IH SkinPerm
READ ME
Help Manual

Rosalie S. Tibaldi
Wil ten Berg
Daniel Drolet

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I. General Information

1. IH SkinPerm is a model for estimating dermal absorption. It is formatted in Microsoft® Excel and is compatible with Excel 2003, 2007 and 2010. Basic knowledge of Excel is all that is needed to operate IH SkinPerm.

2. Apple® computers running Excel may not handle the Visual Basic coding in IH SkinPerm**.** The project team has not verified this. Therefore be aware IH SkinPerm may not run correctly or at all on Apple® computers.

3. Embedded in IH SkinPerm are Visual Basic macros (Microsoft® Excel) and Quantitative Structural Activity Relationships (QSARs) which drive the application. More detailed explanations of the QSARs in IH SkinPerm are published elsewhere[1]

4. Spreadsheet protection is provided to prevent inadvertent changes to the equations and other functions. As stated in the “disclaimer”, users unlocking and modifying the spreadsheet accept all responsibility for their modifications.

5. IH SkinPerm is a work product of the AIHA Exposure Assessment Strategies Committee (EASC) and the Dermal Project Team (DPT) in collaboration with Wil ten Berg, author of the original SkinPerm model.[2]

6. Although various parameters and data outputs have been explained or defined in IH SkinPerm through comments tagged on individual fields, users are encouraged to read Chapter 13 of the *Mathematical Models for Estimating Occupational Exposure to Chemicals*, 2nd edition, AIHA Press, 2009, C. Keil Editor.[3] This is a useful reference for understanding the science and terminology associated with skin permeation.

II. Method / Process

<u>IH Skin Perm models the following</u>:

In essence IH Skin Perm tracks the fate of a chemical after and as it is applied to the skin surface. The rate of mass build-up (or loss) on the skin comes from the deposition rate onto the skin minus the absorption rate into the Stratum Corneum and the amount evaporating from the skin to the air. The equation for this primary relationship in IH Skin Perm is:

$$\frac{dLiqFilm_{neat}}{dt} = DespositionRate - AbsorptionRate(\text{into SC}) - EvaporationRate(LF)$$

$dLiqFilm_{neat}/dt$ = the rate of substance mass build up (or loss) on the skin ($mg/((cm^2)(hr))$)

DepositionRate = the rate at which the substance is being put onto the skin surface (mg/((cm2)(hr))

AbsorptionRate(into SC) = the rate at which the substance is being absorbed into the Stratum Corneum (SC) (mg/((cm2)(hr)). This absorption rate is controlled by the mass, that can be maximally absorbed in the stratum corneum. If the stratum corneum is completely filled up, the absorption rate(SC) decreases to zero.

Absorption rate (viable epidermis) = the rate at which the substance is transferred from the Stratum corneum through the viable epidermis to the blood capillaries and becomes biologically available to the body. This is the absortion rate, which is plotted against the time of observation in the graphical picture of the absorption rate. The maximum absorption rate is equal to that observed from a saturated aqueous solution.

EvaporationRate(LF) = the rate at which the substance is being evaporated from the liquid film to the air (mg/((cm2)(hr))

EvaporationRate(SC) = the rate at which the substance is being evaporated from the Stratum Corneum to the air, when the liquid film has fully evaporated (mg/((cm2)(hr)).

IH Skin Perm provides two primary dermal exposure modes to the modeler. The first is "instantaneous deposition" in which the substance is assumed to be on the skin as the result of a single exposure event. The second is "deposition over time" in which the substance is assumed to be applied at a constant rate over time. In the first case (instantaneous deposition) the above DepositionRate is zero and IH Skin Perm then works to keep track of this single dose over time as it is absorbed into the SC or evaporates from the surface of the skin. In the second case (deposition over time) the rate of the substance going to the skin is assumed constant and the thickness of the film on the skin will either increase or decrease with time depending on the relative rates of deposition and removal.

The user inputs the amount going onto the skin as a single dose or as a constant rate and IH Skin Perm calculates the amount of chemical absorbed into the SC (AbsorptionRate(into SC) X time) over time until all the material disappears from the surface via absorption and evaporation or the exposure is considered to be over. Ultimately, the program estimates the amount of chemical absorbed into the systemic circulation of the body using clearly defined assumptions. IH Skin Perm does all of this using relatively few physical chemical inputs for the substance. Some of the details of these calculations are available below and all are presented in references available from Dr. ten Berge (ref: specific documents http://home.planet.nl/~wtberge/qsarperm.html).

A. Data Input

1. Substance Selection

Users can choose from the robust library of 137 substances already built into IH SkinPerm or enter and select from their own library of substances. A click on the drop down box will display substances for selection in the IH SkinPerm library. Substances in the library vary in chemical and physical properties. For example the Log $(Kow)_{at\ pH\ 5.5}$ of the library ranges from -7 (Sodium Iodide) to 7.6 (Diethylhexylphtalate). Likewise there is a mix of compounds of low to high molecular weight and varying vapor pressure.

To assess your own substance and scenarios within IH SkinPerm click on the + sign to enter required physical and chemical property information for your substance. These include molecular weight, water solubility, vapor pressure, density, and the Log octanol-water partition coefficient (Log K_{ow}). These properties have been shown to greatly influence whether the substance will partition into the skin and/or vaporize. This data can be retrieved from various resources.[6] Use of the substance Partition coefficient measured at pH 5.5 is preferred as this is the pH of the skin.[11] Where available, it is important to use data based on the same pH as skin because ionic compounds (e.g., nicotine) will permeate less readily at lower pH and therefore Log Kow values taken at higher pH 7.0 can overestimate substance permeation rates.[1]

2. Scenario Parameters

IH SkinPerm can be used to assess risks of dermal absorption from an instantaneous contact or from a substance deposited over time.

a. Instantaneous Exposure

Instantaneous deposition dose - In work environments, instantaneous type exposures can occur through surface contact with wet containers, from a splash, or other accidental exposure.

Users must estimate the mass deposited onto the skin. An example of how to estimate the mass is provided as follows:

Example: Deposited mass determination (Liquids)

The supplier safety data sheet indicates the concentration of furfural is 90-100% by weight. A person comes into contact with a wet surface. An estimated 2 ml** covers the palms of both hands or surface area of 420 cm^2.

$$\text{Mass}\,(\mu g) = \text{Product. conc.}\left(\frac{\mu g}{mL}\right) * \text{Volume}(\mu L) * \frac{mL}{1000\,\mu L}$$

$$\text{Furfural}\left(\frac{mg}{mL}\right) = \text{Mass frac.}\left(\frac{g}{100g}\right) * Density\left(\frac{g}{cm^3}\right) * \frac{10^3 mg}{g} * \frac{cm^3}{mL}$$

$$\text{Furfural}\left(\frac{mg}{mL}\right) = \left(\frac{95g}{100g}\right) * 1.16\left(\frac{g}{mL}\right) * \frac{10^3 mg}{g}$$

$$= 1102\,\frac{mg}{mL}$$

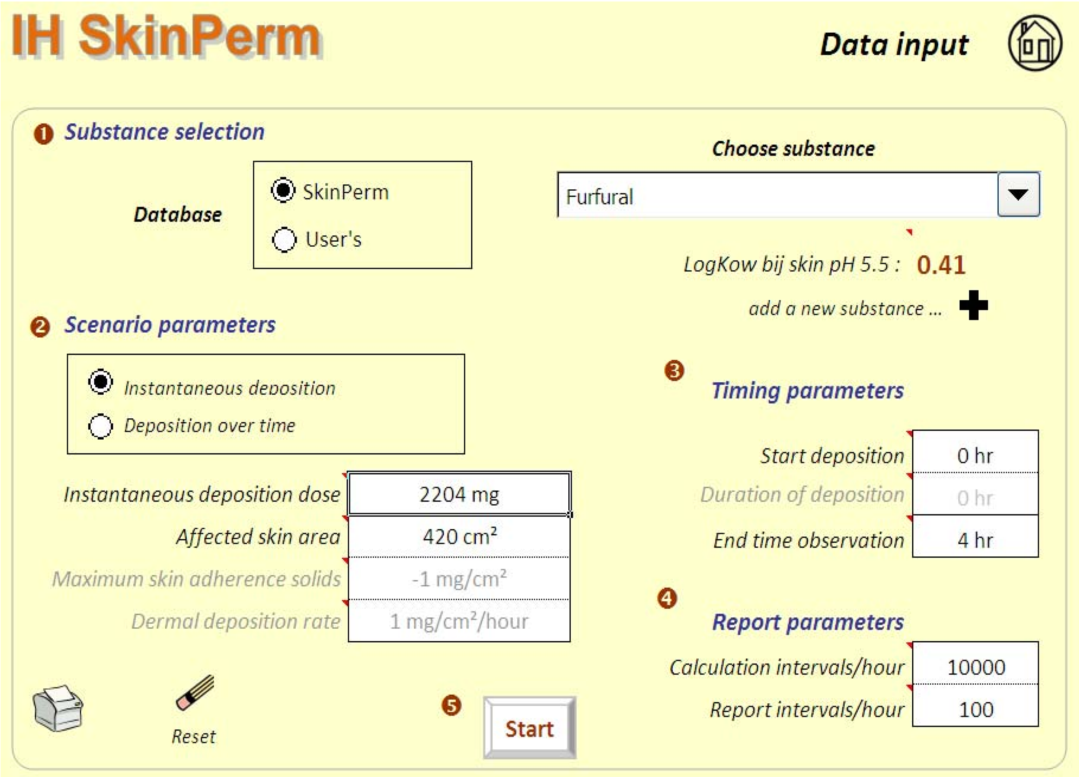
$$\text{Furfural}\,(mg) = 1102\,\frac{mg}{mL} * 2\,mL$$

$$= 2204\,mg$$

The 2 ml translates to about 2204 mg of furfural in contact with the skin. Assumed furfural concentration is 95 wt%.

** Approximately 2 mL of a liquid having a viscosity similar to water will practically wet the palms of two hands. It is reasonably expected more liquid will be excess and wash/fall off.

Figure 1: Example Data Inputs for an Instantaneous dermal exposure scenario



Affected Skin Area - The surface area exposed must be estimated by the user. Body surface areas from the US EPA Exposure Factors Handbook 2009 are typically used to estimate skin surface areas[7] Mean values reported for males over 21 years old are normally used to represent the average occupational worker. The minimum is set to 1 cm², the finger tip in contact with liquid or solid. The commonly assumed maximum full body surface of an adult is 20000 cm².

Maximum Skin Adherence - The skin adherence field is greyed out and a default of -1 is indicated if the substance is a liquid at 25°C. Smart logic is built into IH SkinPerm; the program recognizes whether a substance is a solid or liquid at standard temperature (25°C) based on its' physicochemical properties. For substances that are solids at 25°C a maximum adherence value up to 2 mg/cm² is allowed based on studies of soil-on-skin adherence.[13] If the deposition rate results in an increase above the input figure (0.2-2 mg/cm²), it is assumed that the surplus disappears just by removal from the skin.

b. Deposition Over time

Dermal exposure by deposition of a substance may be continuous during activities like painting or repeated transfer of a substance from one container to another. A second type of scenario estimates dose from a deposition over time type of exposure condition. This scenario simulates absorption from continuous or repeated dermal exposures over a work period. Several assumptions or observations may be required to arrive at a deposition rate. Dermal deposition rates can be determined from surface measurements or from published data. Various references provide guidance on dermal deposition rates.[8-10,12-14] One source is the Targeted Risk Assessment (TRA) model which is accepted as a Tier I screening measure for European REACh chemical safety risk assessments. For example, the TRA suggests a predicted dermal exposure rate of 1 mg/cm² per work day in some worker exposure scenarios. Although the TRA model conservatively assumes 100% absorption, comparative estimates might be made with IH SkinPerm by converting the daily estimate into an hourly rate e.g., 0.125 mg/cm²/hour for duration of 8 hours as a practical example.The instantaneous deposition is not considered in this calculation if the checkbox "longer duration" has been marked.

Example Deposition rate determination:

A physician re-applies an alcohol based sanitizer during an operation. It is estimated 4 mg of benzyl alcohol sanitizer is applied 20 times during a one hour operation to cover both hands and forearms.

$$\text{Deposition rate } (\text{mg/cm}^2/\text{hr}) = \frac{\text{mass (mg)} \times \text{frequency}}{\text{surface area (cm}^2)} \times \frac{1}{\text{time (hr)}}$$

$$= \frac{4\ \text{mg} \times 20\ \text{applications}}{1000\ \text{cm}^2} \times \frac{1}{\text{time (hr)}}$$

$$= 0.08\ \text{mg/cm}^2\text{/hour}$$

Other examples include application of agent to a mechanical part several times an hour, periodic exposure to overspray during metal cutting, additive loading, bag handling, or other regular contacts with moist, damp, or lightly powdered surfaces.

Figure 2: Example data inputs for Deposition over time exposure

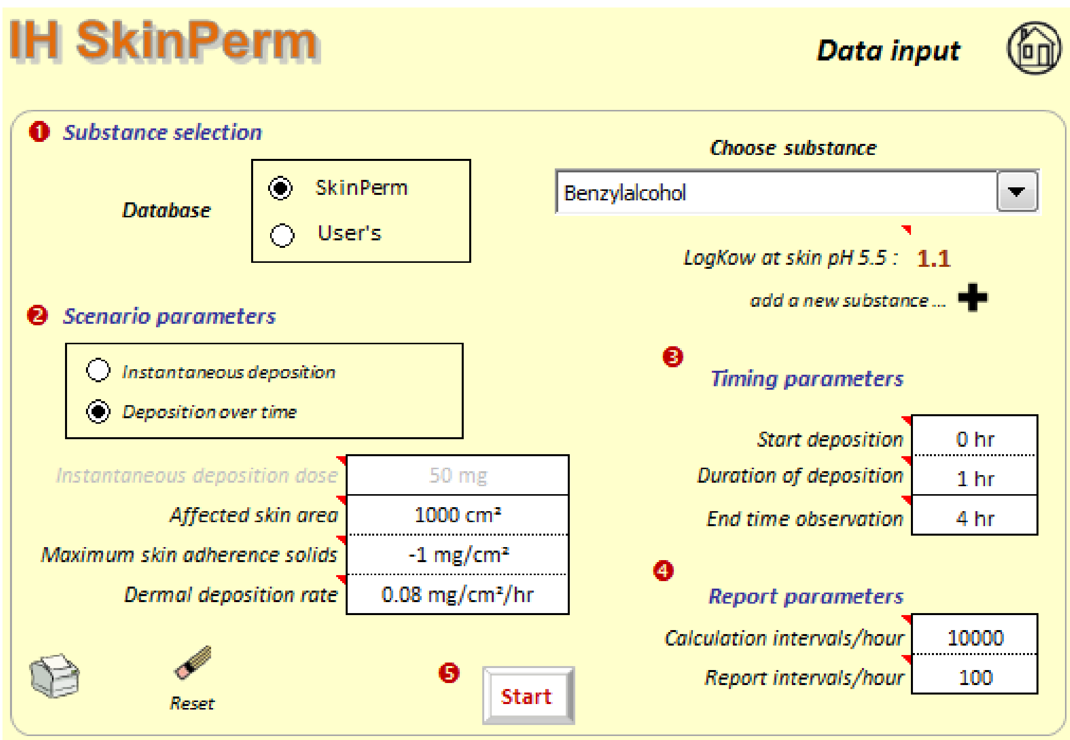
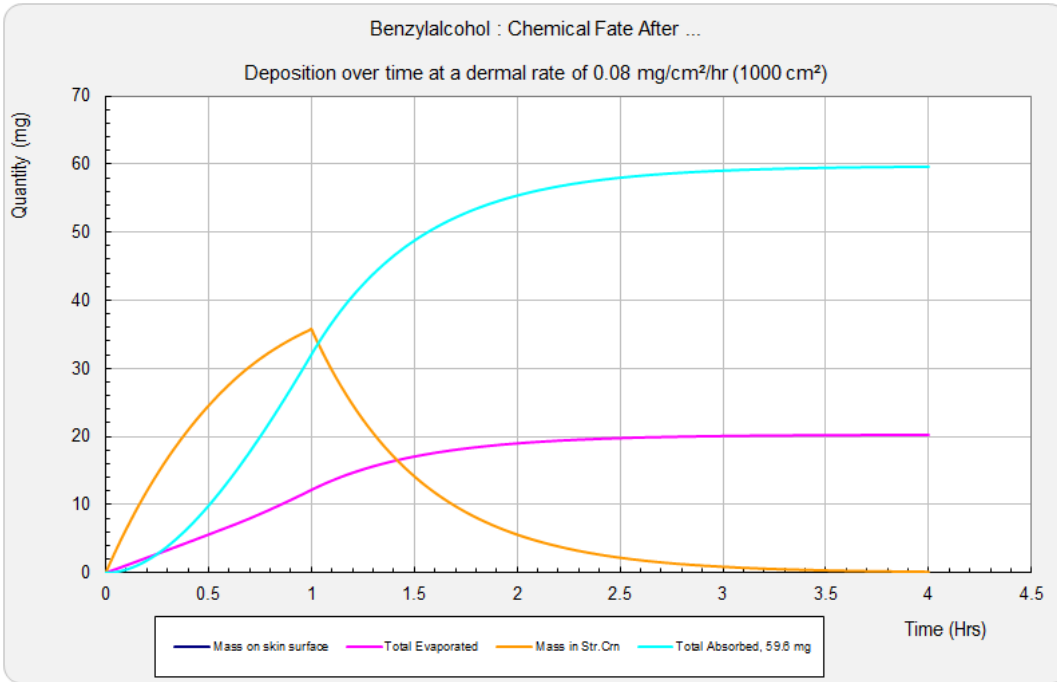


Figure 3: Example Chemical fate graph output for Deposition over time exposure



3. Timing Parameters:

Start Deposition - It is assumed that the start of dermal exposure occurs between 0 and 7 hours after starting work. The default is 0. This setting affects only the onset of skin loading and dermal absorption dependent on the observation time. Inputting a start time other than zero allows functionality for graphical display of the chemical fate relative to the actual time the exposure(s) begin during the shift or observation time.

Duration of Deposition - Duration of deposition is related to the duration of exposure or can be the duration of the task. The maximum duration of exposure is set to 8 hours.

End time Observation - End time of observation can be different from the duration of deposition. After cessation of exposure the dermal absorption may continue. Substances may be dissolved in the lipid matrix of the skin and remain in the skin for many hours.

The minimum observation time is set to 1 hour. The maximum observation time is set to 200 hours. The user may change and enter shorter or longer times for the simulation in order to better see the early or later concentrations. Example inputs could be the length of the workshift (e.g., 8-12 hrs) or a shorter period such as the time the task is completed; assuming the individual washes or removes the substance upon completion of the task.

Other report parameters can remain as their default values or be adjusted to enhance resolution of the graphical output produced in the Report sheet.

4. Report Parameters

Calculation intervals/hour - The estimating calculations are carried out by numerical integration over very small time periods. The higher the calculation intervals rate, the more detailed output data and higher resolution of the graph. The minimum time steps has been set to 1/1000 hour, that is a minimum of 1000 time steps per hour. The maximum number of time steps per hour is set to 100000 time steps per hours, but using this setting will slow down the speed of calculation depending on the speed of the processor in your PC. The default is 10,000 calculation intervals per hour.

Report intervals/hour - This setting affects the level of detail of the resulting graphs. Setting this value to 1 will only plot 1 data point per hour on the graph. Setting this value to 100 will plot 100 calculated points starting at 0.01 hours. For very volatile substances a larger number of report intervals/hr (e.g., 1000) is advised. However, the Report intervals/hour value can never be larger than the number of calculation intervals/hour.

B. Report Sheet

IH Skin Perm provides an estimate of several important parameters used in dermal exposure assessment.

- Partition coefficient stratum corneum/water
- Permeation coefficient liquid from aqueous solution (cm/hr)
- Absorption rate from saturated aqueous solution (mg/cm2/hour)
- Evaporation rate from liquid film on skin surface (mg/cm2/hour)

Key assumptions built in IH SkinPerm based on scientific reasoning are:

- The stratum corneum cannot absorb more than 20% of its volume. If it absorbs more, the structure of the stratum corneum is damaged and no longer mimics intact skin. If the evaporation rate plus the absorption rate are less than the deposition rate, a film of liquid may appear on the skin. The stratum corneum thickness is assumed as 20 micrometers (2×10^{-5} meters).

- Maximum absorption from the stratum corneum into the blood can never exceed the absorption, observed from a saturated aqueous solution of the substance.

- IH SkinPerm model assumes the epidermis provides no barrier against permeation due to the lipid content of the blood and interstitial fluids around ~0.4%.

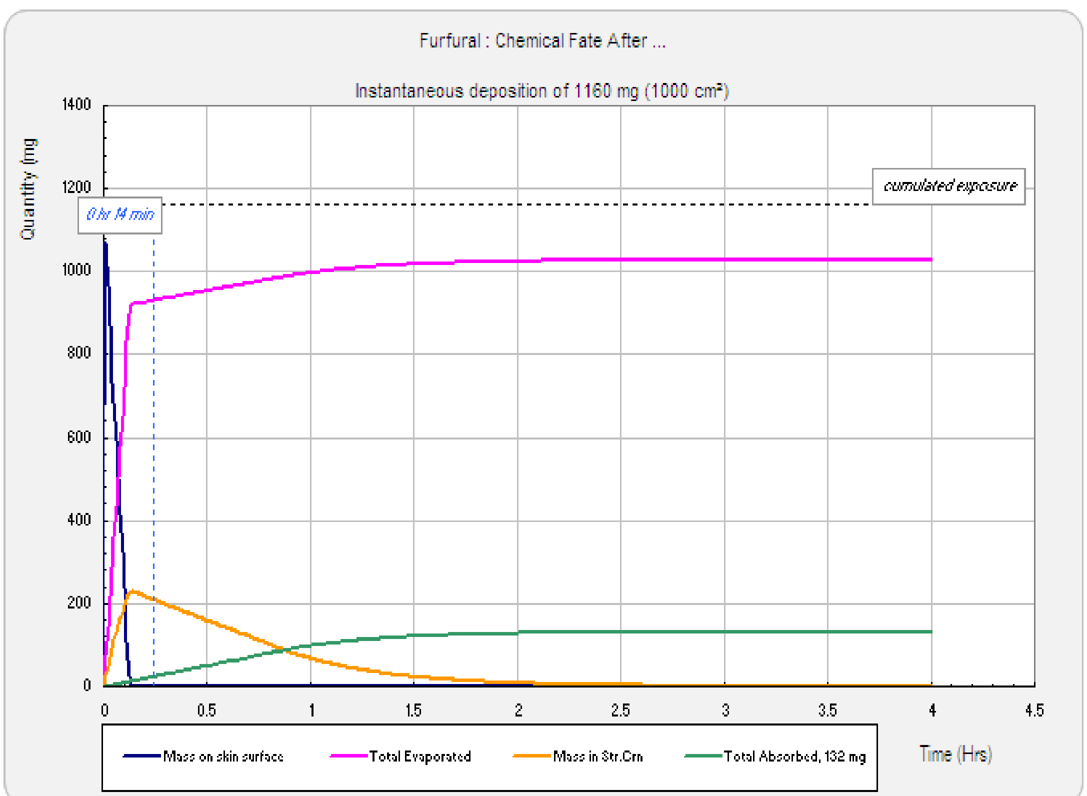
- Most applicable to substances with Log Kow -3 to 6 and MW < 600. However the report sheet includes confidence limits to indicate the representative range for the skin permeation coefficient from an aqueous solution.

1. Chemical Fate Graphs

A drop of substance deposited upon the skin (Dark Blue Line), starts to be absorbed into the stratum corneum (Yellow) and to evaporate simultaneously (Pink) The mass absorbed during the observation period is displayed by the Light Blue Line.

Figures 4 and 5 displays the dynamics of a substance present on the skin. The graph is the Chemical Fate for the Instantaneous scenario involving hand contact with Furfural. The mass on the skin upon contact is displayed by the Dark Blue Line. In Figure 4 for this scenario a residual amount of Furfural remains on the skin surface and the hands would appear moist for about 7 minutes based on the quantity unless other wised rubbed off.

Figure 4: Chemical Fate



The rate of skin absorption into the stratum corneum (Yellow) is considered to be directly related to the thickness and diffusivity of the stratum corneum. Diffusivity is estimated from the skin permeation and partition coefficient of the substance from aqueous solutions. As long as the substance has not been fully evaporated from the skin surface, the stratum corneum is loaded and absorption in the blood starts. The maximum rate is achieved after a period of time (ie lag time). If the liquid evaporates much faster than absorbed into the stratum corneum, the maximum absorption rate will not be achieved and only a small fraction of the substance will enter the body.

Evaporation rate (Pink Line) is calculated based on REACh technical guidance[14] and uses the following equations and assumptions:

$$Evaporation\ rate(LF) = \frac{\beta * Mw * Vp}{R * T * 10} \qquad eq.\ 8$$

$$\beta = \frac{0.0111 * V^{0.96} * D_g^{\ 0.19}}{\nu^{0.15} * X^{0.04}} \qquad eq.\ 9$$

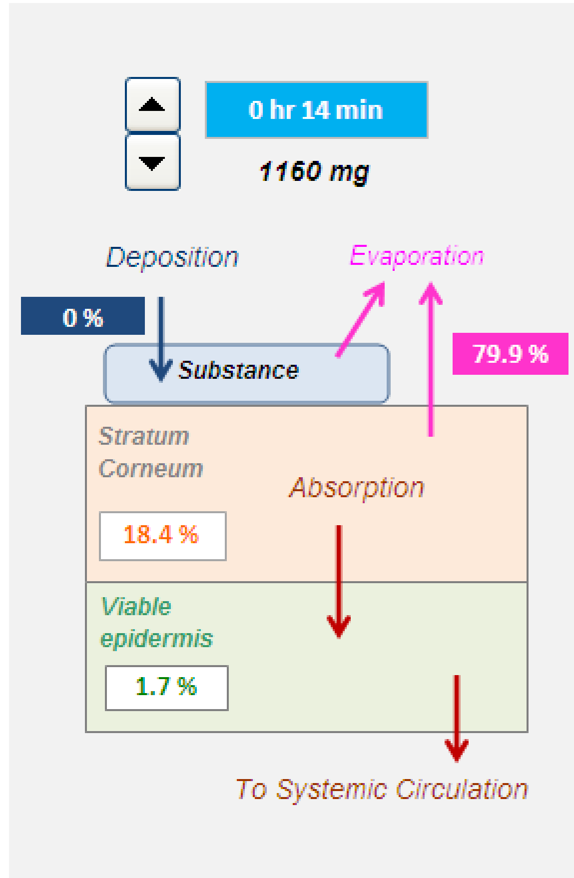
Mw	Molecular weight
Vp	Vapor pressure of the liquid at skin temperature in Pascal
R	Gas constant in J/Mol/°K
T	Skin temperature in°K (normal range 28-32°C) (assume 303°K)
β	Coefficient of mass transfer in the vapour phase in meter/hour
V	Velocity of air (at workplaces ranges 0.3 to 0.6 m/s) (assume or 0.3 m/s ie. 1080 meter/hour)
D_g	Diffusivity of the liquid in the gas phase (range 0.03 to 0.06 m2/hr) (assume 0.05 m2/hr)
v	Kinematic viscosity of air (Literature value 0.054 m2/hour)
X	Length of the area of evaporation in the direction of the air stream (assume 0.1 meter)

Figure 5: Chemical Fate using Drolet Spinner

Chemical fate is alternatively presented using the Drolet spinner. Deposition, Evaporation, and Absorption may be modeled at various times by clicking the arrows on the spinner.

Figure 5 shows that after 14 minutes the instantaneous deposition of 1160 mg of Furfural is no longer present on the skin surface (ie. 0%). The fate after 14 minutes is:

- 79.9% Evaporates after 14 minutes
- 18.4% permeated into the stratum corneum
- 1.7% permeated into the viable epidermis



NOTE: The time increments in the spinner is a function of the report intervals per hour and observation time set on the Data input screen. e.g.if the report interval/hour is set to 100 and the observation period is set to 8 hours, the time increments in the spinner will increase or decrease by (1% x 8 hr x 100) = 8 minute increments.

2. Absorption Rate Over Time Deposition Graph

The absorption rate graph in Figure 5 shows the estimated flux rate for the pure substance moving from the stratum corneum of the contaminated skin area into the body. It is related to the mass of substance in the stratum corneum of the contaminated skin area, but not in a linear way. The maximum absorption rate from the stratum corneum is limited by the maximum solubility of the pure compound in water. If the mass of substance in the stratum corneum exceeds the mass, which is in the stratum corneum in equilibrium with a saturated aqueous solution of the substance, the flux does no longer increase. This graph emphasizes that it takes time for the substance to be fully absorbed to the 100% total amount dependent on the mass of the substance in the stratum corneum.

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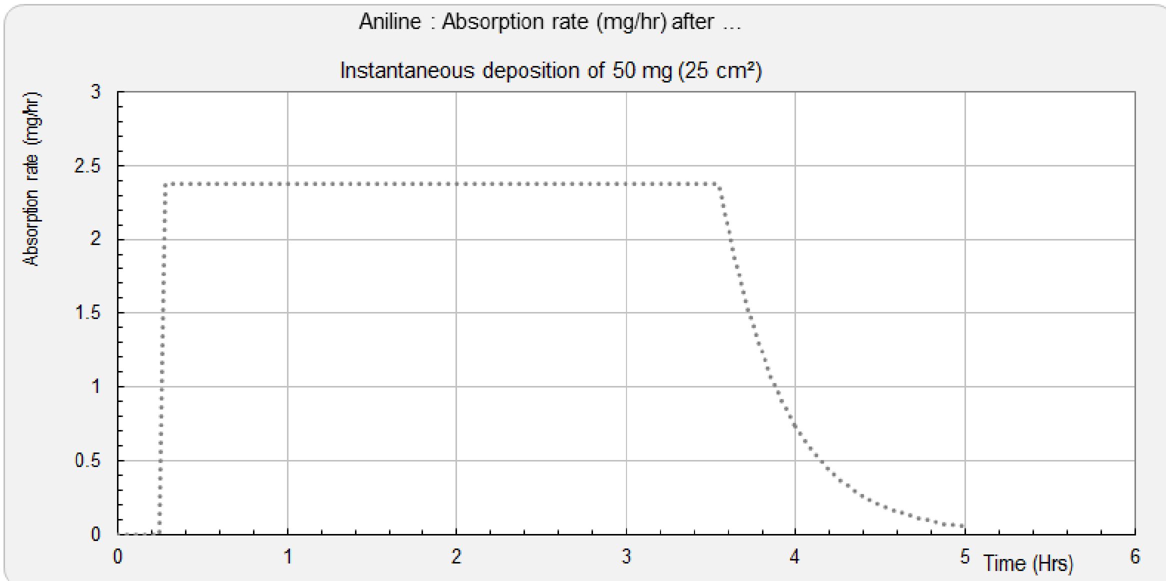
Figure 6: Absorption Rate



3. Parameter Fields Definition

Tot. Deposition- This is the total mass that was deposited during the observation period.

Fraction absorbed- This is the fraction of the total mass exposed that was absorbed during the observation period

Amount absorbed- This is the total mass that was absorbed during the observation period.

Kp-lipids (vehicle water) - This Permeability Coefficient (Kp, cm/hr) is a constant that describes the speed at which a chemical diffuses through the lipid mortar between skin cells.

Kp-keratins (vehicle water) - This Permeability Coefficient (Kp, cm/hr) is a constant that describes the speed at which a chemical diffuses through the dead skin cells.

Lag time stratum corneum - Period for the substance to reach a steady state full loading in the stratum corneum

Diffusivity of Stratum Corneum (Dsc): A dependent variable describing the effective diffusion of a chemical through the stratum corneum. The path length of the stratum corneum in IH SkinPerm assumes a thickness of 0.002 cm.

Skin/Water partition ratio - The partition coefficient is the ratio of the concentration in the Stratum Corneum (SC) to that in the aqueous solution (Vecchia and Bunge 2002)[4-5]. The experimental protocol consists of taking a weighed sample of SC allowing it to equilibrate with an aqueous solution containing the absorbing compound and radio labeled C14 or H3. After sufficient time, the concentration in the aqueous solution and in SC is measured by scintillation counting. Since essentially everything diffuses into a water medium into the skin, the solubility of a substance in water is important. IH Skin Perm makes a basic assumption that the dermal absorption rate would never exceed the amount absorbed from a saturated aqueous solution of the liquid (assuming undamaged skin and there are no compounds in the mixture to enhance water solubility). IH Skin Perm QSARs determine the skin permeation coefficient of the substance from an aqueous solution and the stratum corneum water partition coefficient. Both parameters are needed to estimate the lag time of the substance. Having both parameters enables a better estimation of maximum dermal absorption over time.

Permeation coefficient water - This is an estimate of the mean overall permeation coefficient (cm/hr) of the substance dermally absorbed into the Stratum Corneum from an aqueous solution. If this Skin/Water permeation coefficient is multiplied with the substance concentration in mg/cm^3 this gives us the flux or mass transfer permeation rate in $mg/cm^2/hr$. A protocol for measuring permeation coefficients is described in OECD 428.

5^{th} percentile water - This is the minimum value that is representative of the mean permeation coefficient for the substance in an aqueous solution. Variability is associated with experimental permeation measurements. Wider confidence intervals suggest more variability.

95^{th} percentile water - This is the maximum value that is representative of the mean permeation coefficient for the substance in an aqueous solution. Variability is associated with experimental permeation measurements. Wider confidence intervals suggest more variability

Max. derm. abs. - The QSARs in IH SkinPerm mathematically estimate the maximal dermal absorption rate ($mg/cm^2/hr$) at the maximum solubility of the pure compound in water at steady state.

Kp-lipids (vehicle air) - This is the estimated Permeation Coefficient (Kp, cm/hr) of the substance as vapor in air, valid for the stratum corneum lipid mortar. If multiplied by the airborne concentration (mg/cm^3) a permeation or mass transfer rate ($mg/cm^2/hr$) of chemical diffusion from air through the lipid pathway between skin cells is determined. This is one parameter that enables you to estimate dermal uptake from vapor in air.

Kp-keratins (vehicle air) - This is the estimated Permeation Coefficient (Kp, cm/hr) of the substance as vapor in air, valid for the dead corneocytes of the stratum corneum. If multiplied by the airborne concentration (mg/cm^3), a permeation rate mg/cm²/hr of chemical diffusion from air through the cellular pathway of dead skin cells is determined. This second parameter nables you to estimate dermal uptake from vapor in air.

Kp-stagnant air layer - This is the air boundary layer at the skin. This is the permeation coefficient (Kp) of this air space. The thickness of the air layer is estimated to be 3 cm for light work clothing. The permeation of the substance in this air space is dependent on the diffusivity of the substance in air. Some substances permeate through the stratum corneum so fast (eg aniline, nitrobenzene, phenol, glycolethers, etc.), that delivery from the ambient air becomes the rate limiting step.

Skin/Air partition ratio - This is the vapor partitioning ratio of the substance comparing what is in the skin versus the air.

Permeation coefficient air - This is an estimate of the mean overall permeation coefficient of the substance dermally absorbed from vapor in air. The permeation coefficient in air is derived from the aqueous permeation coefficient according to the following equations.

$$\begin{aligned}
&\textit{Adaptation of aqueous permeation coefficient into a vapour permeation coefficient}\\
Kwa &= \frac{R*T*Sb}{Mw*Vp} \quad \textit{partition coefficient water / air}\\
R &= \textit{gasconstant } 8.314 \ Nm/Mol/°K\\
T &= \textit{temperature in } °K\\
Sb &- \textit{water solubility in } g/m3\\
Mw &= \textit{molecular weight}\\
Vp &= \textit{vapour pressure in Pascal } (= N/m2)\\
Kp_{sk-air} &= Kp_{sk-water} * Kwa \quad (\textit{permeation coefficient skin air, cm/hour})\\
\partial &= \textit{stagnant air layer } (3\ cm, \textit{ simulating barrier of clothing})\\
Dair &= 360 * \sqrt{76/Mw} \quad (cm2/hour, \textit{ diffusivity in air})\\
Kp_{air} &= Dair/\partial \quad (cm/hour, \textit{ permeation coefficient stagnant air layer})\\
Kp_{sk\ air\ air} &= \frac{1}{\frac{1}{Kp_{sk-air}} + \frac{1}{Kp_{air}}} \quad (\textit{overall permeation coefficient skin air})
\end{aligned}$$

5th percentile air - This is the minimum value that is representative of the mean permeation coefficient for the vapor in air. Variability is associated with experimental permeation measurements. Wider confidence intervals suggest more variability.

95th percentile air - This is the maximum value that is representative of the mean permeation coefficient for the vapor in air. Variability is associated with experimental permeation measurements. Wider confidence intervals suggest more variability.

III. Example Comparative Analysis

The report sheet contains a section which provides additional substance relevant information independent of the scenarios modeled. The following information highlights advanced applications and considerations of skin permeation.

A. Maximum Dermal Absorption for 2000 cm2 in one hour (mg) (from liquid)

A surface area of 2000 cm2 is the approximate skin surface area of the hands and forearms. If the dermally absorbed amount (mg) in one hour is greater than a tenth of the OEL inhalation dose equivalent (mg) then the substances meets the EU Skin Notation criteria

Example determination:

Reference value for Furfural = 2 ppm

Furfural reference value in mg/m3 $= \frac{\text{ppm * MW}}{24.45}$

$= \frac{2 * 96.08}{24.45}$ or 7.86 mg/m3

OEL Inhalation dose equivalent (furfural) = 7.86 mg/m3 x 10 m3 = 78.6 mg**

** NOTE: Toxicologically this dose is also dependent on lung retention which is a factor of the water/air ratio and octanol/air ratio of the substance and the extent of metabolism in the body. In practice this may vary between 1% and 100%, but 75% is the regulatory default setting in Europe.

OEL * 1/10 = 78.6 mg * 1/10 = **7.86 mg**

QSARs in IH SkinPerm mathematically estimate the maximal dermal absorption (mg/cm²/hr) at the maximum solubility of the pure compound in water measured at steady state. This value is indicated on the Report Sheet as Max. derm. Abs.

Furfural Max. derm. Abs rate = 0.10102 mg/cm^2/hr

Maximum Dermally absorbed in 1 hour over 2000 cm^2 as calculated by IH SkinPerm: = Max. derm. Abs (mg/cm^2/hr) * 1 hr * 2000cm^2
= 0.10102 mg/cm^2/hr * 1 hr * 2000 cm^2
= **202.04 mg**

NOTE: the value reported as Max. derm abs for 2000 cm^2 must then be compared to one tenth the OEL.

Answer: EU $_{Skin}$ Notation is applied because:

Dermal Absorbed amount 202.04 mg >> 7.86 mg OEL $_{1/10}$ Furfural

NOTE: Determination of EU $_{Skin}$ Notation is not dependent any IH SkinPerm exposure scenario. It is simply provided for informational comparative analysis.

B. Dermal/Respiratory uptake ratio measuring dermal absorption risk from vapor in air.

The purpose of this data is meant to highlight that dermal absorption of certain substances can occur from airborne vapor. Respirators in some cases may not be sufficient. The Dermal/Respiratory uptake ratio indicates the risk of dermal absorption from vapor in air.

Multiply the value for this field by 100% to express % of airborne vapor that is potentially absorbed by skin.

The percentage of protection against absorption by wearing a respirator is calculated by IH SkinPerm as follows:

The Dermal/Respiratory uptake Ratio R = Dermal absorption/Inhalation absorption

Or Ratio R = RX/X

The ratio of absorption between the 2 pathways = RX/X = R

		Determination using Furfural Example
RX	Total Dermal absorption by dermal exposure to airborne vapor	Kpa*Ca*Sa*Du = (cm/hr*mg/cm^3*cm^2*hr = mg) Kpa = Air permeation coefficient (e.g. furfural: 11.1 cm/hour) Ca = Air concentration (e.g. furfural: 7.9 mg/m3, or 7.9E-6 mg/cm^3) Sa = skin area e.g.18000 cm^2 Du = duration of exposure ie. 8 hours like the OEL = 11.1*7.9E-06*18000*8 = 12.63 mg
X	Total Inhalation absorption from airborne vapor	OEL mg/m^3 x 10 m^3 x 0.75 = mg e.g. 7.86 mg/m^3 x 10 m^3 x 0.75 = 59.25 mg

RESULTS:

Dermal/Respiratory Uptake Ratio R = RX/X = 12.63/59.25 = 0.21
Or 21% of airborne Furfural vapor is potentially absorbed by the skin.

Assuming Full Respiratory Protection provides 100% efficiency

Percent protection from respirator = 100*X/(RX+X)

= 100/(R+1)

= 100/(0.21+1) = 82.4 %

IV. Applicability of the Model

IH Skinperm is based on 2 critical QSARs for:

- human aqueous permeation coefficient of the stratum corneum, predicted from the log(Kow) and the molecular weight. This QSAR was derived from 182 measured and validated human aqueous skin permeation coefficients in vitro (ten Berge 2009, Vecchia and Bunge 2002a).

- stratum corneum/water partition coeffcient, predicted from the log(Kow). This QSAR was derived from 97 measured and validated human stratum corneum/water partition coeffcients in vitro (ten Berge 2009 and Vecchia and Bunge 2002b).

V. References:

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