2
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No data

Molecular weight: 323.4
Density: 1.659 g/cm³
Melting point: -136.8°C
Boiling point: ~200°C
Vapour pressure: 27 Pa (at 20°C)
Evaporation rate: Not available
Log Kow: 4.15

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

No consensus document by the Swedish Criteria Group.

According to ACGIH (2001), tetraethyl lead can be absorbed percutaneously in amounts that cause systemic poisoning.

Substance: Tetrahydrofuran
CAS: 109-99-9
Scientific basis: AoH 1991:8

Skin notation: No
Skin permeability: Low

Molecular weight: 72.1
Density: 0.886 g/cm³
Melting point: -108.4°C
Boiling point: 66°C
Vapour pressure: 18 kPa (at 20°C)
Evaporation rate: 8
Log Kow: 0.46

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Hum	Br	Fl	280	0.64	0.2	Neat	5	24	24	0.33	0.2	0.46	*41*	Wilkinson & Williams (2001)
Hum	Br	Fl	280	0.64	0.2 H2O	3	5	24	24	0.35	1.7	61	*18*	Wilkinson & Williams (2001)
In vivo														
No data available														

Asessment

The only available data are those of Wilkinson & Williams (2001), given as a conference presentation. Human breast skin was exposed in vitro to neat and aqueous solutions of tetrahydrofuran.

The Kp value of neat tetrahydrofuran corresponds to "low" permeability.

It should be noted that the Kp measured from aqueous solutions is over two orders of magnitude higher, suggesting a strong vehicle effect.

Substance: Tetramethyl lead
CAS: 75-74-1
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No data

Molecular weight: 267.3
Density: 2.0 g/cm³
Melting point: -27.5°C
Boiling point: 110°C
Vapour pressure: 2.9 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 2.97

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The ACGIH-TLV committee (ACGIH (2001)) base their skin notation on a study with dogs demonstrating toxicity after dermal exposure.

Substance: Thioglycolic acid
CAS: 68-11-1
Scientific basis: AoH 1994:30

Skin notation: Yes
Skin permeability: No data

Molecular weight: 92.1
Density: 1.325 g/cm³
Melting point: -16.5°C
Boiling point: 120°C
Vapour pressure: 1.3 kPa (at 18°C)
Evaporation rate: Not available
Log Kow: 0.09

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The skin notation assigned by ACGIH-TLV is based on systemic toxicity in animals following dermal application.

According to theoretical calculations by Fiserova-Bergerova et al. (1990) the potential for dermal absorption and resulting toxicity is significant.

Substance: Titanium dioxide
CAS: 13463-67-7
Scientific basis: Not available

Skin notation: No
Skin permeability: Extremely low

Molecular weight: 79.9
Density: 4.26 g/cm³
Melting point: 1855°C
Boiling point: 2900°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: 2.23 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Pig	Ab	St	500	1		H2O + oil	10% (240 µg/cm^2)	3	24	24		< 0.1	*0.001*	*0.01*	Gamer et al. (2006)
In vivo															
No data available															

Asessment

Micro fine TiO_2 (10 wt%) in oil/water emulsion was applied to the skin. Mean particle size was 80 nm with 90% of the particles < 160 nm. Dermatomed pig skin was used in the static cells, and bovine serum albumin (5%) was added to the saline as receptor medium. High recovery rates (98-100%) were achieved, still no TiO_2 was detected in the receptor medium.
The reported detection limit was 0.3 µg Ti, corresponding to 0.1% absorbed dose.

Thus, the calculated Kp value is lower than $1 \cdot 10^{-7}$ cm/h, suggesting "extremely low" permeability (or lower).

Substance: Toluene
CAS: 108-88-3
Scientific basis: AoH 2002:18

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 92.1
Density: 0.867 g/cm³
Melting point: -93°C
Boiling point: 110.6°C
Vapour pressure: 3.7 kPa (at 20°C)
Evaporation rate: 2.2
Log Kow: 2.73

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum		St	500	1.1		JP-8			24	24			2	0.095	Kanikkannan et al. (2001)
Hum	Br	St	300-600	0.64			Neat	6	6	6			*1*	130	Ursin et al. (1995)
Hum	Br	Fl	280	0.64	0.2		Neat	5	24	24	0.01	0.22	0.14	12	Wilkinson & Williams (2001)
Hum	Br	Fl	280	0.64	0.2	H2O	20	5	24	24	0	79	830	1.7	Wilkinson & Williams (2001)
Hum		Fl	250	1	0.2-0.3		Neat	3	24	24		1.9	*1.6-2.4*	*140-210*	Boman & Maibach (2000)
Hum		Fl	250	1	0.2-0.3	n-Bu	*430* (50%)	4	20	20		*9.5*	*9.2-14*	*400-620*	Boman & Maibach (2000)
Hum		Fl	250	1	0.2-0.3	Chf + Me	*430* (50%)	5	20	20		*2*	*2-3*	*85-130*	Boman & Maibach (2000)
MP		Fl	900	3.1			Neat	6	14.5	14.5			*3.7*	320	Jacobs & Phanprasit (1993)
MP		Fl	900	3.1		Vap	0.12 (Saturated)	6	14.5	14.5			*14000*	160	Jacobs & Phanprasit (1993)
MP	Ear	St	500	1.1		JP-8			24	24			2.5	0.12	Kanikkannan et al. (2001)
Rat	Ba	St	560	4.9	2	JP-8	0.06%	8	4	4	0.5		11	0.54	McDougal et al. (2000)
Rat	Ab	St	Full	2.6	1		Neat	34	1-5	1-5	1.55	10-430 µg	*0.54*	47	Tsuruta (1982)
In vivo															
HM	Ba			0.8	0.0045		Neat	12	0.033	4		90 µg	*34*	2900	Susten et al. (1990)
HM	WB					Vap	3000ppm	6	2-6	2-6			*12000*	14	Tsuruta (1989)
HM	WB					Vap	1000ppm	6	2-6	2-6			*12000*	4.6	Tsuruta (1989)
HM	WB					Vap	200ppm	6	2-6	2-6			*12000*	0.9	Tsuruta (1989)
Hum	Arm			17	0.2		Neat	10	1	1		71 mg	*210*	18000	Dutkiewicz et al. (1968a)
Hum	Ha					H2O	0.19-0.61	16	1	1		130 mg	*6200-20000*	380	Dutkiewicz et al. (1968a)
Hum	Ha						Neat	10	1				*220*	19000	Dutkiewicz & Tyras (1968b)
Hum	Arm/Ha			1000		Vap	*0.065* (0.7 mmol/L)	5	0.33	6			1400	*9*	Kezic et al. (2000)
Hum	WB			19000		Vap	*0.0023* (600ppm)	2	3.5	24		26 mg	*1700*	0.4	Riihimaki & Pfaffli (1978)
Hum	Fi				Inf	H2O	1%	12	15s	0.3			*0.89*	0.77	Naitoh et al. (2002)
Hum	Fi				Inf	H2O	1%	12	15s	0.3			*23*	20	Naitoh et al. (2002)
Hum	WB				Inf	H2O	0.0005	6	0.3-0.5	0.75-1			30-200	*0.0015-0.01*	Thrall et al. (2002a)

Sp	Loc	Cell	L (µm)	A (cm^2)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_p (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
Mou	Ba			0.8	0.004		Neat	12	4	4		2.1	*0.27*	*23*	Susten et al. (1990)
Mou	Ab			3.1	0.5		Neat	15	0.25-1				*0.01*	69	Tsuruta (1996)
Mou	Ab			3.1	0.5	Me	50%	15	0.25-1				*0.1*	260	Tsuruta (1996)
Mou	Ab			3.1	0.5	DMSO	50%	15	0.25-1				*0.12*	310	Tsuruta (1996)
Mou	Ab			3.1	0.5	DMF		15	0.25-1				*0.08*	220	Tsuruta (1996)
Rat	WB							6	4	4			7200	21	McDougal et al. (1990)
Rat	Ba			4.9	2	H2O	0.2	3	5	5		45	760	*15*	Thrall et al. (2002b)
Rat	Ba			4.9	2	H2O	0.5	3	5	5		42	700	*35*	Thrall et al. (2002b)

Asessment

The human skin in vitro studies with neat toluene show relatively consistent results with Kp values ranging from $1 \cdot 10^{-5}$ to $2 \cdot 10^{-4}$ cm/h.
The in vivo studies by Dutkiewicz et al. (1968a) and Dutkiewicz & Tyras (1968b) show two orders of magnitude higher Kp values.

The preferred experiment is the one by Boman & Maibach (2000) where human skin was exposed to neat toluene.

The Kp value of $2 \cdot 10^{-4}$ cm/h corresponds to "moderate" permeability.

It should be noted that the Kp value of toluene vapour and in aqueous solution is around 4 orders of magnitude higher than in the preferred study.

Substance: Tributyltin
CAS: 56573-85-4
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No data

Molecular weight: 290.0
Density: Not available
Melting point: 53°C
Boiling point: 193°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: 4.76

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment
The Swedish skin notation applies to organotin compounds in general (including tributyltin).

Dermal application of various organotin compounds causes systemic toxicity in laboratory animals.
For example, daily application of 10 mg/kg tributyltin oxide to the shaved skin of male guinea pigs caused reduced body weight and renal tubular degeneration (ACGIH (2001)).

The dermal LD50 value in rats was reported to 605 mg/kg (ACGIH (2001)).

Substance: Trichlorethane, 1,1,1-
CAS: 71-55-6
Scientific basis: AoH 1982:9

Skin notation: No
Skin permeability: Moderate

Molecular weight: 133.4
Density: 1.338 g/cm³
Melting point: -32.6°C
Boiling point: 74.1°C
Vapour pressure: 13 kPa (at 20°C)
Evaporation rate: 13
Log Kow: 2.49

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
Hum	Arm/Ha		1000			Vap	1.6 mmol/L	5	0.33	6			210	*4.4*	Kezic et al. (2000)
Hum	WB		19000			Vap	600ppm	2	3.5	24		2 mg	*90*	*0.03*	Riihimaki & Pfaffli (1978)
Mou	Ab		2.9		0.5		Neat	6	0.25			270 µg	*2.7*	370	Tsuruta (1975)

Asessment

The study by Tsuruta (1975) suggest "moderate" permeability of neat 1,1,1-trichloroethane. However, absorption was measured by homogenizing the whole animal. This method may severely underestimate skin permeability.

The remaining experiments exposed the skin to 1,1,1-trichloroethane vapour, which probably gives overestimated Kp values.

Substance: Trichloroethylene, 1,1,2-
CAS: 79-01-6
Scientific basis: AoH 1981:21

Skin notation: No
Skin permeability: Moderate

Molecular weight: 131.3
Density: 1.462 g/cm³
Melting point: -86°C
Boiling point: 86.7°C
Vapour pressure: 7.2 kPa (at 20°C)
Evaporation rate: 6.4
Log Kow: 2.42

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_p (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Ab	Fl	200-400	0.2	Inf	H2O	32-82 µg/l	23	6	6			1200	*0.0038-0.0098*	Nakai et al. (1999)
Hum	Ab	Fl	200-400	0.2	Inf	H2O	34-79 µg/l	17	6	6			1100	*0.0037-0.0087*	Nakai et al. (1999)
Hum	Br	Fl	Full	0.79		H2O	*7.3 ng/ml* (5ppb)	105	0-1	0-1			2800	*0.002*	Bogen et al. (1998)
Rat	Fk	St	Full	0.79	0.005		Neat	5	10	10		1.3	*0.082*	*12*	McCormick et al. (1991)
Rat	Fk	St	Full	0.79	0.005		Neat	5	6	10		1.1	*0.12*	*17*	McCormick et al. (1991)
Rat	Fk	St	Full	0.79	0.005		Neat	5	4	10		1	*0.16*	*23*	McCormick et al. (1991)
Rat	Fk	St	Full	0.79	0.005		Neat	5	3	10		0.9	*0.19*	*28*	McCormick et al. (1991)
Rat	Fk	St	Full	0.79	0.005		Neat	5	2	10		0.7	*0.22*	*32*	McCormick et al. (1991)
Rat	Fk	St	Full	0.79	0.005		Neat	5	1	10		0.5	*0.32*	*46*	McCormick et al. (1991)
Rat	Fk	St	Full	0.79	0.005		Neat	5	0.5	10		0.3	*0.38*	*55*	McCormick et al. (1991)
Rat	Fk	St	Full	0.79	0.005		Neat	5	10	10		2.5	*0.16*	*23*	McCormick et al. (1991)
Rat	Fk	St	Full	0.79	0.005		Neat	5	6	10		2.2	*0.23*	*34*	McCormick et al. (1991)
Rat	Fk	St	Full	0.79	0.005		Neat	5	4	10		1.9	*0.3*	*44*	McCormick et al. (1991)
Rat	Fk	St	Full	0.79	0.005		Neat	5	3	10		1.7	*0.36*	*52*	McCormick et al. (1991)
Rat	Fk	St	Full	0.79	0.005		Neat	5	2	10		1.4	*0.45*	*65*	McCormick et al. (1991)
Rat	Fk	St	Full	0.79	0.005		Neat	5	1	10		1	*0.63*	*92*	McCormick et al. (1991)
Rat	Fk	St	Full	0.79	0.005		Neat	5	0.5	10		0.5	*0.63*	*92*	McCormick et al. (1991)
Rat	Ab	St	Full	2.6	0.5		Neat	27	1-5	1-5	1.1		*0.46*	68	Tsuruta (1978)
In vivo															
HGP	WB			~300	Inf	H2O	*28-160 ng/ml* (19-110 ppb)	5	1.2	2-4w			2300	*0.0064-0.037*	Bogen et al. (1992)
HGP	WB			~300	Inf	H2O	*0.15* (100000 ppb)	5	1.2	2-4w			2100	*32*	Bogen et al. (1992)
Hum	Arm/Ha			1000		Vap	1.3 mmol/L	5	0.33	6			490	*8.4*	Kezic et al. (2000)
Hum	Arm			50	80	H2O	1	3	2	2	0.3	3 mg	190	*19*	Poet et al. (2000)
Hum	Ha			510	4000	H2O	1	3	2	2	0.3	40 mg	150	*15*	Poet et al. (2000)
Mou	Ab			2.9	0.5		Neat	21	0.083-0.25			91-340 µg	*3.2*	470	Tsuruta (1978)

Asessment

A wide range of Kp values are reported, depending on vehicle and species.
The preferred study is that of Tsuruta (1978), using mouse skin in vivo with neat trichloroethylene.
The calculated Kp value of $3 \cdot 10^{-4}$ cm/h, suggests "moderate" permeability.

Substance: Trichlorophenol
CAS: 25167-82-2
Scientific basis: Not available

Skin notation: Yes
Skin permeability: No data

Molecular weight: 197.4
Density: ~1.5 g/cm³
Melting point: ~70°C
Boiling point: 150 to 200°C
Vapour pressure: Not available
Evaporation rate: Not available
Log Kow: 3.69

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

The Swedish consensus report (AoH 1989:35) states that reported cases of poisoning indicate that the chlorophenols (tri-, tetra-, penta-) can be absorbed effectively through the skin, and that this is probably the major exposure route at sawmills.

Substance: Trichlorophenol, 2,4,6-
CAS: 88-06-2
Scientific basis: Not available

Skin notation: Yes
Skin permeability: Extremely high

Molecular weight: 197.4
Density: 1.49 g/cm³
Melting point: 69.5°C
Boiling point: 244.5°C
Vapour pressure: 133 Pa (at 76.5°C)
Evaporation rate: Not available
Log Kow: 3.69

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
Mou			Full	0.79		0.5				0.5		1700	*85*	Huq et al. (1986)
In vivo														
No data available														

Asessment

Only one study on 2,4,6-trichlorophenol was found.

In Huq et al. (1986) the reported Kp value suggests "extremely high" permeation.

It should be noted that for phenol, Huq et al. (1986) reported a Kp value which was two orders of magnitude higher than the preferred value.

Substance: Triethanolamine
CAS: 102-71-6
Scientific basis: AoH 1983:36

Skin notation: No
Skin permeability: High

Molecular weight: 149.2
Density: 1.126 g/cm³
Melting point: 21.6°C
Boiling point: 335.4°C
Vapour pressure: <1 Pa (at 20°C)
Evaporation rate: <0.005
Log Kow: -1.00

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
No data available															
In vivo															
Mou	Ba			2	0.04-0.06		Neat (2000 mg/kg bw)	24	48	48		*78*	*3.7*	*410*	Stott et al. (2000)
Mou	Ba			2	0.2	Ac	*Neat* (1000 mg/kg bw)	3	24	24		*92*	*4.2*	*480*	Stott et al. (2000)
Mou	Ba			2	0.2	H2O	*250* (2000 mg/kg bw)	3	24	24		*79*	*33*	*820*	Stott et al. (2000)
Mou				1		Ac	20	9	24	24			*380*	780	Knaak et al. (1997)
Mou				1.8		H2O	23	21	48	48			*170*	410	Knaak et al. (1997)
Mou				1.8			Neat	3	24	24			*360*	840	Knaak et al. (1997)
Mou				2			Neat	24	48	48			*200*	410	Knaak et al. (1997)
Mou				1.8			Neat	24	48	48			*180*	420	Knaak et al. (1997)
Rat	Ba			2	*0.4*		Neat (1000 mg/kg bw)	3	48	48		*76*	*18*	*2000*	Stott et al. (2000)
Rat				1.8			Neat	3	48	48			*190*	2500	Knaak et al. (1997)

Asessment

The data presented by Knaak et al. (1997) are based on an industry report by Waechter 1988 (unavailable). The original data appear to be the same as those presented in Stott et al. (2000), however, the calculation of concentration and, hence, Kp values of Knaak et al. (1997) are seemingly erroneous.

The first two experiments by Stott et al. (2000) are disregarded due to small volume and acetone as vehicle, respectively. The next two experiments are in good agreement considering known species differences between mouse and rat skin. The rat skin data is preferred as being closer to human skin. The Kp value of $2 \cdot 10^{-3}$ cm/h corresponds to "high" permeability.

However, the experiments of Stott et al. (2000) have high %absorption, which suggest that the fluxes and Kp values may have been underestimated.

Substance: Trinitrotoluene, 2,4,6-
CAS: 118-96-7
Scientific basis: AoH 1992:6

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 227.1
Density: 1.654 g/cm³
Melting point: 80.9°C
Boiling point: 240°C
Vapour pressure: 0.004 kPa (at 80°C)
Evaporation rate: Not available
Log Kow: 1.60

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro														
Pig	Ba	St	500-900	0.8	9.9 mg/cm² Soil (Ti)	*1.5* (9.5 µg/cm²)	6	8	8		1.3	*0.095*	*0.015*	Reifenrath et al. (2002)
Pig	Ba	St	500-900	0.8	10 mg/cm² Soil (Yo)	*1.8* (11 µg/cm²)	6	8	8		5	*0.39*	*0.068*	Reifenrath et al. (2002)
Pig	Ba	St	500-900	0.8	0.005 Ac	*2.2* (11 µg/cm²)	6	8	8		19	*1.2*	*0.25*	Reifenrath et al. (2002)
In vivo														
No data available														

Asessment

The only found study was that of Reifenrath et al. (2002), where pig skin was exposed to 2,4,6-trinitrotoluene with soil or acetone as vehicles. It should be noted that the use of acetone as vehicle may have severely affected the skin properties.

The preferred experiment is that with acetone, suggesting a "moderate" permeability.

Substance: Turpentine
CAS: 8006-64-2
Scientific basis: AoH 1987:39

Skin notation: Yes
Skin permeability: No data

Molecular weight: Not available
Density: 0.9 g/cm³
Melting point: -50 to -60°C
Boiling point: 150 to 180°C
Vapour pressure: 0.66 kPa (at 25°C)
Evaporation rate: Not available
Log Kow: Not available

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
No data available															
In vivo															
No data available															

Asessment

No quantitative experimental data on dermal uptake were found in the literature.

According to the Swedish Criteria Group, α-pinene (a major component of turpentine) is readily absorbed via the skin (AoH 1987:39).

ACGIH (2001), mention that skin may be a significant route of exposure to turpentine but that there is no evidence of organ damage as a result of this absorption.

Substance: Vinyl chloride
CAS: 75-01-4
Scientific basis: AoH 1986:17

Skin notation: Yes
Skin permeability: High

Molecular weight: 62.5
Density: 0.911 g/cm³
Melting point: -153.7°C
Boiling point: -13°C
Vapour pressure: 340 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 1.62 (estimated)

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
No data available															
In vivo															
Mon	WB				Inf	Vap	*0.018* (7000 ppm. 3400 mg)	1	2	2		0.02	*62*	*0.11*	Hefner et al. (1975)
Mon	WB			3500	Inf	Vap	*0.0021* (800 ppm. 390 mg)	1	2.5	2.5		0.03	*66*	*0.014*	Hefner et al. (1975)

Asessment

The only found study was that of Hefner et al. (1975), were a monkey was exposed to vinyl chloride vapour.

The reported Kp values suggest a "high" permeability.

It should be noted that vinyl chloride is a gas at skin temperature (b.p. -14°C).

Substance: Vinyl toluene; methyl styrene
CAS: 25013-15-4
Scientific basis: AoH 1992:6

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 118.2
Density: 0.89 g/cm³
Melting point: -77°C
Boiling point: 170°C
Vapour pressure: 0.15 kPa (at 20°C)
Evaporation rate: Not available
Log Kow: 3.48

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro														
Hum	Ab	St	46-63	0.64	0.064	Neat	6	48	48		25	2.3	200	Fasano et al. (2006)
Hum	Ab	St	46-63	0.64	0.006	Neat	6	0.2	0.2			*0.74*	66	Fasano et al. (2006)
Hum	Ab	St	46-63	0.64	0.006	Neat	6	1	1			*1.1*	100	Fasano et al. (2006)
In vivo														
No data available														

Asessment

The only found study was that of Fasano et al. (2006), were human skin was exposed to neat viny ltoluene.

The reported Kp values suggest a "moderate" permeability.

Substance: Xylene, m-
CAS: 108-38-3
Scientific basis: AoH 2005:16

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 106.2
Density: 0.868 g/cm³
Melting point: -47.9°C
Boiling point: 139.1°C
Vapour pressure: 0.86 kPa (at 20°C)
Evaporation rate: 0.51
Log Kow: 3.20

Reported data

Sp	Loc	Cell	L (µm)	A (cm²)	V	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm²/h)	Reference
In vitro															
Hum	Br	Fl	280	0.64	0.2		Neat	5	24	24	0.22	0.59	0.3	26	Wilkinson & Williams (2001)
Hum	Br	Fl	280	0.64	0.2	H2O	20	5	24	24	0.18	58	590	0.15	Wilkinson & Williams (2001)
In vivo															
Hum	WB			19000	Inf	Vap	*0.0080* (600ppm)	3	3.5	24		44 mg	*2400*	1.9	Riihimaki & Pfaffli (1978)
Hum	WB			19000	Inf	Vap	*0.0040* (300ppm)	2	3.5	24		21 mg	*2400*	0.94	Riihimaki & Pfaffli (1978)
Hum	Arm/Ha			1000	Inf	Vap	*0.073* (5500ppm)	5	0.33	6			1200	*8.8*	Kezic et al. (2000)
Hum	Has			810-1000	Inf		Neat	9	0.25	6		35 mg	*1.4*	120	Engstrom et al. (1977)
Hum	Has			810-1000			Neat	10	0.25	22			*4.4*	380	Riihimaki (1979)
Hum	Arm			1178	Inf	Vap	0.001	6	0.33	6			*910*	0.091	Kezic et al. (2004a)
Hum	Arm			1178	Inf	Vap	0.001	6	0.75	6			*720*	0.072	Kezic et al. (2004a)
Hum	Arm			1178	Inf	Vap	0.001	6	2	6			*660*	0.066	Kezic et al. (2004a)
Hum	Arm			1178	Inf	Vap	0.001	6	3	6			*610*	0.061	Kezic et al. (2004a)
Rat	WB					Vap		6	4	4			7200	15	McDougal et al. (1990)

Asessment

There is a wide range of Kp values (o-, m-, p-xylene and xylene mixture), depending on vehicle and species.
The preferred experiments are those with neat xylene by Riihimaki (1979) and Engstrom et al. (1977).

The Kp value of $4 \cdot 10^{-4}$ cm/h suggests "moderate" permeability.

It should be noted that the permeabilities of aqueous and vaporous xylene are several orders of magnitude higher.

Substance: Xylene, o-
CAS: 95-47-6
Scientific basis: AoH 2005:16

Skin notation: Yes
Skin permeability: Low

Molecular weight: 106.2
Density: 0.897 g/cm³
Melting point: -25.2°C
Boiling point: 144°C
Vapour pressure: 0.66 kPa (at 20°C)
Evaporation rate: 0.51
Log Kow: 3.12

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Hum	Br	Fl	280	0.64	0.2		Neat	5	24	24	0.3	0.35	0.22	20	Wilkinson & Williams (2001)
Hum	Br	Fl	280	0.64	0.2	H2O	31	5	24	24	0.3	25	350	1.1	Wilkinson & Williams (2001)
Rat	Ab	St	Full	2.6	1		Neat	37	3-6	3-6	2.2	10-59 µg	0.07	6.2	Tsuruta (1982)
In vivo															
No data available															

Asessment

The preferred study is the one using neat o-xylene and human skin.

The Kp value of $2 \cdot 10^{-5}$ cm/h, suggests "low" permeability.

It should be noted that the preferred study of m-xylene suggest a Kp value that is one order of magnitude higher.

Substance: Xylene, p-
CAS: 106-42-3
Scientific basis: AoH 2005:16

Skin notation: Yes
Skin permeability: No data

Molecular weight: 106.2
Density: 0.861 g/cm³
Melting point: 13.3°C
Boiling point: 138.3°C
Vapour pressure: 0.79 kPa (at 20°C)
Evaporation rate: 0.51
Log Kow: 3.15

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V Vehicle (ml)	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro														
No data available														
In vivo														
No data available														

Asessment

Based on similarities in chemical structure and physical properties, p-xylene may be assumed to have similar permeability to that of o- and m-xylene.

Substance: Xylenes
CAS: 1330-20-7
Scientific basis: AoH 2005:16

Skin notation: Yes
Skin permeability: Moderate

Molecular weight: 106.2
Density: 0.862 g/cm³
Melting point: -50°C
Boiling point: 140°C
Vapour pressure: 0.66 kPa (at 20°C)
Evaporation rate: 0.7
Log Kow: 3.12

Reported data

Sp	Loc	Cell	L (µm)	A (cm^2)	V (ml)	Vehicle	C (mg/ml)	n	T_{Exp} (h)	T_{Obs} (h)	T_{Lag} (h)	Abs (%)	K_P (10^{-4} cm/h)	Flux (µg/cm^2/h)	Reference
In vitro															
Rat	Ba	St	560	4.9	2	JP-8	*5.1* (0.59%)	8	4	4	0.5		1.7	0.8	McDougal et al. (2000)
In vivo															
Hum	Arm						Neat	10	1				*52-110*	4500-9600	Dutkiewicz & Tyras (1968b)

Asessment

No information on the content of the xylene mixture was available in the two studies.

The results of the study by Dutkiewicz & Tyras (1968b) seems very unrealistic. Xylene absorption was calculated as difference between applied and recovered amount. As xylene is nonpolar and volatile this method may result in significant losses and, hence, overestimates of flux and Kp.

The preferred study is that of McDougal et al. (2000), were the reported Kp value of $2 \cdot 10^{-4}$ cm/h suggests "moderate" permeability.

It should be noted that the permeabilities for neat o- and m-xylene were determined as "low" and "moderate", respectively. See also data on each xylene isomer (o-, m-, p-)

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