

Welcome to ConsExpo 4.0

This guide introduces you to using ConsExpo 4.0, a program to estimate exposure to compounds from consumer products. The tutorial in this guide leads you through a step-by-step exposure assessment using physicochemical properties of the compound of interest and information on the product.

The screenshot shows the ConsExpo 4.00 software window. The title bar reads 'ConsExpo 4.00'. Below the title bar is a menu bar with 'File' and 'Help'. A toolbar with icons for file operations is located below the menu bar. The main interface has a yellow sidebar on the left with the RIVM logo and text 'Rijksinstituut voor Volksgezondheid en Milieu'. The main area is divided into several sections: 'Product & Compound' with a 'Product' text box and a 'Compound' dropdown; 'Exposure Scenario' with a 'defaults database' button and a 'General Scenario Data' section; 'Exposure Routes' with sections for 'Inhalation', 'Dermal', and 'Oral', each containing 'Exposure' and 'Uptake' sub-sections and a 'Clear' button; and 'Output' with options for 'Point values', 'Graphs', 'Sensitivity', 'Distributions', and 'Report'.

The chapters in these tutorials will explain the different sections of ConsExpo 4.0. In this tutorial, we will demonstrate an exposure assessment for a person cleaning a kitchen countertop with a kitchen detergent containing the anti-bacterial ingredient 'License-to-kill'. It is recommended to go through the chapters in the following order:

[1. Product & Compound](#)

[2. Exposure Scenario](#)

[3. Exposure routes first tier](#)

[4. Output first tier](#)

[5. Exposure routes refined](#)

[6. Output refined](#)

Please proceed to the [Product & Compound](#) section, and fill out the values as provided in this tutorial.

Product & Compound

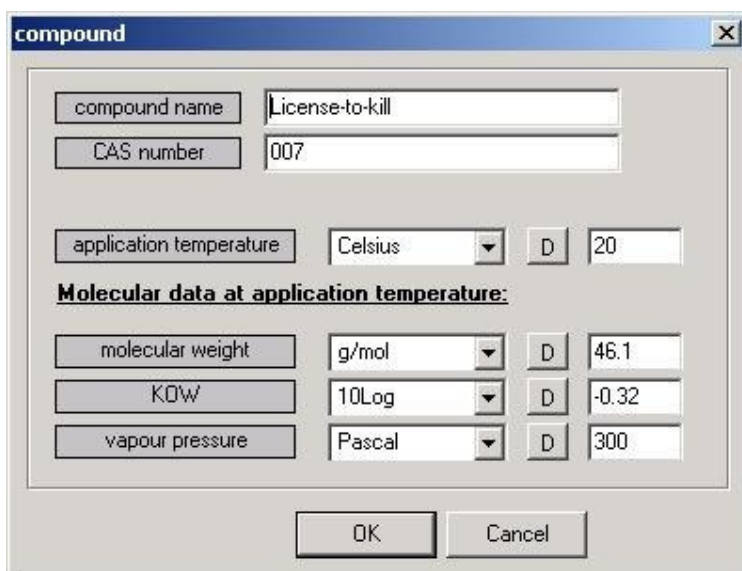
In ConsExpo 4.0, an exposure study is identified by the product name. This name can be edited in the product name edit control on ConsExpo's main screen. The product name will appear in the output of the exposure assessment. In this tutorial on a detergent, we will use the working name 'Kitchen detergent'.



Product & Compound	
Product	Kitchen detergent
▶ Compound	

Editing the compound parameters

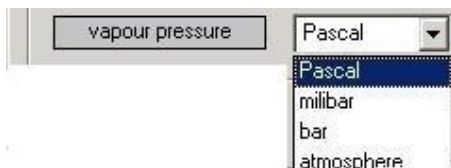
We can edit the properties of the compound in the product for which we want to do the exposure assessment by clicking the arrow button ▶ in front of the 'Compound' topic. The following screen is displayed:




compound			
compound name	License-to-kill		
CAS number	007		
application temperature	Celsius	D	20
Molecular data at application temperature:			
molecular weight	g/mol	D	46.1
KOW	10Log	D	-0.32
vapour pressure	Pascal	D	300
OK		Cancel	

The values for the parameters filled out in this example apply to the compound of interest in the kitchen detergent: 'License-to-kill'. Please fill out the values presented above.

If necessary, the units of the parameters can be changed by clicking the arrow-down button behind the units, displaying a list of available units.



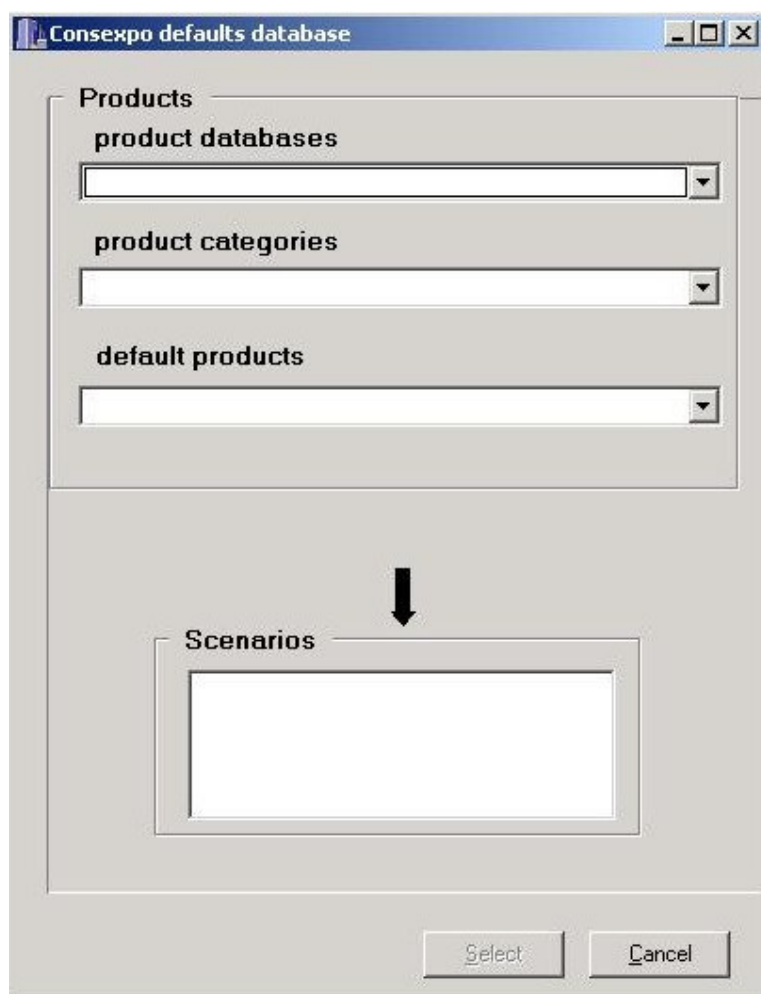
vapour pressure	Pascal
	▼
	Pascal
	milibar
	bar
	atmosphere

Once all parameters have been filled out, clicking the  button brings us back to the main screen. We can now start to define our ['Exposure Scenario'](#).

Exposure Scenario

In this tutorial, we will assess the exposure of an adult to 'License-to-kill' in kitchen detergent while cleaning a kitchen countertop. The exposure scenario can be described as follows: a cloth immersed in water containing kitchen detergent is used to clean the kitchen countertop by wiping the surface. This activity takes place regularly, as it is usually associated with doing the dishes. Exposure to 'License-to-kill' takes place during and after wiping the surface of the kitchen countertop.

ConsExpo 4.0 has a database of default scenarios with associated models and parameter values for a number of products, which can be accessed by pressing the **defaults database** button, displaying the following screen:




These scenarios and accompanying default values are explained in ConsExpo fact sheets and can be used for the exposure assessment^a. However, it is recommended to

^a While performing an exposure assessment using ConsExpo 4.0, the appropriate exposure scenario and values for many parameters may sometimes be unknown. In these instances, default scenarios and default values are available in ConsExpo fact sheets, which are available for a number of product categories. The fact sheets are in the process of being updated and will be available soon on www.rivm.nl/ConsExpo.

check whether the models or values used are applicable to the exposure scenario at hand. If no appropriate scenario is available in the database, the models can be selected manually. Similarly, if better values than the defaults are available, these are preferred and can be filled out manually. In this tutorial, we will manually select the

appropriate models and values. Click  to return to the main screen.

Back in the main screen, we can edit the general exposure scenario parameters by clicking the arrow button  in front of 'General scenario data'. The following screen is displayed:




The dialog box titled 'General Exposure Parameters' contains two rows of input fields. The first row has a label 'body weight', a unit dropdown menu set to 'kilogram', a default value dropdown set to 'D', and a text box containing '75'. The second row has a label 'use frequency', a unit dropdown menu set to '1/year', a default value dropdown set to 'D', and a text box containing '426'. At the bottom right are 'OK' and 'Cancel' buttons.

Values for these parameters are needed for all exposure models.

Assuming that in today's society, both men and women clean kitchen countertops, we take the default body weight value for adults from ConsExpo's general fact sheet: 75 kg^a.

We assume that the frequency of doing the dishes is 426 times per year^a. As stated before, cleaning the kitchen countertop is associated with doing the dishes and the same frequency can be used.

Clicking the  button brings us back to the main screen. The checkmark in front of the General Scenario Data item tells us that all general parameters have been filled out:



The main screen shows a header 'Exposure Scenario' with a 'defaults database' button. Below it, a list item 'General Scenario Data' is preceded by a red checkmark and a right-pointing arrow button.

Other model specific parameters will be filled out in the next section: [Exposure routes first tier screening approach](#).

^a While performing an exposure assessment using ConsExpo 4.0, the appropriate exposure scenario and values for many parameters may sometimes be unknown. In these instances, default scenarios and default values are available in ConsExpo fact sheets, which are available for a number of product categories. The fact sheets are in the process of being updated and will be available soon on www.rivm.nl/ConsExpo.

Exposure Routes - first tier screening approach

An exposure assessment in ConsExpo 4.0 can be performed at different levels of detail, depending on the models selected. Relatively simple models are available as a first tier approach, when the goal of the assessment is screening the product or the ingredient. This approach may be used to screen whether the use of the product will lead to exposure levels of the ingredient that are close to the relevant health based exposure limits. The models for a more detailed exposure assessment need more specific information, but generally lead to a more accurate exposure assessment. In the first part of this tutorial, we will use models that are appropriate for the first tier screening approach.

Defining an exposure scenario

In defining an exposure scenario for a compound, one can select one or more of the different exposure routes: inhalation, dermal and oral exposure. The appropriate route depends on the use of the product containing the compound of interest. It is wise to describe for oneself the events taking place during the exposure. In this tutorial, we assess the exposure to 'License-to-kill' in kitchen detergent for a person cleaning a kitchen countertop. The exposure scenario can be described as follows: an adult wipes the surface of a kitchen countertop with a cloth immersed in water containing kitchen detergent after each time he or she does the dishes. Exposure takes place via inhalation of 'License-to-kill' evaporating from the surface of the countertop during and after the cleaning. In addition, dermal exposure takes place via the hands, while immersing and handling the cloth in water containing kitchen detergent. The most relevant routes of exposure in this scenario are the inhalation and the dermal route. The oral route is not considered in this example. In addition, the mixing and loading of the kitchen detergent in the water is also not considered in the scope of this tutorial. The latter could significantly contribute to the exposure, but the scenario is different to such an extent from that of the actual cleaning scenario that it needs a separate exposure assessment. More information on the exposure assessment for mixing and loading events can be found in ConsExpo fact sheets^a.


The values to be filled out for each parameter refer to a single event of cleaning the kitchen countertop. ConsExpo 4.0 will calculate exposure levels for one event, but also for more events based on the 'use frequency' value, which was filled out in the ['Exposure Scenario'](#) section.

^a While performing an exposure assessment using ConsExpo 4.0, the appropriate exposure scenario and values for many parameters may sometimes be unknown. In these instances, default scenarios and default values are available in ConsExpo fact sheets, which are available for a number of product categories. The fact sheets are in the process of being updated and will be available soon on www.rivm.nl/ConsExpo.


The inhalation route

Exposure via the inhalation route in this tutorial consists of inhaling 'License-to-kill' that evaporates from the surface of the kitchen countertop. To estimate exposure via this route, information is needed both on the use of the kitchen detergent and on the uptake of 'License-to-kill' by the body through the lungs.

Inhalation exposure

Selecting the 'Exposure' topic under the 'Inhalation' header by pressing the arrow button  gives access to the exposure models selection dialog. At present, two inhalation models are available:



In our exposure assessment, exposure takes place via inhalation of 'License-to-kill' vapour from the kitchen countertop surface. We therefore select the 'Exposure to vapour'- model and press .

The parameter edit dialog for this model is shown:

Inhalation: evaporation model

general

exposure duration: minute D 30

product amount: gram D 68.4

weight fraction compound: fraction D 0.00014

room volume: m3 D 15

ventilation rate: 1/hr D 2.5

☒ limit the air concentration to the vapour pressure of pure substance

vapour pressure: Pascal D 300

molecular weight: g/mol D 46.1

temperature: Celsius D 20

mode of release

instantaneous release

☒ All of the chemical is released at once into the room.
Use as a first tier approach

constant rate

☐ The chemical is released with a constant rate in a certain time.
Use when details of evaporation are not exactly known

evaporation

☐ The chemical is released by evaporation.
Use when details of evaporation are known

OK Cancel Help

While cleaning the kitchen countertop surface, the 'License-to-kill' vapour will be released in the air at a certain rate, depending on a number of factors such as the use of the product, characteristics of the exposure location, but also compound specific factors. ConsExpo 4.0 offers three modes of release to describe the evaporation process. Parameter values needed for all modes of release are:

- Exposure duration: the total amount of time spent in the exposure location during and after the event. It is assumed that the person cleaning the kitchen countertop will stay in the kitchen around 30 minutes in total.
- Product amount: The amount of product applied to the surface, in this case the amount of suds containing kitchen detergent that is used to clean the countertop. We assume that 40 ml/m² is used for cleaning surfaces with all purpose cleaners^a. We further assume that the surface of a kitchen counter top is 1.71 m²^a. Therefore, the amount of suds used for this surface is 1.71 x 40 = 68.4 ml, or 68.4 grams.
- Weight fraction compound: the weight fraction of the compound of interest in the product. The 'product' in this case is not the pure kitchen detergent, but the suds containing the kitchen detergent. If we assume that 7 grams of kitchen detergent containing 10% 'License-to-kill' is dissolved in 5 liters (5000 grams) of water^a, the weight fraction of 'License-to-kill' in the suds is 7 / 10 / 5000 = 0.00014.
- Room volume: the volume of the room in which the exposure takes place, in this case the kitchen. In the general fact sheet, the default value for kitchen volume is 15 m³^a.


^a While performing an exposure assessment using ConsExpo 4.0, the appropriate exposure scenario and values for many parameters may sometimes be unknown. In these instances, default scenarios and default values are available in ConsExpo fact sheets, which are available for a number of product categories. The fact sheets are in the process of being updated and will be available soon on www.rivm.nl/ConsExpo.

- Ventilation rate: The number of times all the air in the room of exposure is replaced, per unit of time. In the general fact sheet, the default value for kitchen ventilation rate is 2.5 times per hour^a.

The three modes of release offered by ConsExpo 4.0 all describe the release of a compound in the air, but differ in model detail and the required information. The instantaneous release mode can be used when very little information is available on the product and the properties of the compound, or when one is interested in a worst case estimation as a first tier approach for the exposure assessment. To get an upper estimate of the exposure level, we will first use the instantaneous release mode.

The instantaneous release mode assumes that the total amount of compound is released in the air at once. In practice, the air concentration is limited to the saturated vapour pressure. If information on the vapour pressure of the compound is known, the box in front of the phrase 'limit the air concentration to the vapour pressure of pure substance' can be checked. Parameters needed for this option are vapour pressure, molecular weight and temperature. The values for these parameters will already be displayed, as they were already filled out in the [Product&Compound](#) section. ConsExpo 4.0 automatically imported these values in this section.


We now have filled out all the required values for the inhalation exposure to a vapour.

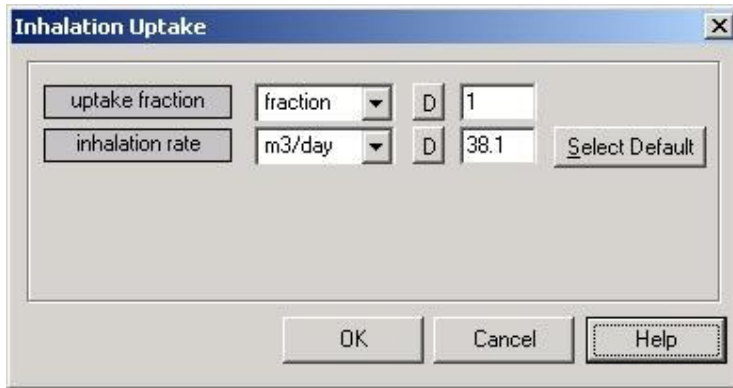
Pressing  brings us back to the main screen. There is now a checkmark before the inhalation exposure item, but a question mark before the inhalation uptake field, indicating that values for parameters in that item are missing:

Exposure Routes	
Inhalation	
  Exposure	Exposure to vapour : instantaneous release
  Uptake	

^a While performing an exposure assessment using ConsExpo 4.0, the appropriate exposure scenario and values for many parameters may sometimes be unknown. In these instances, default scenarios and default values are available in ConsExpo fact sheets, which are available for a number of product categories. The fact sheets are in the process of being updated and will be available soon on www.rivm.nl/ConsExpo.

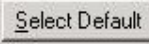
Inhalation uptake

Selecting the 'Uptake' topic under the 'Inhalation' header by pressing the arrow button  gives access to the inhalation uptake model dialog:



The 'Inhalation Uptake' dialog box contains two rows of input fields. The first row has a label 'uptake fraction', a dropdown menu set to 'fraction', a unit dropdown set to 'D', and a text box containing '1'. The second row has a label 'inhalation rate', a dropdown menu set to 'm3/day', a unit dropdown set to 'D', a text box containing '38.1', and a 'Select Default' button. At the bottom are 'OK', 'Cancel', and 'Help' buttons.



In this dialog, values for two parameters need to be filled out:

- uptake fraction: the fraction of inhaled compound that will be taken up in the body by the lungs. Experimental studies indicate that 'License-to-kill' is taken up relatively easy by the lungs. The value is therefore set to 100% or fraction 1.
- inhalation rate: the inhaled volume per unit of time by the exposed subject. ConsExpo 4.0 offers the possibility to calculate a default value based on body weight and level of exercise. Pressing the  button displays the following screen:



The 'Inhalation rate' dialog box has a 'body weight' label, a unit dropdown set to 'kilogram', a unit dropdown set to 'D', and a text box containing 'Distr.'. Below this is an 'exercise level' section with four radio buttons: 'Sleep', 'Rest', 'Light Exercise' (which is selected and highlighted with a dashed border), and 'Heavy Exercise'. At the bottom, it displays 'inhalation rate: 38.1 m3/day'. 'OK' and 'Cancel' buttons are at the bottom.

The body weight parameter displays the distribution filled out in the ['Exposure Scenario'](#) section. The exercise level while cleaning the kitchen countertop can be considered light. When the 'Light Exercise' option is selected, the default inhalation rate at this exercise level is displayed: 38.1 m3/day. This value is automatically filled out in the inhalation uptake model dialog, to which we can return by

clicking . Clicking  once more brings us back to the main screen where the two checkmarks tell us that all required parameter values are now filled out for the inhalation exposure route:





The 'Exposure Routes' dialog box has a title bar 'Exposure Routes'. Below it is a tab labeled 'Inhalation' with a 'Clear' button next to it. There are two rows of parameters, each with a red checkmark and a right-pointing arrow button. The first row shows 'Exposure' with the value 'Exposure to vapour : instantaneous release'. The second row shows 'Uptake' with the value 'Fraction'.

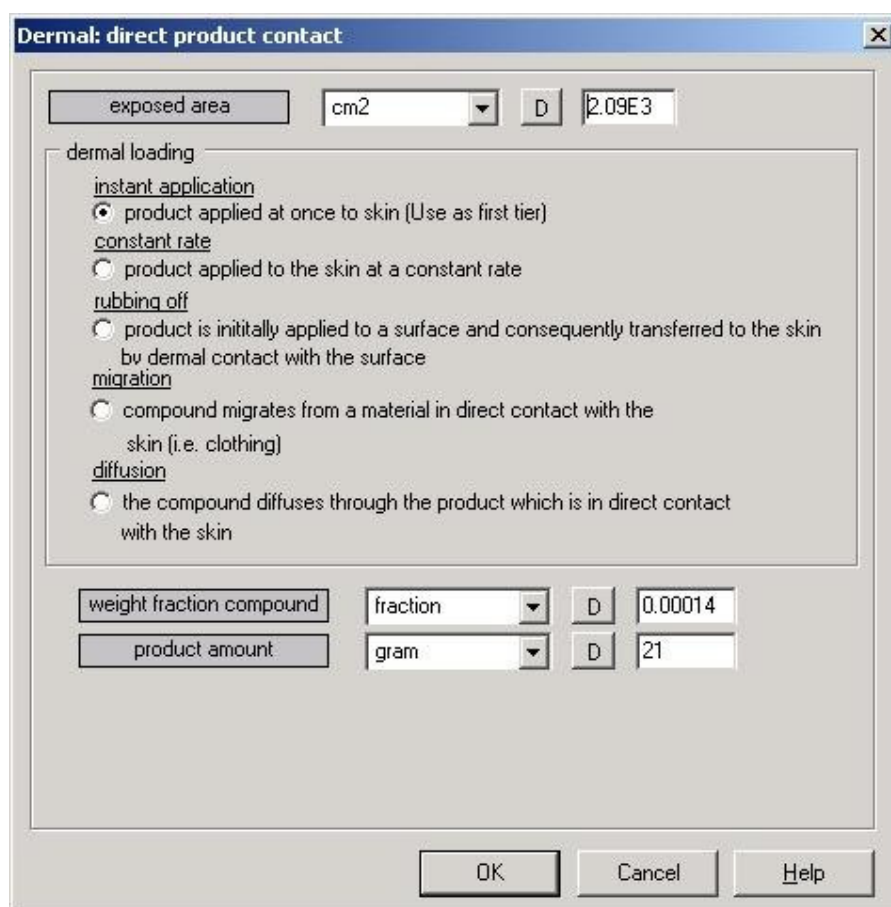
We now move on to the dermal route.

Dermal route

The dermal route of exposure while cleaning a kitchen counter top consists of immersing the hands in the suds containing the kitchen detergent with 'License-to-kill' and subsequently wiping the surface with a cloth.

Dermal exposure

Selecting the 'Exposure' topic under the 'Dermal' header by pressing the arrow button  gives access to the exposure models selection dialog. At present, only one dermal model is available. We select the 'Direct dermal contact with the product'- model and press . The parameter edit dialog for this model is shown:




The 'Dermal: direct product contact' dialog box has a title bar with the same text and a close button. It contains several input fields and radio buttons. At the top, there is a field for 'exposed area' with a unit dropdown set to 'cm2', a 'D' button, and a value field containing '2.09E3'. Below this is a section titled 'dermal loading' with four sub-sections, each with a radio button: 'instant application' (selected), 'constant rate', 'rubbing off', and 'migration'. Under 'instant application' is the text 'product applied at once to skin (Use as first tier)'. Under 'constant rate' is 'product applied to the skin at a constant rate'. Under 'rubbing off' is 'product is initially applied to a surface and consequently transferred to the skin by dermal contact with the surface'. Under 'migration' is 'compound migrates from a material in direct contact with the skin (i.e. clothing)'. Below these is a section titled 'diffusion' with a radio button and the text 'the compound diffuses through the product which is in direct contact with the skin'. At the bottom, there are two rows of input fields: 'weight fraction compound' with a unit dropdown set to 'fraction', a 'D' button, and a value field containing '0.00014'; and 'product amount' with a unit dropdown set to 'gram', a 'D' button, and a value field containing '21'. At the very bottom are 'OK', 'Cancel', and 'Help' buttons.

A compound can reach the skin via different ways of 'dermal loading'. Depending on what dermal loading option is chosen, a number of parameters need to be filled out. A parameter needed for all options is the 'exposed area' parameter - the area of skin exposed to the compound. While cleaning the kitchen countertop, the skin exposed to 'License-to-kill' consists of the hands and lower arms which are immersed in the suds. We assume the surface area of the hands and lower arms is 2085 cm²^a.


The instant application mode can be used when very little information is available on the product and the properties of the compound, or when one is interested in a worst case estimation as a first tier approach. To get an upper estimate of the dermal exposure level, we will first use the instant application mode, which assumes that all of the compound is directly in contact with the skin. The parameters needed for this mode are:

- weight fraction compound: the weight fraction of the compound of interest in the product. The 'product' in this case is not the pure kitchen detergent, but the suds containing the kitchen detergent. As before, if we assume that 7 grams of kitchen detergent containing 10% 'License-to-kill' is dissolved in 5 litres (5000 grams) of water^a, the weight fraction of 'License-to-kill' in the suds is $7 / 10 / 5000 = 0.00014$.
- product amount: It is assumed that not the total amount of suds is in contact with the skin but only a layer around the exposed skin. Consistent with the EU Technical Guidance Document on Risk Assessment (2003), we assume the thickness of a product layer on the skin is 0.01 cm^a. The exposed area of hands and lower arms is 2085 cm²; the amount of diluted product is 20.85 cm³ or 21 g. The latter is used as the product amount.

When all parameters are filled out, clicking the  button brings us back to the starting screen. There is now a checkmark in front of the dermal exposure field, but a question mark before the dermal uptake field, indicating that values for parameters in that item are missing:


Dermal		Clear
✓	▶ Exposure	Direct dermal contact with product : instant application
?	▶ Uptake	










Dermal uptake

Selecting the 'Uptake' topic under the 'Dermal' header by pressing the arrow button  gives access to the uptake model dialog:

^a While performing an exposure assessment using ConsExpo 4.0, the appropriate exposure scenario and values for many parameters may sometimes be unknown. In these instances, default scenarios and default values are available in ConsExpo fact sheets, which are available for a number of product categories. The fact sheets are in the process of being updated and will be available soon on www.rivm.nl/ConsExpo.

Two modes of uptake can be chosen: 'fixed fraction' or 'diffusion through skin'. For our upper estimation of the dermal exposure, we chose the fixed fraction mode. A worst case value for the uptake fraction - the fraction where all of the compound will be absorbed by the skin - is 1.

We have now filled out all the values needed for our upper estimation of exposure to 'License-to-kill'. Clicking the  button brings us back to the starting screen where the exposure and the uptake fields are now checked for both the inhalation and the dermal route:

Exposure Routes		
Inhalation 		
✓ 	Exposure	Exposure to vapour : instantaneous release
✓ 	Uptake	Fraction
Dermal 		
✓ 	Exposure	Direct dermal contact with product : instant application
✓ 	Uptake	fraction
Oral 		
	Exposure	
	Uptake	

Note that all selected models are displayed in the main screen. Since we do not consider oral exposure in this tutorial, no models or checkmarks are displayed in these fields.

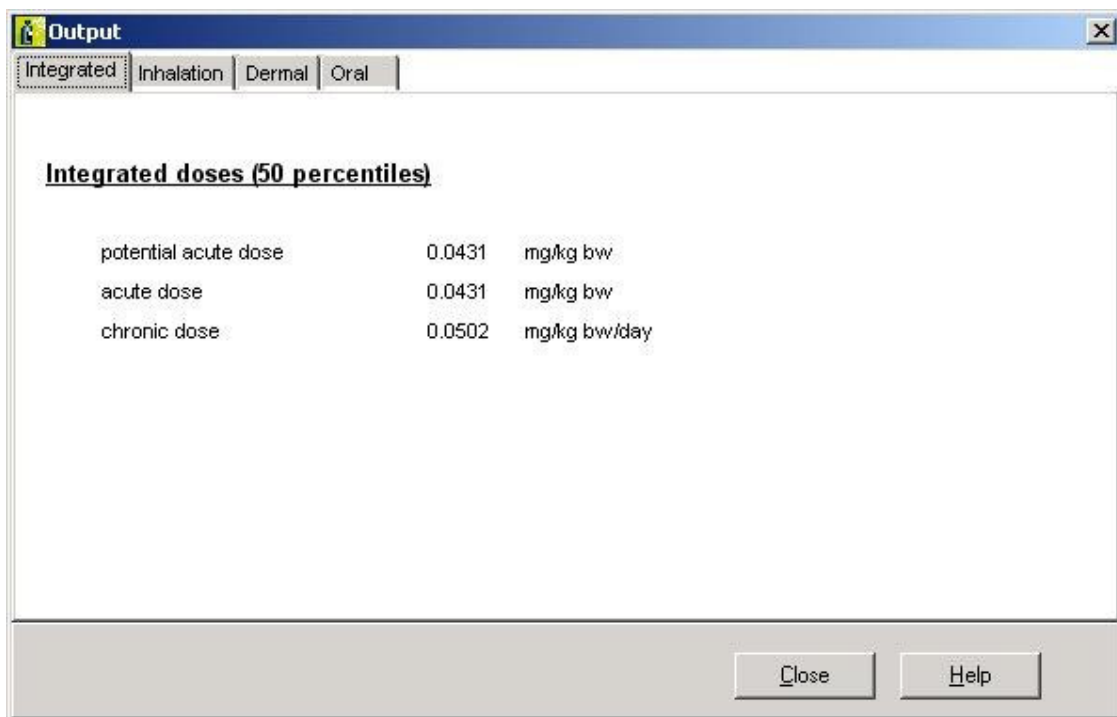
The information needed for our exposure assessment is now complete and the estimated upper exposure levels can be viewed in the [Output first tier](#) section.

Output first tier

The output section allows the user to view the results of the exposure assessment in a number of ways. In this section, we will view the results of the upper exposure levels estimated by using worst case first tier approach models. For a correct interpretation of the results, it is recommended to not just look at the point values but also at the graphs, the sensitivity and, if applicable, the distributions.

Point values

The point values field allows us to quickly view our mean acute and chronic exposure levels. Under the integrated tab, we find the estimated exposure levels combined for all exposure routes:

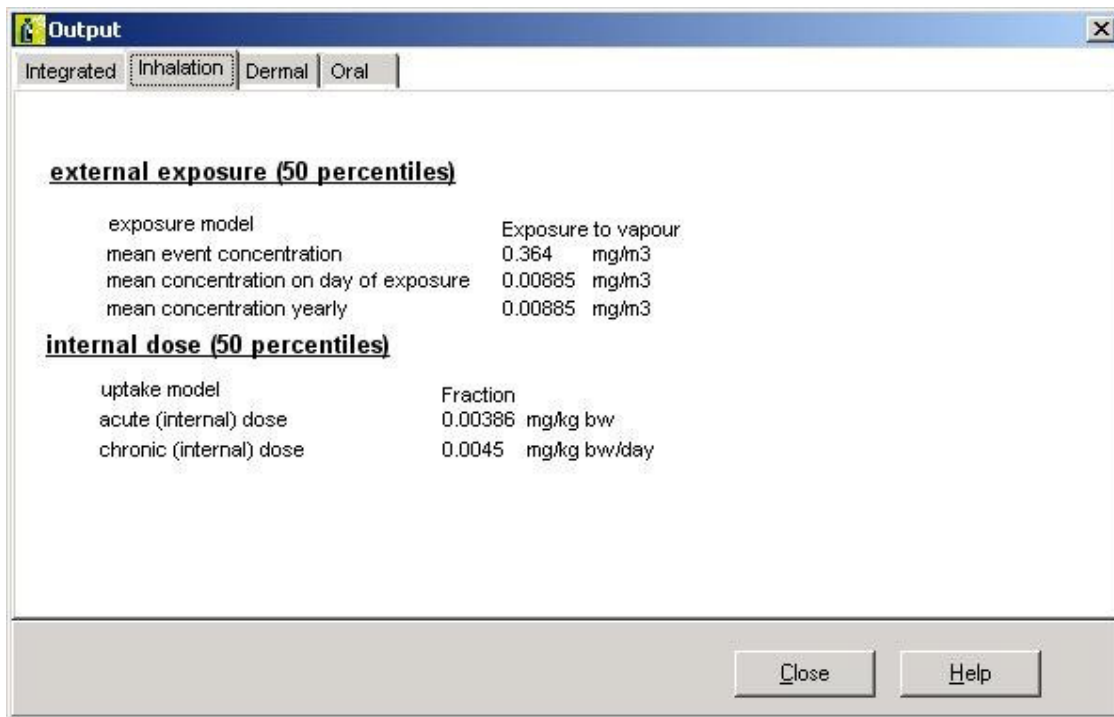


The screenshot shows a software window titled 'Output' with four tabs: 'Integrated', 'Inhalation', 'Dermal', and 'Oral'. The 'Integrated' tab is selected. Below the tabs, the text 'Integrated doses (50 percentiles)' is displayed. A table lists three exposure scenarios with their corresponding values and units. At the bottom right of the window are 'Close' and 'Help' buttons.

<u>Integrated doses (50 percentiles)</u>		
potential acute dose	0.0431	mg/kg bw
acute dose	0.0431	mg/kg bw
chronic dose	0.0502	mg/kg bw/day

The worst case potential acute dose of 'License-to-kill', i.e. the total dose the person cleaning the kitchen countertop is exposed to, is 0.043 mg/kg bw per cleaning event. The actual acute dose, i.e. the total dose taken up in the body, is also 0.043 mg/kg bw per cleaning event, as we defined that all 'License-to-kill' would be taken up by the lungs and the skin. The estimated chronic dose of 'License-to-kill' taken up in the body as a result of cleaning the kitchen countertop 426 times per year is 0.0502 mg/kg bw/day.

By selecting the different tabs, we can also view each exposure route separately. Selecting the inhalation route gives the following display:



The screenshot shows a software window titled 'Output' with four tabs: 'Integrated', 'Inhalation', 'Dermal', and 'Oral'. The 'Inhalation' tab is selected. The window displays two sections of data, both labeled '(50 percentiles)'. The first section, 'external exposure', lists three metrics: 'exposure model' (Exposure to vapour), 'mean event concentration' (0.364 mg/m3), 'mean concentration on day of exposure' (0.00885 mg/m3), and 'mean concentration yearly' (0.00885 mg/m3). The second section, 'internal dose', lists two metrics: 'uptake model' (Fraction) and 'acute (internal) dose' (0.00386 mg/kg bw), and 'chronic (internal) dose' (0.0045 mg/kg bw/day). At the bottom right, there are 'Close' and 'Help' buttons.

external exposure (50 percentiles)	
exposure model	Exposure to vapour
mean event concentration	0.364 mg/m3
mean concentration on day of exposure	0.00885 mg/m3
mean concentration yearly	0.00885 mg/m3

internal dose (50 percentiles)	
uptake model	Fraction
acute (internal) dose	0.00386 mg/kg bw
chronic (internal) dose	0.0045 mg/kg bw/day

The display gives information on the selected models and the external and internal exposure levels. The external exposure level represents the concentration of 'License-to-kill' in the kitchen air. It is given as a mean event concentration and a mean concentration throughout the day or year. The internal dose level represents the level of 'License-to-kill' taken up by the lungs while inhaling air containing 'License-to-kill'. It is given as an acute dose, based on a single cleaning event, and a chronic dose, based on cleaning the kitchen countertop 426 times per year.

Selecting the dermal route gives the following display:

The screenshot shows a software window titled 'Output' with four tabs: 'Integrated', 'Inhalation', 'Dermal' (which is selected), and 'Oral'. The window displays results for the 50th percentile of external exposure and internal dose.

external exposure (50 percentiles)

exposure model	Direct dermal contact with product
dermal load	0.00141 mg/cm ²
external dose	0.0392 mg/kg bw


internal dose (50 percentiles)

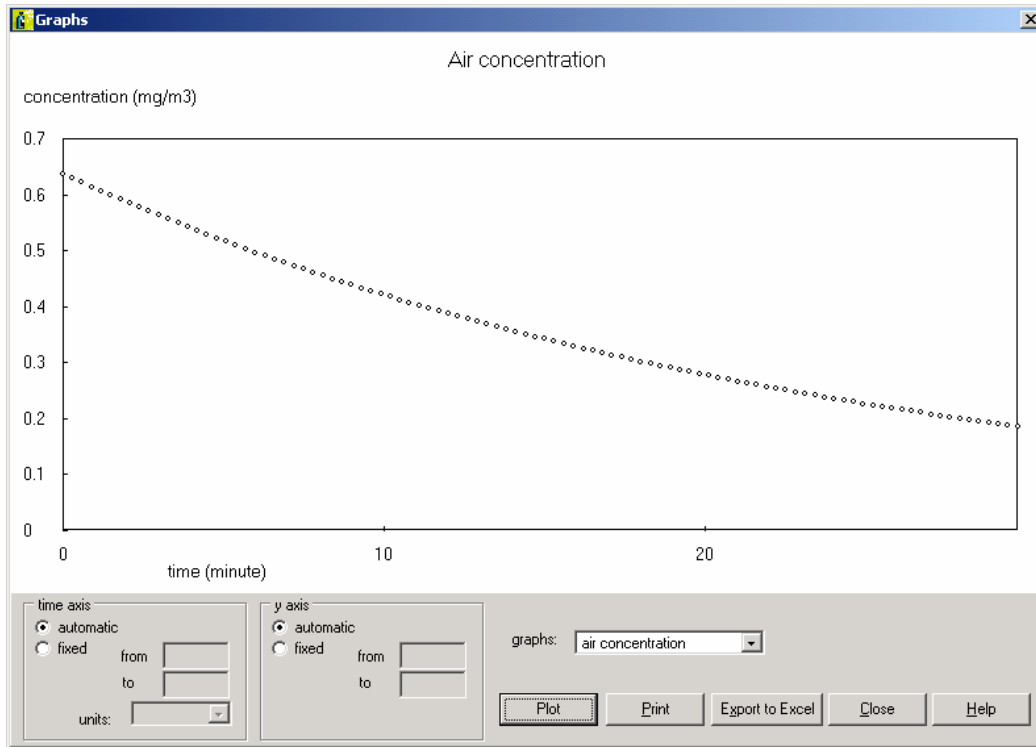
uptake model	fraction
acute (internal) dose	0.0392 mg/kg bw
chronic (internal) dose	0.0457 mg/kg bw/day


At the bottom right of the window are two buttons: 'Close' and 'Help'.

Again, the selected models and external and internal exposure levels are given. The external exposure is given in dermal load, which is the amount of compound per cm² of exposed skin, or as external dose - the amount that can potentially be taken up per kg bodyweight. The internal dose represents the amount of compound taken up through the skin. It is given as an acute dose, referring to the dose taken up after one cleaning event, and a chronic dose, based on cleaning the kitchen countertop 426 times per year.

Graphs

The graphs allow the user to study the process of exposure in time. For example, if we plot the air concentration of 'License-to-kill' against time and press , the following graph is displayed:

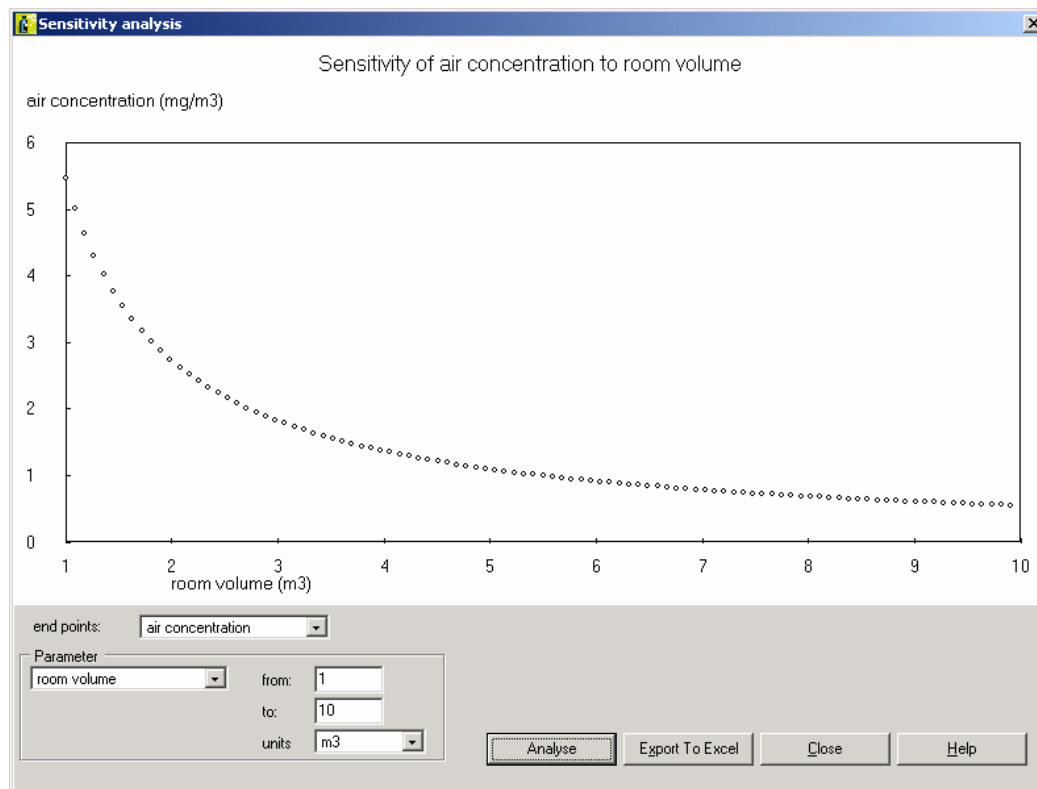


From this graph we can see that the maximum air concentration of 'License-to-kill' in the kitchen air is approximately 0.6 mg/m3 and gradually decreases throughout the cleaning event. The data points of the graph can be exported to Microsoft Excel by clicking the  button, such that the graph can be reproduced in this program.

Sensitivity

The sensitivity analysis allows the user to investigate graphically the consequences for the exposure results when changes in one single parameter are made. In our example of 'License-to-kill' in kitchen detergent, our mean event air concentration of 'License-to-kill' was 0.364 mg/m3. For this estimate, we assumed that the room volume of the kitchen was 15 m3. However, it is possible that the size of the kitchen is much smaller or much bigger than this.

We can use the sensitivity analysis to **Analyse** what happens to the mean air concentration when we vary the kitchen room volume between 1 and 20 m³:



The graph demonstrates that the mean event air concentration of 'License-to-kill' would be higher in a smaller kitchen, whereas there is relatively little difference for larger kitchens. The data points of this graph can also be exported to Microsoft Excel by clicking the **Export To Excel** button, such that the graph can be reproduced in this program.

Distributions

Distributions are typically part of a more detailed exposure assessment. We will therefore demonstrate the use of distributions at a later stage of this tutorial.

Report


The report presents a summary of the exposure assessment, including the selected models and values of the parameters. Print the report and save the ConsExpo file before moving to the next part of the tutorial.

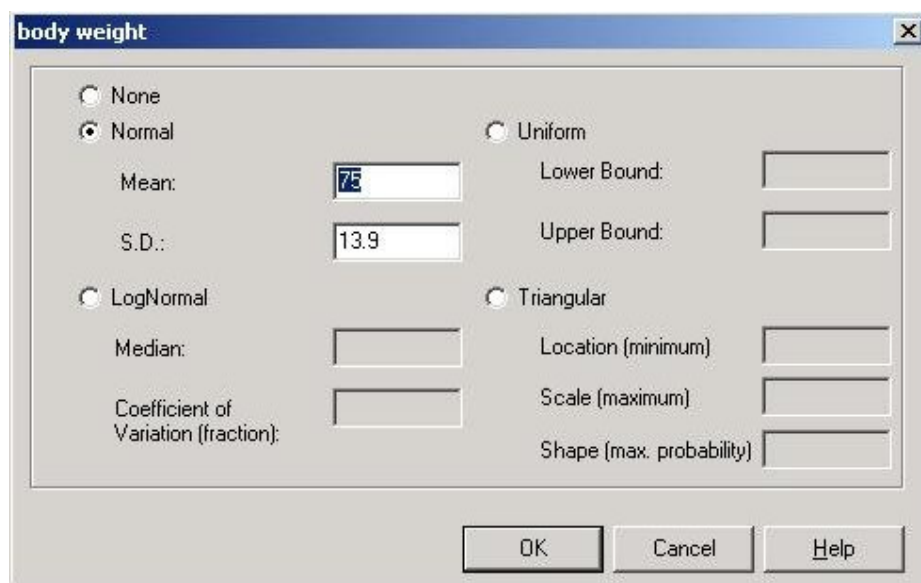
We have now evaluated the results of the upper exposure levels estimated by using worst case first tier approach models. In the next two sections, we will refine our exposure assessment with more specific models. Please proceed to the ['Exposure Routes Refined'](#) section.

Exposure Routes - refined

In the previous chapters, we assessed the upper estimate for the exposure to 'License-to-kill' in kitchen detergent for a person cleaning a kitchen countertop. We would now like to refine the exposure assessment by using more specific models, which require more information on the use of our product and the properties of 'License-to-Kill'. Some parameter values are the same as those used in the first tier approach. It is therefore recommended to save the previous ConsExpo file under a different name and alter the values as described below.

As the product and compound have not changed, we can leave the parameter values in the [Product & Compound](#) section unaltered. The exposure scenario has not changed either, but in this refined exposure assessment, we would like to give a stochastic distribution rather than a point value for the body weight parameter. We can do this in the [Exposure Scenario](#) section, under the General Scenario Data field.

Clicking on the  button in front of the body weight value field displays the following screen:



We assume that the different values of body weights in our population occur with frequencies that can be plotted in a so-called bell shaped graph, with the mean body weight in the middle: a normal distribution. Assuming that in today's society, both men and women clean kitchen countertops, we take the mean and standard deviation values for adult body weights from the general fact sheet^a. In subsequent calculations, ConsExpo 4.0 randomly draws values out of this distribution to estimate the exposure levels and displays the results in a distribution graph. This is explained in more detail

^a While performing an exposure assessment using ConsExpo 4.0, the appropriate exposure scenario and values for many parameters may sometimes be unknown. In these instances, default scenarios and default values are available in ConsExpo fact sheets, which are available for a number of product categories. The fact sheets are in the process of being updated and will be available soon on www.rivm.nl/ConsExpo.

in the [Output refined](#) section. Return to the main screen by clicking the button.

OK

We now move on to the [Exposure Routes](#) section, where in this refined exposure assessment, we will 'translate' the exposure scenario in more specific models. Exposure takes place via inhalation of 'License-to-kill' evaporating from the surface of the countertop during and after the cleaning. In addition, dermal exposure takes place via the hands, while immersing the cloth in water containing kitchen detergent. We will use more refined models for both the inhalation and the dermal route. Again, the oral route and the mixing and loading scenario are not considered in this tutorial.

The inhalation route

Exposure via the inhalation route in this tutorial consists of inhaling 'License-to-kill' that evaporates from the surface of the kitchen countertop. To estimate exposure via this route with the 'refined approach', more information is needed on the use of the kitchen detergent.

Inhalation exposure

In our exposure assessment, exposure takes place via inhalation of 'License-to-kill' vapour from the kitchen countertop surface. The three modes of release offered by ConsExpo 4.0 all describe the release of a compound in the air, but differ in the assumptions and required information. The instantaneous release mode can be used when very little information is available on the product and the properties of the compound, or when one is interested in a worst case estimation as a first tier approach. We have used this mode in the estimation of the upper exposure level in the [Exposure routes first tier](#) section. Now we will use the more complex mode of release, the evaporation mode, where information is required on the release area and the release rate.

Inhalation: evaporation model

general

exposure duration: minute D 30

product amount: gram D 68.4

weight fraction compound: fraction D 0.00014

room volume: m3 D 15

ventilation rate: 1/hr D 2.5

mode of release

instantaneous release

☒ All of the chemical is released at once into the room.
Use as a first tier approach

constant rate

☐ The chemical is released with a constant rate in a certain time.
Use when details of evaporation are not exactly known

evaporation

☒ The chemical is released by evaporation.
Use when details of evaporation are known

release area

release area: m2 D 1.71

application duration: minute D 3.2

☐ evaporation is from a constant surface (i.e. from a can)

☒ the area of release increases over time (i.e. in case of painting)

release rate

Note: all data at application temperature

temperature: Celsius D 20

molecular weight: g/mol D 46.1

vapour pressure: Pascal D 300

mass transfer rate: m/min D 5.5E3 default

☐ the product is the compound in pure form

mol weight matrix: g/mol D 18

OK Cancel Help

Parameter values that are needed for all modes of release were already filled out when we used the first tier approach and will remain the same.


Parameter values needed in the evaporation mode of release are:

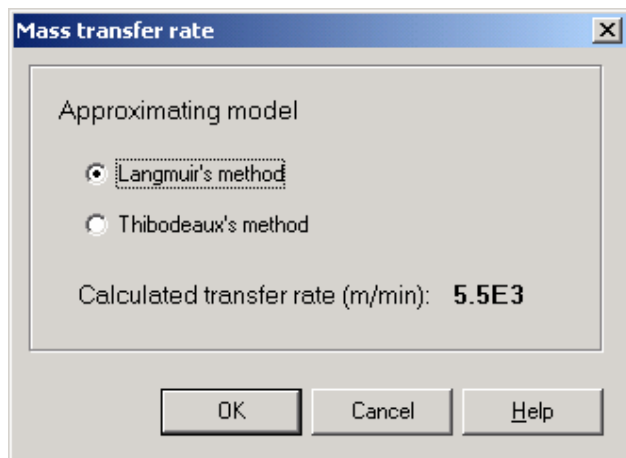
- Release area: The area from which the compound can evaporate. As before, we assume the surface area of a kitchen countertop is 1.71 m²^a.
- Application duration: The time it takes to apply the product to the surface. We assume that cleaning a kitchen counter top takes 3.2 minutes^a.


Two options are available for the release area:

- Evaporation is from a constant surface. This option is appropriate if the compound is released from a surface area that remains the same size over time, for example, from a stick-on or plug-in house perfume.
- The area of release increases over time. This option is appropriate when the area from which the compound is released is not of a constant size. While cleaning the kitchen countertop, the area to which the suds are applied increases in time while wiping the surface. This option is therefore selected.

The other parameters needed for the evaporation mode of release relate to the physicochemical properties of the product and the compound of interest. The values for these parameters have already partially been filled out in the ['Product & Compound'](#) section. The parameter not filled out yet is the 'mass transfer rate'. This parameter describes how fast a compound is transferred between the liquid and the air. ConsExpo 4.0 offers two methods to calculate a default value. Clicking the

 button displays the following screen:




The Help file and the ConsExpo 4.0 manual can assist in selecting the appropriate model. For this scenario involving the evaporation of a compound from an aqueous solution, both models can be used. The Langmuir method will predict higher peak concentrations and will be selected for the purpose of this tutorial. Selecting the desired method will automatically display the calculated value. Clicking 

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brings us back to the evaporation model dialog where the calculated value is filled out.

In our tutorial example, the 'License-to-kill' is contained in a kitchen detergent which is dissolved in water. We will therefore leave the checkbox in front of 'the product is the compound in pure form' unchecked. This requires us to fill out a value for the 'molecular weight of the matrix', meaning the average molecular weight of the rest of the total product minus the compound of interest. Since the product in this tutorial is the suds containing the kitchen detergent, it consists mostly of water. The molecular weight is therefore approximately 18 g/mol.

Click  to go back to the main screen. Since we have only one model for the inhalation uptake, and we have used this already in the first tier approach, the values will be the same and we can skip this part.

We now move on to the dermal route.

Dermal route

The dermal route of exposure while cleaning a kitchen counter top consists of immersing the hands in the suds containing the kitchen detergent with 'License-to-kill' and subsequently wiping the surface with a cloth.

Dermal exposure

A compound can reach the skin via different ways of 'dermal loading'. Depending on what dermal loading option is chosen, a number of parameters need to be filled out. For the estimation of the upper level of exposure we used the instant application mode. To refine the exposure assessment, we would like to use a more specific mode. The dermal loading of 'License-to-kill' on the skin during the immersion of the hands in the suds can be described by the diffusion mode: 'License-to-kill' diffuses through the suds which are in direct contact with the skin:

Dermal: direct product contact

exposed area: cm2 D 2.09E3

dermal loading

instant application

☐ product applied at once to skin (Use as first tier)

constant rate

☐ product applied to the skin at a constant rate

rubbing off

☐ product is initially applied to a surface and consequently transferred to the skin by dermal contact with the surface

migration

☐ compound migrates from a material in direct contact with the skin (i.e. clothing)

diffusion

☒ the compound diffuses through the product which is in direct contact with the skin

compound concentration: g/cm3 D 0.00014

diffusion coefficient: cm2/min D 2.4E-5

layer thickness: centimeter D 0.01

exposure time: minute D 3.2

OK Cancel Help

A parameter needed for all modes is the 'exposed area' parameter - the area of skin exposed to the compound. The value for this parameter is the same as that used for our estimation of the upper exposure level: the surface area of the hands and lower arms is 2085 cm²^a.


The parameters needed for the diffusion mode are:

- compound concentration: it is assumed that 7 g of kitchen detergent containing 10% 'License-to-kill' was dissolved in 5 litres water^a. The concentration of 'License-to-kill' in the suds is therefore 0.7g / 5 liter = 0.14 g/liter
- diffusion coefficient: the rate at which the compound moves in the product by diffusion. For 'License-to-kill' in water, the diffusion coefficient is 2.4 x 10⁻⁵ cm²/sec.
- layer thickness: the thickness of the layer of product on the skin. It is assumed that not the total amount of suds is in contact with the skin but only a layer around the exposed skin. Consistent with the EU Technical Guidance


^a While performing an exposure assessment using ConsExpo 4.0, the appropriate exposure scenario and values for many parameters may sometimes be unknown. In these instances, default scenarios and default values are available in ConsExpo fact sheets, which are available for a number of product categories. The fact sheets are in the process of being updated and will be available soon on www.rivm.nl/ConsExpo.

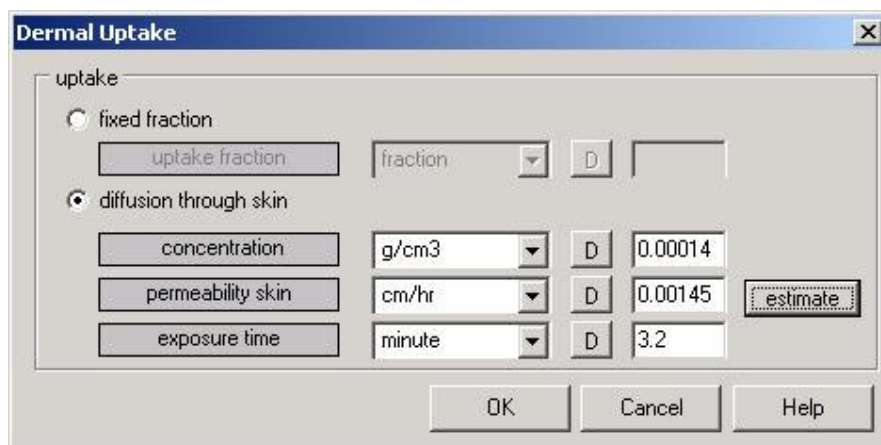
Document on Risk Assessment (2003), we assume the thickness of a product layer on the skin is 0.01 cm.

- exposure duration: The time it takes to apply the product to the surface. We assume it takes 3.2 minutes to clean a kitchen countertop^a.

When all parameters are filled out, clicking the  button brings us back to the starting screen.

Dermal uptake

Selecting the 'Uptake' topic under the 'Dermal' header by pressing the arrow button  gives access to the uptake model dialog:



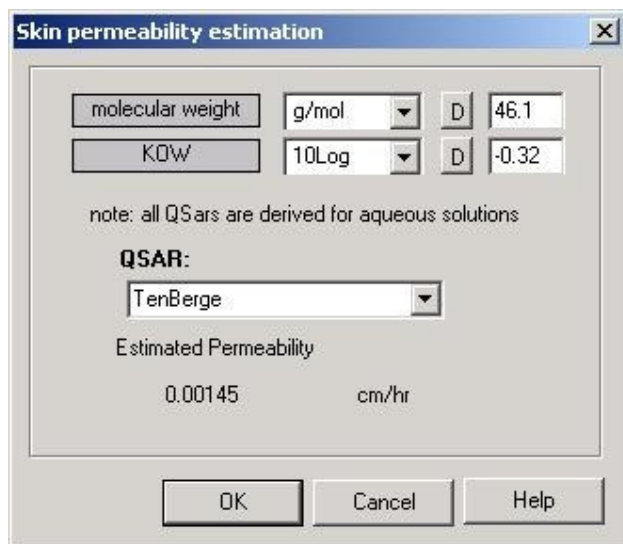
Two modes of uptake can be chosen: 'fixed fraction' or 'diffusion through skin'. We have used the first mode for our estimation of the upper exposure level. We will now use the latter mode, which can be used when information is available on diffusion of the compound in an aqueous solution. The required parameter values for this mode are:

- Concentration: the concentration of the compound in the product. We assume that 7 g of kitchen detergent containing 10% 'License-to-kill' was dissolved in 5 liters water^a. The concentration of 'License-to-kill' in the suds is therefore $0.7\text{ g} / 5\text{ liter} = 0.14\text{ g/liter}$ or 0.00014 g/cm^3 .
- Exposure time: the duration of exposure to the compound via the dermal route. Although the person cleaning the kitchen countertop is assumed to remain in the kitchen for 30 minutes, the actual dermal exposure only takes place while wiping the surface, which we previously assumed to take 3.2 minutes^a.
- Permeability skin: the rate at which the compound can be taken up through the skin, which depends on the molecular weight and the KOW. Usually this value

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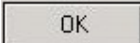
should be obtained from experimental data. For the purpose of this tutorial, we will demonstrate the use of one of the five QSARs offered by ConsExpo 4.0 to estimate this permeability.


Clicking on  displays the following screen:



The dialog box titled "Skin permeability estimation" contains the following elements:

- Input fields for "molecular weight" (g/mol) and "KOW" (10Log), both with units and values (46.1 and -0.32 respectively).
- A note: "note: all QSARs are derived for aqueous solutions".
- A dropdown menu labeled "QSAR:" with "TenBerge" selected.
- A label "Estimated Permeability" followed by the value "0.00145 cm/hr".
- Buttons for "OK", "Cancel", and "Help".

Values for the molecular weight and KOW are already displayed, as they were filled out in the ['Product & Compound'](#) section. The help file and the ConsExpo 4.0 manual give more information on the available QSARs. When we select the desired QSAR, the estimated permeability of the compound is automatically displayed. Clicking  brings us back to the dermal uptake dialog, where the estimated value is filled out.

Clicking the  button again brings us back to the starting screen.

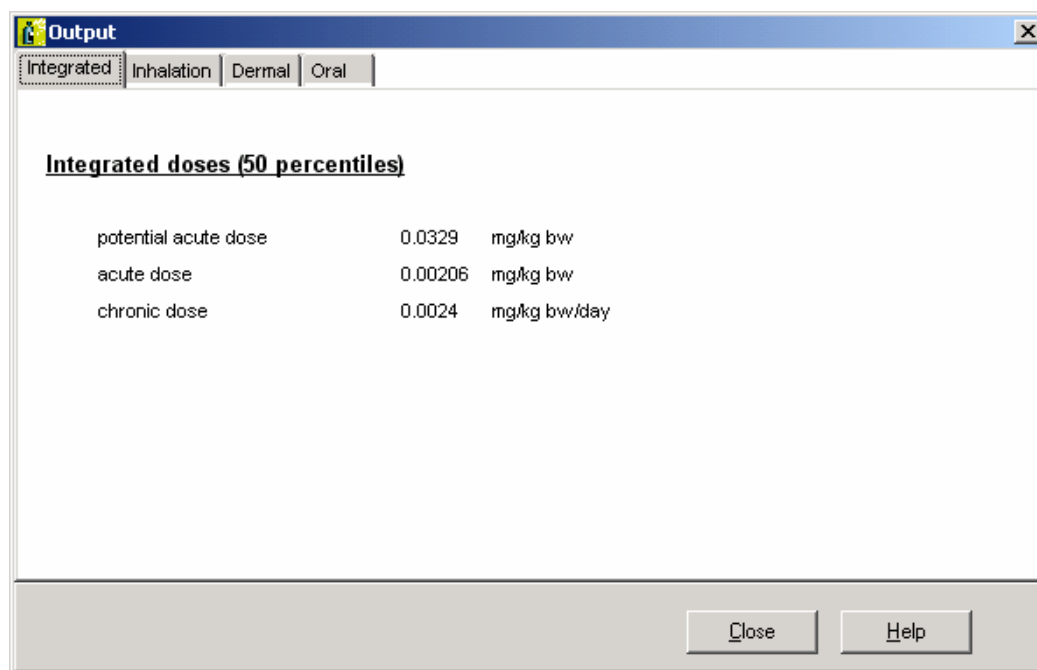
The information needed for our more refined exposure assessment is now complete and the estimated exposure levels can be viewed in the ['Output refined'](#) section.

Output - refined

In the '[Output first tier](#)' section, we looked at the results of our exposure assessment using first tier models for a worst case upper exposure level. In this section we will look at the results of our more refined exposure assessment using more specific exposure and uptake models for the inhalation and dermal routes. For a correct interpretation of the results, it is always recommended to not just look at the point values but also at the graphs, the sensitivity and the distributions.

Point values

The point values field allows us to quickly view our mean acute and chronic exposure levels:

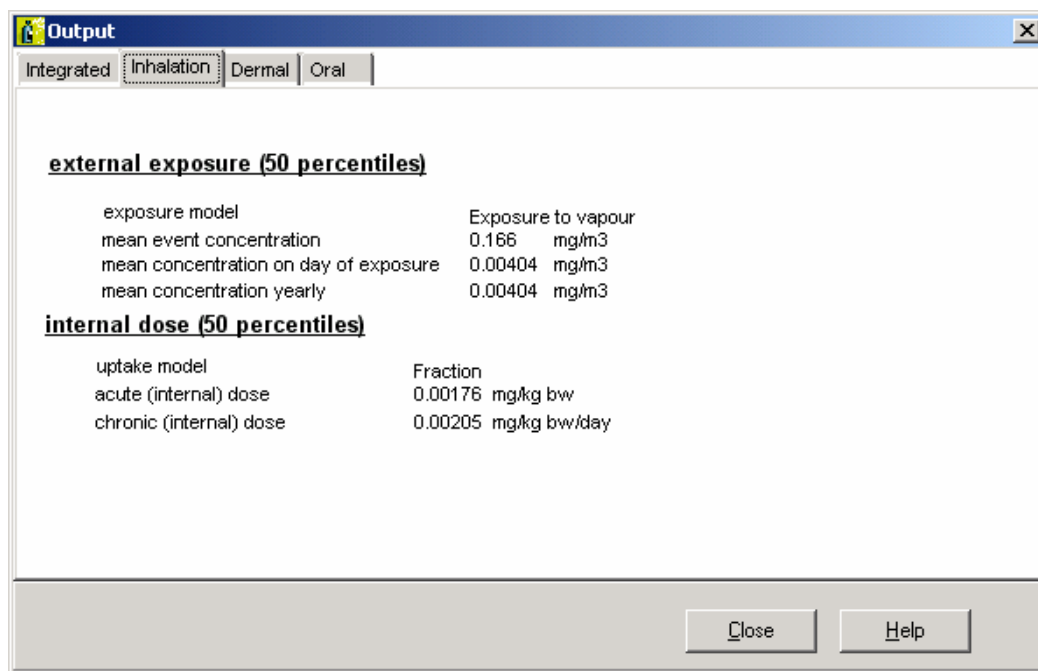


The screenshot shows a software window titled 'Output' with four tabs: 'Integrated', 'Inhalation', 'Dermal', and 'Oral'. The 'Integrated' tab is selected. Below the tabs, the text 'Integrated doses (50 percentiles)' is displayed. A table follows with three rows of data. The first row shows 'potential acute dose' as 0.0329 mg/kg bw. The second row shows 'acute dose' as 0.00206 mg/kg bw. The third row shows 'chronic dose' as 0.0024 mg/kg bw/day. At the bottom right of the window are 'Close' and 'Help' buttons.

<u>Integrated doses (50 percentiles)</u>		
potential acute dose	0.0329	mg/kg bw
acute dose	0.00206	mg/kg bw
chronic dose	0.0024	mg/kg bw/day

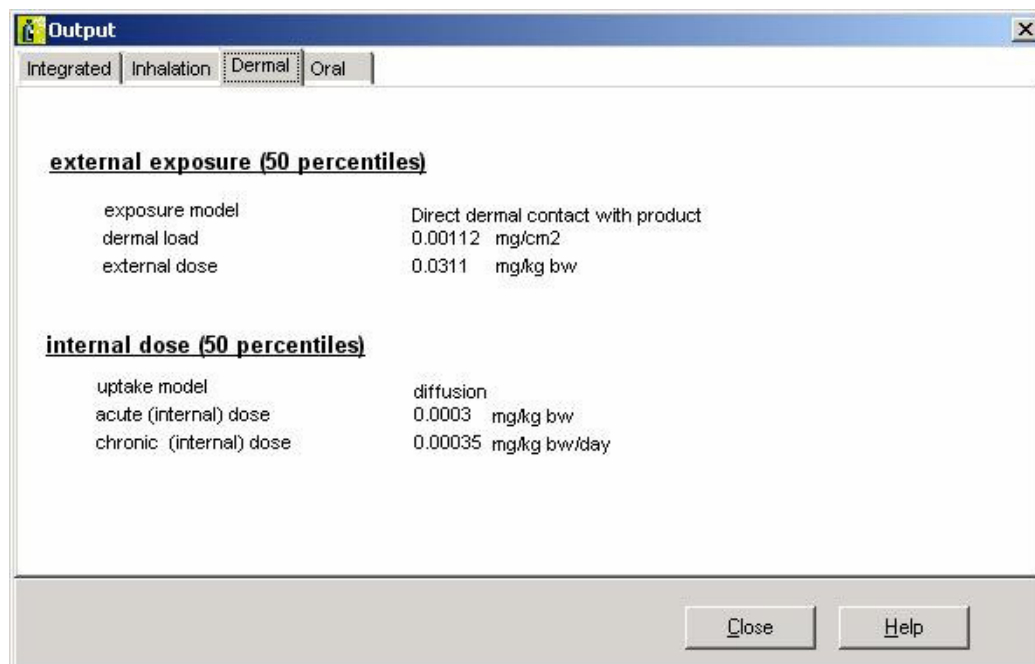
The potential acute dose of 'License-to-kill', i.e. the dose the person cleaning the kitchen countertop is exposed to, is 0.0329 mg/kg bw per cleaning event. This is only slightly lower than the upper potential dose calculated with the first tier models (0.0431 mg/kg). However, the actual acute dose, i.e. the dose taken up in the body, is now 0.00206 mg/kg bw per event compared to the 0.0431 mg/kg calculated before. In addition, the estimated chronic dose of 'License-to-kill' taken up in the body as a result of cleaning the kitchen countertop 426 times per year is now 0.0024 mg/kg bw/day compared to the 0.0502 mg/kg bw calculated with the first tier models. We can investigate the origin of this difference by looking at the data for the individual exposure routes.

Selecting the inhalation route gives the following display:



Compared with the results of the first tier approach, all exposure concentrations are lower than with the refined exposure assessment, demonstrating the value of performing a more detailed exposure assessment. Whereas the results of the first tier approach may have been a cause for concern, the more specific models in the refined exposure assessment may show the risk is much lower.

We would also like to know whether the refined exposure assessment had any effect on the estimated dermal exposure levels. We therefore switch to the 'Dermal' tab:



The screenshot shows a software window titled 'Output' with four tabs: 'Integrated', 'Inhalation', 'Dermal' (selected), and 'Oral'. The 'Dermal' tab displays two sections: 'external exposure (50 percentiles)' and 'internal dose (50 percentiles)'. The first section lists 'exposure model' as 'Direct dermal contact with product', 'dermal load' as '0.00112 mg/cm2', and 'external dose' as '0.0311 mg/kg bw'. The second section lists 'uptake model' as 'diffusion', 'acute (internal) dose' as '0.0003 mg/kg bw', and 'chronic (internal) dose' as '0.00035 mg/kg bw/day'. At the bottom right are 'Close' and 'Help' buttons.

external exposure (50 percentiles)	
exposure model	Direct dermal contact with product
dermal load	0.00112 mg/cm2
external dose	0.0311 mg/kg bw

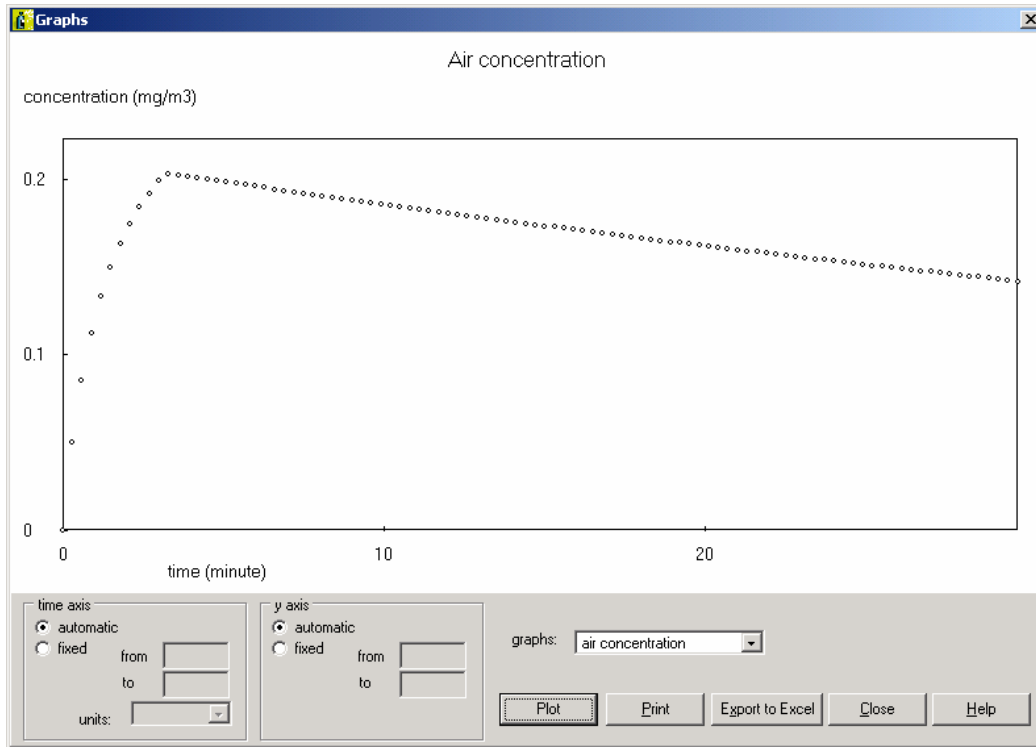
internal dose (50 percentiles)	
uptake model	diffusion
acute (internal) dose	0.0003 mg/kg bw
chronic (internal) dose	0.00035 mg/kg bw/day

As we can see, the external exposure levels are not much lower than the exposure levels calculated with the first tier approaches for which estimates were 0.0014 mg/cm² or 0.039 mg/kg. Apparently, for 'License-to-kill', it makes little difference whether the instant application mode or the diffusion mode is used to calculate the external exposure level. This is apparently due to the fact that 'License-to-kill' diffused through the suds on the skin at a very high rate, such that it resembles the scenario of instantly applying the compound to the skin.

However, the internal doses are significantly lower than those calculated with the first tier approach (0.0392 mg/kg bw and 0.0457 mg/kg bw for acute and chronic dose, respectively). In the first tier approach, we assumed that all of the 'License-to-kill' would be taken up by the skin. Based on the properties of 'License-to-kill', the diffusion model used in the refined exposure assessment estimated a much lower uptake, leading to a much lower systemic exposure. Needless to say this may be of great importance in the risk assessment.


Graphs

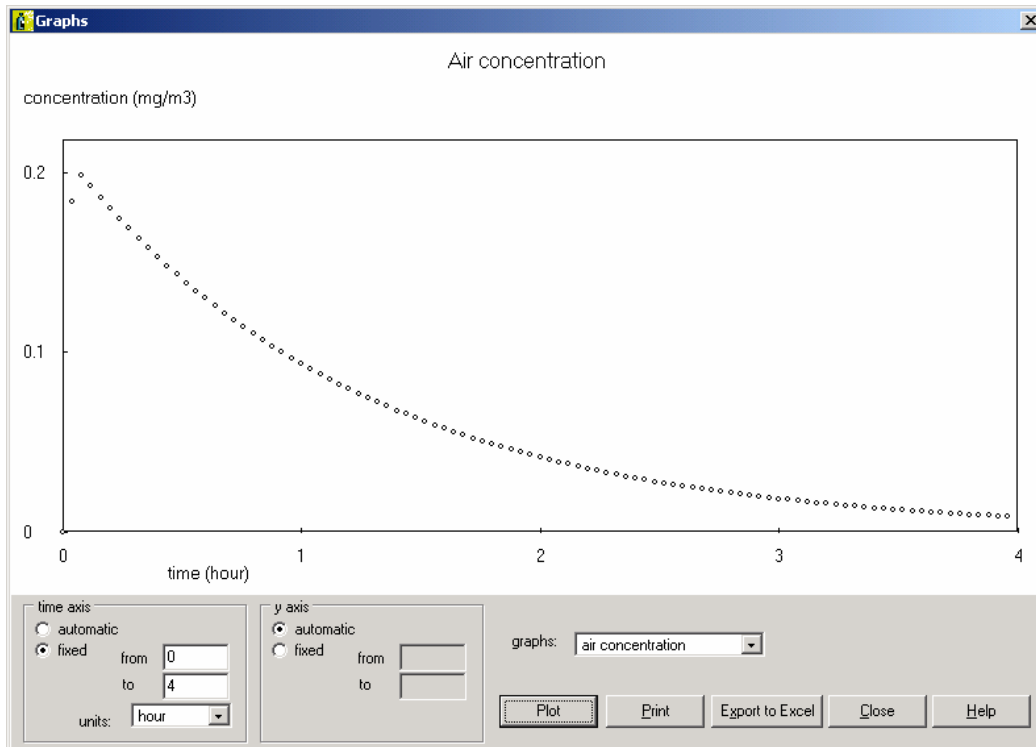
The graphs allow the user to study the process of exposure in time. For example, if we plot the air concentration of 'License-to-kill' against time, the following graph is displayed:



As we left the time axis on 'automatic', ConsExpo 4.0 automatically only displays the air concentration during the actual exposure time. We can see that the air concentration of 'License-to-kill' is at its maximum after approximately 5 minutes and, similar to the first tier approach, gradually decreases throughout the cleaning event.

However, we may also be interested in what a person is exposed to when entering the kitchen a few hours after the cleaning event. For this purpose we can enter our time period of interest, say 0-4 hours, by selecting the 'fixed' option under 'time axis'. The

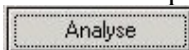
following graph is displayed when we press :



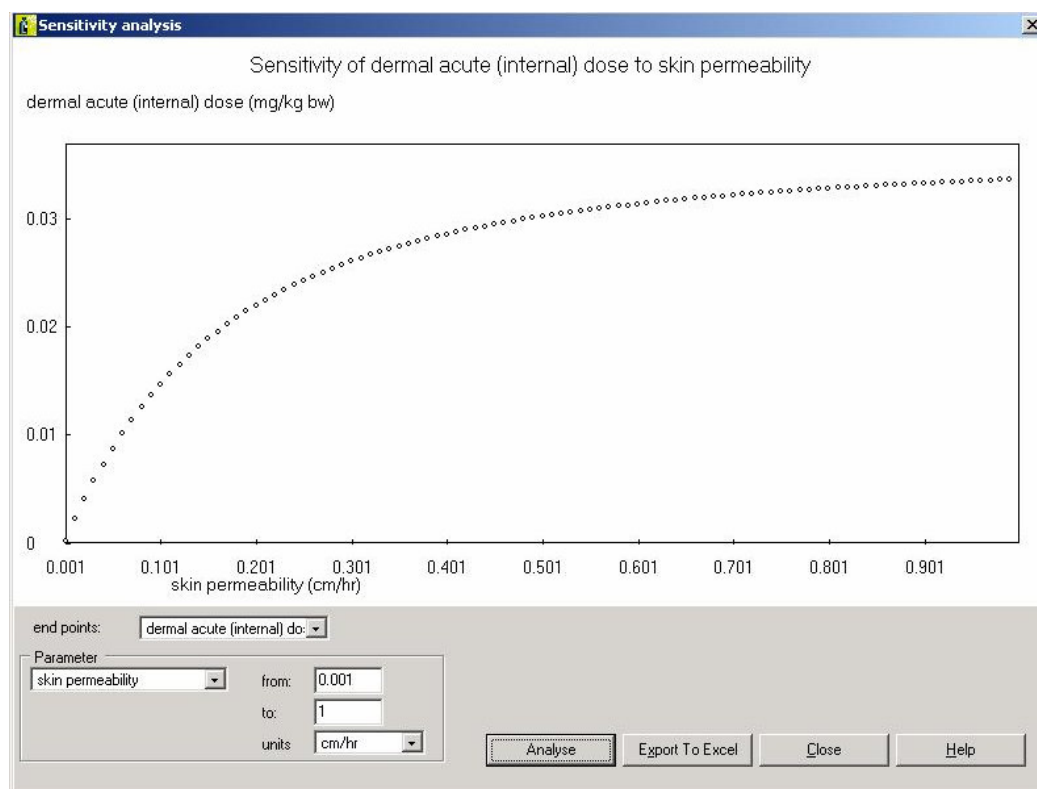
The new graph gives a broader idea of the course of the air concentration of 'License-to-kill' in the hours after the cleaning event. The data points of the graph can be exported to Microsoft Excel by clicking the button, so that the graph can be reproduced and further analysed in this program.

Sensitivity

As discussed before, we have seen that the estimated dermal uptake is significantly lower using the diffusion model instead of the fraction model used in the first tier approach. To determine how the skin permeability influences the results, we can do a sensitivity analysis. We select under 'endpoints' the dermal acute (internal) dose define under 'parameter' a skin permeability varying from 0.001 to 1 cm/hr and press




The following graph is displayed:

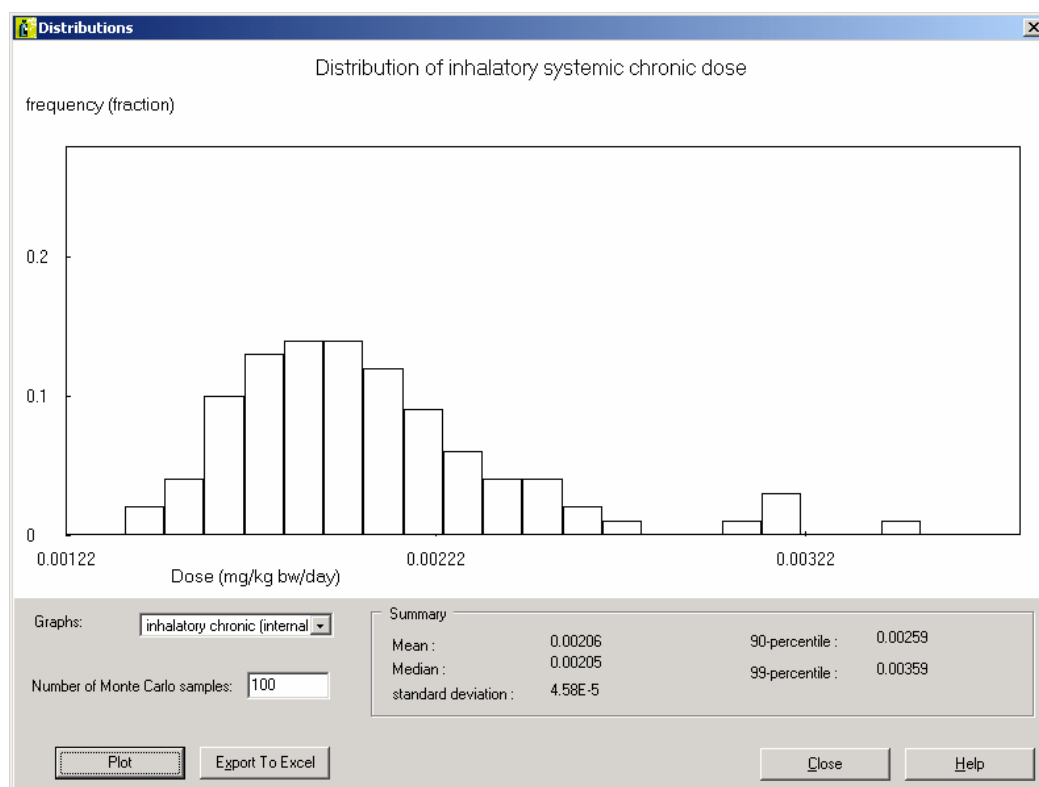


As suspected, the skin permeability greatly influences the dermal uptake of 'License-to-kill', and at a skin permeability of 1 cm/hr, the uptake nearly approaches that calculated with the first tier approach, assuming a 100% uptake.

Distributions

For this more refined exposure assessment, we have used a stochastic distribution for the body weight parameter. ConsExpo 4.0 can calculate the exposure levels based on this distribution, for example, the chronic inhalation dose level. For this, we select the inhalatory chronic (internal) dose level from the scroll list next to 'Graphs'. We also have to define the number of Monte Carlo samples that should be drawn from the pool of distributed body weight values. The calculations become more accurate with an increasing number of Monte Carlo samples, and a suitable number would be 1000 samples. However, with the models used in this refined exposure assessment, the calculations take a lot of time. For the purpose of this tutorial, we will therefore use 100 Monte Carlo samples.

Pressing  starts the calculations of the distributed inhalatory systemic chronic dose. Note that these calculations still may take up to 5 minutes. The following graph is displayed:



This graph represents the distribution of chronic inhalation dose levels for a population whose average body weight is 75 kg and normally distributed with standard deviation 13.9. Note that with a Monte Carlo distribution, the calculated values for mean, median, 90- and 99-percentile are not exactly the same every time the calculation is repeated. This is because the calculations are based on random drawings from the pool of distributed values of, in this case, body weight.

Report

The report presents a summary of the exposure assessment, including the selected models and values of the parameters. The report can be printed for easier comparison with the results of the first tier exposure assessment.