National Institute for Public Health
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PACEM background information

Version 1.1

Including guidance on how to perform an analysis using PACEMweb in chapters 8 and 9.

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1 Aggregate exposure and PACEM

Some chemical substances, for example some fragrances and preservatives, are used in many consumer products. Examples are personal care products, household cleaning products and do-it-yourself products. On a single day a person can be exposed to these substances via multiple products. To estimate the total daily exposure of a person, the exposures from all products used on that day need to be summed. For this purpose the Probabilistic Aggregate Consumer Exposure Model (PACEM) has been developed by RIVM, in cooperation with ETH Zürich and Radboud University of Nijmegen. The development of the model has been funded by the Dutch Ministry of Public Health, Welfare and Sports and by the CEFIC Long Range Initiative program.

Within PACEM aggregate exposure is defined as the combined exposure to one substance from multiple sources, and if applicable, via multiple routes of exposure (such as ingestion, inhalation and dermal uptake). Related and sometimes synonymously used denominations for aggregated exposure are total exposure, cumulative exposure and combined exposure.

The model is based on realistic product usage information obtained from surveys. Currently, information on the usage (frequency and amount) of personal care products and household cleaning products in various European countries is included. PACEM has previously been applied and tested in a number of cases studies considering several substances: diethyl phthalate, parabens, decamethylcyclopentasiloxane (D5), geraniol, isothiazolinones and bisphenols (Delmaar et al. 2014; Dudzina et al. 2015; Ezendam et al. 2018; Gacia-Hidalgo et al. 2018; Gosens et al. 2014; Jongeneel et al. 2018; Karrer et al. 2019; Nijkamp et al. 2015). In 2021, in a project funded by the Long Range Science Strategy (LRSS) program of Cosmetics Europe, the PACEM model as described in Ezendam et al. (2018) has been made available in the web tool called PACEMweb. If you have any comments or questions you can contact us via pacemweb@rivm.nl.

1.1 How does PACEM calculate aggregate exposure?

PACEM evaluates the aggregate exposure of a population. The basis for the assessment of exposure is data on product usage in the population, obtained from surveys. The survey data contain two aspects of information: information on the persons using the products (e.g. body weight, sex) and information on the product usage.

The product usage of the persons in the survey will vary from day to day and this is taken into account in PACEM. From each survey, the product usage information is formatted in a standardized way, namely as a product use diary (see chapter 3 for details).
The product use diary of a person consists of records in the PACEM database that contain the day on which a product is used, the product that is used and the amount of the product used on the particular day.

To evaluate exposure, the information on product usage is combined with information on product composition (i.e. which products contain the substance in which concentration).

Calculation of exposure in PACEM is done according to the following steps:

1) Construct a model population by copying the personal information and product usage data for all individuals in the survey(s)
2) Model product usage in this model population, by copying all days in the diary of each person in sequence or simulate diaries for the surveys in which only summary product usage information is available
3) Combine the product usage information for each person with the information on product substance concentration. Assign concentrations (fraction of substance in the product) to each of the products used
4) Calculate the exposure per product use event for all individuals and all simulation days
5) Aggregate the calculated exposure per day by summation of all exposure events for all individuals and all simulation days
6) Determine exposure in different exposure metrics per individual from the daily exposure estimates

Step 1 and 2 are described in detail in chapter 3, taking the surveys described in chapter 2 as a starting point for creating the diaries for the model population. These two steps are generic and result in the diary of a model population.
The following steps 3 to 6 are specific for a substance or exposure assessment purpose, and are described in the chapters 4 to 8. The exposure metric is addressed first (chapter 4), because it determines the how the exposure is to be calculated. To calculate the exposure, user input is needed on exposure fractions (chapter 5) and product composition (chapter 6). The exposure calculation itself (chapter 7) requires an assumption on the time frame of aggregation (7.1). Finally the results of a calculation can be expressed in several ways, which are addressed in section 7.2.

Chapters 8 and 9 describe the inputs and settings to perform an aggregate exposure assessment with PACEMweb.

2 Product usage information

PACEM requires product usage patterns across populations to derive the exposure to some substance from the use of consumer products. Two surveys describing personal care product (PCP) usage are available in PACEM, and one considering household cleaning products (HCPs). The PCP surveys are designated as the Dutch PCP survey and the European PCP survey. The HCP survey is referred to as the European HCP survey. Short descriptions of these three surveys are provided below. The experimental setup of the surveys do not necessarily meet the general requirements on data information needed by the conceptual model implemented in PACEM. The various strengths and weaknesses of the surveys will be highlighted, and the conversions made to enable application of the surveys in PACEM.

2.1 PACEM data requirements

PACEM is a person-oriented model, i.e. the exposed person is taken as the central entity in the exposure calculation. Aggregation is performed by adding-up of the product exposures based on the exposed person's product use pattern. In principle, person-oriented modelling can be deterministic, in which case the person represents a homogeneous group of product users sharing a common pattern of product use. In PACEM, however, the person-oriented model is probabilistic and the exposed person is considered to represent a specific individual in an exposed population. By taking the exposed person rather than the product as the central unit of exposure evaluation, unrealistic combinations of product exposures that will not co-occur in reality are prevented.

To derive the aggregate exposure of a population, PACEM requires the product usage patterns of the individuals of the population. The product usage pattern of an individual exist of the products used by the individual on a specific day, and the amount of the products used. This information is termed the product use diary (of an individual). Depending on the type of assessment (see chapter 7) multiple days may be required in a diary. In addition to the individual's diary, some anthropometric data needs to be known for each individual, e.g. sex and body weight, to enable the exposure assessment of various subpopulations and express exposure in various units.

2.2 Dutch PCP survey

2.2.1 *General description*

Biesterbos et al. (2013) report the frequency of use and the amount of 32 PCP among 516 adult (age 18-70) men and women from the Netherlands. General information of the participants was recorded, i.e. their body weight, age, sex, level of education, skin type, skin colour, smoking habits and alcohol use.

The participants indicated their frequency of use of each of the 32 PCP by selecting one of the provided frequencies: <1, 1-2, 3-4, 5-6 times per week or 1 or ≥2-3 times per day.
The amount of product used per application was surveyed using photographs to visualize the amount of product used in the following product categories: general hygiene (e.g. deodorant), shaving products, hair care, skin care and tanning products (Annex I). The photographs contained three images displaying an increasing amount of product. The weight of the amount of product shown in each of the images was recorded. This information was used to transform the categorical data provided by the respondents into amounts (see section 2.2.3).
For several PCPs the visual display of amounts was not meaningful. For these products the participants were asked to indicate how often they sprayed (spray products), where they applied the product (eye shadow, eye pencil and lip pencil), and how many layers they applied (mascara, eyebrow pencil, lip pencil, lipstick, lip balm and nail polish). The amounts corresponding to the answers to these questions were derived based on a small experimental study measuring the amount used per spray, application or layer.

In addition, information was recorded on the type and brand of the product, the application area on the body, the time of day a product was used (e.g. morning or evening), the location of use (indoors or outdoors) and the presence of ventilation. All of the questions concerned use within the past 6 months, except for the questions regarding tanning products, which covered the past year to minimize seasonal influences.

2.2.2 *Representativeness*

Biesterbos and co-workers (2013) consider that the usage patterns and circumstances of use of PCPs collected in their study are fairly representative for the Dutch adult population, as they started with a random sample of Dutch citizens living throughout the entire country and there are no indications for selective non-response. In addition, they note that most results seem to be logic and are generally as expected. However, the authors state that the highly educated respondents may be slightly overrepresented compared to the Dutch general population.

Considering the general information of the participants on age, sex and level of education, the fractions reported in the publication are listed in Table 2.1. This table also shows the fractions found in the entire population according to the Dutch Central Bureau of Statistics (CBS). The CBS data indicate that men and the age group 18-39 are underrepresented in the Dutch PCP survey. The CBS data confirm the author's notion that the highly (≥15 yr) educated respondents are overrepresented (and the 6-10 yr education group is underrepresented). General information on skin type and skin colour is not available in the Netherlands. Therefore, it cannot be determined whether the surveyed population is a representative group considering these characteristics.

Table 2.1

	Fraction (%) in Dutch PCP survey	**Fraction (%) according to Dutch Central Bureau of Statistics (CBS) in 2012**
Men	41	49.5 *
Women	59	50.5 *
Age 18-39 yr	21.6	40.9 #
Age 40-54 yr	36.9	59.1 $
Age 55-71 yr	41.5	
Education 6-10 yr	24.2	29.9 **
Education 11-14 yr	38.6	38.6 **
Education ≥15 yr	37.2	30.7 **

* all ages, # fraction age 20-40 of age 20-65, $ faction age 40-65 of age 20-65
https://opendata.cbs.nl/statline/#/CBS/nl/dataset/37296ned/table?ts=1556544954033
**CBS website: age 25-75, 2012,
https://opendata.cbs.nl/statline/#/CBS/nl/dataset/82816ned/table?dl=19D07

Consumer behaviour (i.e. usage of PCPs) is influenced by socio-cultural and marketing variables. These issues make it hard to generalize the product use patterns from the Dutch PCP survey to other countries or regions outside the Netherlands.

The population size (516) is rather small, which causes limitations on granularity (i.e. smallest size of subsetting a population). In addition, the survey does not contain product use information of children (ages <18).

Survey participants were asked to provide frequency of use per product in the past 6 months, except for the questions regarding tanning products, which covered the past year to minimize seasonal influences. A benefit of obtaining frequencies (compared to diary information) is that low frequency use is included. In this survey no information was obtained on co-use.
Each participant provided the amount of use per application. For more details, see Biesterbos et al. (2013).

The survey covers 32 PCPs (see list in Annex I). For each specific exposure assessment, it should be checked whether this list of PCPs sufficiently covers the products containing the substance of interest

2.2.3 *Conversion of surveyed data*

For the application of the survey information several adjustments and conversions are required to build a product use diary.

For each individual their location (all in the Netherlands), sex and body weight were taken from the survey without any modifications. Subsequently, a 14-day diary was created, which was randomly filled with the products used by the individual. Daily use of the product is simulated for each individual in the population for each day of the 14 days by:

1) (at random) determining whether the product will be used on a particular day, based on the use frequency data available for the

modelled individual. The product-use database contains a list of PCPs applied by each questionnaire respondent. The product use frequencies had to be specified by the questionnaire respondents as value ranges. Accordingly, for these quantities we defined uniform uncertainty distributions in the respective ranges (e.g. the product use frequency of "2–3 times per week" was translated into a uniform distribution with minimum = 2/7 and maximum = 3/7 times per day) (Annex III).

2) Assigning a 'used amount' of product to the use event, based on the product usage information of the modelled individual. Used amounts were surveyed using photographs. The photographs contained three images displaying an increasing amount of product. The weight of the amount of product shown in each of the images was recorded. This information was used to transform the categorical data provided by the respondents into numerical values for exposure calculation. For several PCPs the visual display of amounts was not meaningful, and alternative questions were asked, e.g. on the number of sprays. This information was translated into amounts (Annex III)

2.3 European PCP survey

2.3.1 *General description*

The European PCP survey is constructed from multiple underlying studies surveying the use frequency and use amount. The survey reporting the use frequency of PCPs is referred to as the European Toiletries and Cosmetics Database (ETCD-1) (Hall et al. 2007; 2011). ETCD-1 contains the use frequencies of PCPs for France, Germany, UK and Spain obtained in 2007 and 2008. In each country the study inclusion criteria were as follows: Females and males (ratio 70–30%), age 17–74 years, demographically representative sample, including working status and age, habitual users of all products, brands and categories for toiletries and cosmetics. In total data from 23,232 volunteers were obtained. The volunteers reported their frequencies by filling out a diary for seven consecutive days in one or two non-consecutive weeks.

The following information was obtained from each volunteer: country, year and quarter of survey, age, size of household, sex, working status, marital status, child in household, length of hair, type of hair, hair coloured in last 6 months, where and by whom coloured, hand skin type, body skin type, face skin type, skin colour and BMI. For each product used by a volunteer, the following information was recorded: weekday of use, time of use and body part where the product was applied. Note that products used multiple times a day are recorded separately (with different times of use). The survey included 21 products (see Annex I for product list).

The ETCD does not contain the information on the amount (quantity) of product used per application. These data were obtained with the aid of two other studies.

In the ALBA and ICS studies 501 and 496 volunteers, age 17–74, all habitual users of the cosmetic products selected for the study,

completed the full two week usage period of their own products. ‘‘Regular use’’ was defined as any product use occasion recorded during the two week study period. The use of five products was recorded in the ALBA study and seven other products in the ICS study (Annex I). Volunteers declared that they were the sole users of the studied products. Two-week product use was the minimum period judged necessary to obtain accurate product weight differences. For more details about the selection criteria of the studies see Hall et al. (2007; 2011).
Each participant recorded each usage occasion in a diary throughout the two weeks' test period. The products were weighed at the start and end of the study. By dividing the total quantity of product used during the study period by the number of times the product was used (marked in the diary) the average amount of product per use per occasion, was obtained.
The following information was obtained from each volunteer in the ALBA study: country (all Scotland), year of survey (all 2007), age, household composition, sex, working status and body weight.
For the ICS study volunteer characteristics are available on: country (all Scotland), year of survey (all 2004), age group, sex, body height and body weight. For each product used by a volunteer, the amount per use is available.

2.3.2 *Representativeness*

In each of the four countries (Germany, France, UK and Spain) the study inclusion criteria were as follows: females and males (ratio 70–30%), age 17–74 years, demographically representative sample, including working status and age, habitual users of all products, brands and categories for toiletries and cosmetics.
The ETCD-1 data were collected over the period of one year. The ALBA study was performed from September to February, and the ISC study from January until March. In the latter three studies survey weeks were chosen to avoid any coincidence with any holidays, where usage pattern may be temporarily affected.

In Hall et al. (2007, 2011) the data contained in the ETCD-1 survey (and an additional survey conducted in Denmark) were used to generate (weighted) representative populations for each country, and for the EU15. In Hall, the amount data from Scotland are assumed representative to the EU15. Without weighing of the use frequency data and founded assumptions on the representativeness of the use amounts, caution should be taken on the representativeness of the information in the four underlying studies. The use frequency data are representative for the four surveyed countries, and the use amount data are representative for Scotland. The female to male ratio in all underlying surveys is not representative to the European ratio and neither to the individual member states, which is approx. 50-50%[1].
It should be noted that the number of products in the study is rather low, it does not seem to cover most widely used products and product groups. An exposure assessment using the European PCP survey should

[1] https://ec.europa.eu/eurostat/web/population-demography-migration-projections/data/main-tables Accessed on 23 Jan. 2020

be reconsidered carefully in case the assessed substance also occurs in (many) products which are not included in the survey.

2.4 European HCP survey

2.4.1 *General description*

Household cleaning product usage data in PACEM is obtained from the EPHECT study (Johnson & Lucica, 2012). The EPHECT study collected product use data on a variety of products including HCPs in ten different European countries. The target population was the general public, residents of each of the selected countries, aged 18 and older, who are generally in charge of cleaning tasks in their household, and who have used at least one of the selected product classes during the 6 months prior to the survey. Respondent selection was based on two main criteria: only those who were in sole or shared charge of household cleaning tasks, and who have used at least one of the product classes were able to answer the survey.

A selection of the data available from the EPHECT study is used in PACEM. From the surveyed products the household cleaning products were included (listed in Annex II). Other surveyed products, like air fresheners, insecticides, PCPs and coating products for leather and textiles were excluded.
Regarding product use data, the frequency of use (how often a product is used, whether daily, weekly, monthly or less often), quantities of product used (according to the different formats: quantities of liquid, number of sprayings, number of wipes etc.) and dilution patterns (whether or not people dilute the products they use into water) were included. These use data were converted to the use data required by PACEM as described in section 2.4.3. Other characteristics of the product use were surveyed, but not used in the exposure calculation in PACEM, e.g.:

- time of day when the product is used,
- rooms where the product is used,
- surfaces on which the product is used (walls, doors, floors, furniture, windows etc.),
- protection measures (whether people wear gloves, avoid using the product in combination with others, or whether they ventilate when using the product),
- ventilation patterns (whether people ventilate before/during/after using the product, and for how long), and
- reading product instructions (whether or not people read instructions before using a product for the first time).

Data from four countries, Germany, France, UK and Spain, were included, which correspond to the countries surveyed in the European PCP survey. Data of 12 other European countries are not used in PACEM.

2.4.2 *Representativeness*

Sample sizes varied between countries, ensuring national representativity of consumers of the selected product classes by age, gender and region. The survey was designed to ensure representative

samples of product users in each country. The sample design followed national representative quotas, by age, gender and region.

2.4.3 *Conversion surveyed data*

Use frequencies recorded as daily, once a week, several times per week, etc., which were transformed to daily frequencies (Annex IV). In the survey amounts were indicated as number of sprays, caps, tablespoons, tablets or wipes used. These numbers were converted to grams (Annex IV).

2.5 Overview of PCP and HCP surveys

In Table 2.1 an overview is provided on the main characteristics of each survey included in PACEM.

Table 2.1: Overview with survey characteristics important for PACEM
Co-use info means: "do we, for each individual and day, have the use data of multiple products?"
Freq/diary means whether survey participants are asked for their freq(uency) of use in terms of e.g. every day or once a week, or by filling out a diary form.

	Dutch PCP survey	**European PCP survey**			**European HCP survey**
		ETCD-1	**ISC**	**ALBA**	
N	516	23,232	496	501	1774**
Fraction men and women	Men (59%), women (41%)	Men (30%), women (70%)	Men (30%), women (70%)	Men (30%), women (70%)	Men (39%), women (61%)
Age range	18-71	17-74	17-55+	17-74	18+
Country of survey	The Netherlands	France, Germany, UK, Spain	Scotland	Scotland	France, Germany, UK, Spain
Year	2012	2007-2008	2004	2007-2008	2010-2011
BW recorded?	Yes	No	yes	yes	no
No. products	32	21	7	5	7 in various formulations***
Co-use info	No	yes	Limited*	Limited*	no
Contains info on correlation frequency and amount	yes	no	no	no	yes
Freq/diary	Freq	diary	Not recorded	Not recorded	freq
Amounts recorded?	Yes, indirectly	No	Yes, directly	Yes, directly	Yes, indirectly

*not used because this info is obtained from ETCD studies
** only of the four selected countries

*** only the selected products

3 Daily use profiles

3.1 Constructing a model population

The model population is constructed by duplicating all persons from the product usage survey data, and copying his or hers anthropometric and product usage data, and generating a set of exposure days in the way described in 3.2.
This results in a set of individuals and their product use diaries, that are copies representing the product usage surveys.
In the exposure simulation, the entire model population is always taken as the basis of the calculation. That is, all individuals in the model population are used one or multiple times (e.g. with different product concentrations and exposures per use) to estimate their aggregate individual exposure. All individual exposures are finally pooled to represent exposure in the population at large.

3.2 Incorporating product usage data

Product usage data has been collected in different surveys. Data obtained in these surveys is formatted differently. European PCP product usage is collected in a diary as 14 days with information on which products have been used on that particular day. In contrast, in the Dutch PCP survey and European HCP data have been collected as self-reported use frequencies. Specifying how often a product is typically used in a specific time frame.
To combine the data in a common model framework, the usage data is converted to a common format. For each modelled individual, a set of 14 days of product usage is constructed. For the European PCP data, the entire set of days is simply copied from the database on the product usage data. For European HCP and Dutch PCP data, the days are constructed by random sampling, based on the specified usage information. The number of uses of a product on any day in the 14 day diary is assigned by sampling from a Bernoulli trial where the change p of use equals the frequency per day. For example, if the survey data specify that a product is used once a week, on each of the days in the 14 day diary, it is decided whether this particular product is used by random sampling. The product having a probability of $1/7^{th}$ (once a week) to be used on this day. If the frequency of use of a product exceeds 1 (per day), the number of uses is taken to be the use frequency per day from the database. This is always an integer value. This procedure is repeated for all products included in the assessment, on all days of the diary. In this fashion, product usage is expected to reflect (on average) the use frequencies from the survey data. Note, that there is no correlation between the uses of products on each day. For the Dutch PCP survey the use of a product is assumed to be completely independent of the uses of other products. In case a product is used on a particular day in the diary, the amount of product used is determined by sampling from the amount distributions in de product usage surveys.

3.3 Including and scaling household product usage data

Household product usage information is disjunct from the use information on PCPs, i.e. PACEM does not include data in which the combined use of HCPs and PCPs was monitored in the same population. To combine data from the different product groups, it was assumed that product use is completely uncorrelated between the different product groups.

Joining data from the different surveys has been done on the basis of sex and nationality only. When HCP usage data is combined with PCP usage data, first a person is sampled from the model population based on the PCP usage data. This person has a particular PCP use profile. Next, a HCP usage profile is added by randomly selecting an individual from the HCP data set of the same sex and nationality. The HCP usage profile of this person is then merged with the PCP product usage data of the first sampled individual.

It is thus assumed that there is a fundamental distinction in product usage between men and women and between nationalities, but not in other parameters, such as age.

Product usage information on both PCPs and HCPs is available for Germany, Spain, UK and France. PCP data for The Netherlands has been collected in a separate survey. If 'The Netherlands' are selected in a combined PCP and HCP assessment, the HCP usage data for Germany are selected from the HCP data set and combined with the PCP usage data for The Netherlands.

The EPHECT study was conducted among persons in a household that indicated they were responsible for cleaning activities in the house. Using the data as representative of the entire population introduces a bias to over-including product users in the model population.

To correct for this, an assumption was made that only half of the individuals in a household actually use household products. The other half is assumed not to be exposed to household products. This is accounted for by adding persons that do not use any HCP products to the model population of HCP users.

4 Exposure metric and routes of exposure

In PACEM two different exposure metrics are evaluated:

1) Systemic exposure
2) Dermal load

Dermal load is the amount of substance contacting the skin, per unit surface area of the exposed skin (e.g. g/cm^2). Dermal load is typically needed to evaluate exposure of dermal sensitizers. Systemic exposure refers to the amount of a substance that is absorbed across the body boundary. Systemic exposure may occur along one of following exposure routes:

a) Inhalation
b) Dermal
c) Oral ingestion

PACEM includes all three exposure routes for systemic exposure calculations. Doses taken in via different routes are added in PACEM to obtain the total absorbed amount, i.e. the total systemic exposure.

4.1 Absorption fractions

Exposure calculations for the systemic end point, using the exposure fractions, are assumed to refer to external exposure. That, is to the dose that comes into contact with the body exterior (lung-blood barrier, skin, mouth). To estimate the absorbed dose, and to allow integration of the dose over the different routes, absorption should be specified. This is done by providing values for absorption as absorption fraction. Absorption fractions are specified for inhalation, dermal and oral routes separately. Absorption fractions are point values.

4.2 Dermal load

Next to the systemic dose, PACEM allows the calculation of the dermal load. Dermal load is defined as the amount of substance per unit surface area of the exposed skin (e.g. in g/cm^2). Dermal load is used in the risk assessment of sensitizing substances (both for risks of sensitization and elicitation). It is generally assumed that this surface concentration of a substance on the skin is a more predictive measure of adverse sensitisation effects than the total amount delivered to the systemic circulation (Api et al. 2008a, 2008b; Nijkamp et al. 2015; Ezendam et al. 2018).

An evaluation of dermal load requires an estimation of both the amount of substance delivered to the skin and the surface area of the skin exposed. The exposed skin surface area will in practice not be known for each individual in a population. Therefore the process is simplified as follows:

1) The body surface area is sub-divided in distinct body parts
2) Products that are used are assigned to a selection of these body parts (e.g. hands and forearms)
3) For each of these body parts, a separate exposure fraction is defined (called ‘retention factor’ in the case of dermal load). This fraction specifies how much of the product used ends up on the

skin of the body part. Retention factors are product specific. They have to be provided as user input.

4) Exposure is evaluated per body part. Exposures that take place on the same day on the same body part are aggregated to a single dermal load.
5) Dermal load is determined by dividing the amount on the skin by the surface area of the body part. This assumes that the loading on the skin is uniform for the body part, which may be inaccurate and may potentially lead to under-estimation of the dermal load in some scenarios.

PACEM distinguishes the following body parts: hands, feet, head, trunk, legs and arms.
The surface areas of these body parts are determined by the model on the basis of an individual's body weight in two steps. First, the total skin surface area is estimated from body weight, according to (te Biesebeek, 2014):

$$SA = 10^{-1.02} \times BW^{0.7}$$

Where BW is the person's body weight (in kg), and SA the total body surface area (in m^2).
Next, to estimate the body part's surface area, a fixed list of percentages of each of the identified body parts is used (Table 4.1). These are taken from (US-EPA, 2011). They are the 25th percentiles of relative surface areas of body parts in the US population. They are sex-dependent.

Table 4.1. Fractions of different body parts as used in PACEM. Based on the 25th percentiles as reported in (US-EPA, 2011).

Body Part	**Male**	**Female**
Trunk	0.38	0.34
Head	0.068	0.067
Arms	0.15	0.14
Hands	0.052	0.049
Legs	0.33	0.32
Feet	0.067	0.068

From the retention factors, specified by the user, the total exposed skin area is determined: this is the sum of all body parts for which the retention fraction is larger than 0. It is assumed that the used substance is applied to all the exposed body parts in equal measure (i.e. equal amounts per cm^2). Thus, the amount applied per cm^2 surface area σ is given by the amount applied on the skin, divided by the total exposed skin surface area:

$$SA = \sum_{\substack{exposed \\ body\ parts}} SA_i$$

$$\sigma = A/SA$$

From the load on the skin, the dermal load on each body part is determined by multiplication with the retention factor (RF) for the considered body part:

$$dermal\ load = \sigma \times RF_{body\ part}$$

Aggregation is done by adding all exposures on a specific body part that occur on the same day.

As a measure of daily exposure, the body part of each individual is selected on which the highest dermal load occurs.

5 Exposure fractions & retention factors

The basis of an exposure evaluation in PACEM is the amount of product that a person uses in a particular product use event. This product contains a certain amount of the substance under consideration. The amount of substance that is applied when using the product is the source of exposure during the use event. In principle, for each exposure event, the exposure arising from the use of this amount of substance has to be estimated. To simplify exposure calculations, it is assumed that exposure can be represented by a so-called 'exposure fraction' in case of deriving systemic exposure, or 'retention factor' when the dermal load is derived. By applying exposure fractions or retention factors it is assumed that of the amount of product used, a person will be exposed to a fixed fraction (independent of the amount used) of the product. This exposure fraction is assumed to be the constant for a specific product, but may differ between different products.

5.1 Exposure fractions

Evaluation of the exposure fraction has to be done outside of PACEM. As exposure fractions will likely depend on properties of the substance itself (e.g. volatility), exposure fractions and retention factors will have to be derived or obtained on a case by case basis. Exposure fractions need to be developed outside the PACEM tool. They may be derived by using a dedicated consumer product exposure estimation tool (e.g. ConsExpo [2]) and evaluate exposure in a representative scenario, using a unit amount of substance (e.g. one gram of substance). The resulting calculation will directly yield the exposure fraction (e.g. as gram exposure per gram substance used). See Annex VI for guidance on the derivation of exposure fractions.

Variability in the exposure fraction can be accounted for by using probability distribution to specify the fraction. This distribution is assumed to represent the inter-event variability in the EF. Consequently, for each exposure event, a random value of the EF will be sampled from the probability distribution to represent the EF in the particular exposure event. Probability distributions that are supported in PACEM are described in section 8.3.4.

In the case of multi-route (systemic) exposure, a distinct exposure fraction for each route is used (i.e. one for inhalation, one for dermal and one for the oral route). Exposure fractions are specified as probability distributions, to account for variability in event exposure. Samples for the different route exposure fractions are drawn independently, but afterwards, the fractions are normalized in such a way that their sum does not exceed 1 (i.e. that total exposure cannot be more than the amount of substance available). The same applies when the user enters point values which add up to more than 1. Normalization is done as follows: the sum of exposure fractions $\sum Ef$ is determined. If

[2] https://www.rivm.nl/en/consexpo

this exceeds 1, then each individual exposure fraction is divided by the sum $\sum Ef$. So that the total exposure fraction is normalized to 1.

5.2 Retention factors

For the calculation of dermal load, a similar concept to the exposure fraction is used to describe event exposures: the retention factor. The retention factor gives the fraction of the used substance that remains on the skin, after the exposure event.
Retention factors are specified for each product and each body part independently. Body parts distinguished in PACEM include head, trunk, hands, arms, legs and feet. If a substance is applied on multiple body parts, the amount is divided according to the relative size of the exposed body parts. It is only after this distribution step of the substance that the retention factor is applied. Therefore, no additional normalization has to be performed for the sum of the retention factors (i.e. that they be 1 at maximum in total).
When aggregating the exposure from multiple product use events on a single day, it is assumed that different exposures do not influence each other. Retained amounts are simply added.
Retention factors are specified as distributions. The user has a choice from a set of parametric distributions (see section 8.3.4).

As for the exposure fractions, evaluation of the retention factor has to be done outside of PACEM. SCCS (2018), in their notes of guidance, propose default values for retention factors for personal care products (see Annex V). These may be used as generic inputs in PACEM and are, in fact included in the tool as defaults. In addition, specific retention factors for a product or body part may be derived by using a dedicated consumer product exposure estimation tool (e.g. ConsExpo) in a similar fashion as to derive exposure fractions. See Annex VI for guidance on the derivation of exposure fractions and retention factors.

6 Product composition / concentration data

An assessment of aggregate exposure with PACEM requires user input on the extent to which products contain the substance of interest. This comprises two aspects:

1) The occurrence fraction of the substance. This is the fraction of generic products that contain the substance (e.g. 3% of deodorant sprays contain substance X).
2) The concentration of the substance in the product that does contain the substance.

The occurrence fraction is specified as 'fraction products containing substance'. The concentration is specified by a point value or distribution, representing variations in the concentration. Probability distributions that are supported in PACEM are described in section 8.3.4. Product concentrations are modelled in PACEM by assigning concentrations to each (person, product) combination according to:

$$concentration = Bernoulli(occurence) \times P(concentration),$$

i.e. by drawing from a Bernoulli(occurrence) to estimate the probability a product contains the substance and P(concentration) to estimate the concentration in the product in case the product contains the substance. P() can be a point value or any of the supported parametric probability distributions. The product is assumed to be used by the person throughout the exposure period.

To account for distributed inputs of the product concentrations in the calculations, PACEM takes the following approach.
The model population consists of a duplicate of all persons in the survey, recording their personal properties as well as their product use diaries. For each product the person uses, a sample of size N is taken from the product concentration distribution. The person's personal information and diary is duplicated N times and sequentially combined with a product sample (i.e. which has a specific concentration of the substance). Each of the duplicated records now represents a different individual that has the same use pattern, but uses products with a different concentration. The duplicated records are added to the model population. This procedure increases the size of the modelled population by a factor of N.
Exposure is now calculated for all the individuals' diaries, representing both variability in product usage as well as product concentrations.
N, the size of the product sample taken for each individual, is user input. The input parameter is labelled 'Product sample size per simulated individual' in the PACEM user interface.

7 Exposure calculation

To calculate exposure, for each individual his daily product use profile is generated: for each day in the simulated 14-day period, the product use events on that day are determined. For these product use events exposure is evaluated. This yields a set of exposure estimates for a person on each day in the simulation period. This daily exposure profile is retained for subsequent analyses. From this daily exposure profile, the aggregate exposure on the day is determined by adding all event exposures (see also 7.1). If both PCPs and HCPs are included in the analysis, the exposure to PCPs only and HCPs only is determined on that day .
Exposure for each product use is calculated by combining the amount used with the exposure fraction(s) or retention factor(s) of the product and the substance concentration:

$$Dermal\ load = \frac{[amount]\times[concentration]\times[retention\ fraction]}{[exposed\ skin\ surface\ area]}$$

for the dermal load. For each individual, different loads may be calculated for different body parts. Ultimately, PACEM only reports the dermal load on the body part that had the highest exposure. This may be a different body part for a different individual. When systemic exposure is required, the absorption fraction is included:

$$Exposure = \frac{[amount]\times[concentration]\times[exposure\ fraction]\times[absorption\ fraction]}{[body\ weight]}$$

By aggregating exposures of the single product use events PACEM calculates :

- Total exposure on each day for the subsets PCPs and HCPs separately for each person (if both product groups are included in the analysis).
- Total exposure on each day from all products used combined for each person.

For this set of daily exposure profiles, long term average and short term exposure can be determined (see 7.2) for each person.
The population exposure is given by the distribution of the exposure profiles of all individuals in the model population. PACEM thus evaluates the aggregate exposure of a population to (a subset of) all products combined. And this in measures of long term and short term exposure metrics.
From these distributions, different proportions of the aggregate exposure may be determined (e.g. median, 95th percentile).

7.1 Time frame of aggregation

To determine aggregate exposure, exposures from different product use events that are deemed to occur simultaneously, are added. This requires a notion of a time frame within which exposure events are

considered simultaneous. A proper selection of the time frame depends on a variety of aspects, such as the purpose of the assessment, the kinetics of exposure and absorption and distribution of the substance in the body, the toxico-dynamics of the toxicological effects under consideration, the granularity of the product usage data.
The time frame of aggregation in PACEM is chosen as one (calendar) day, meaning that exposures that take place on one specific calendar day are added, and are treated as distinct when they occur on different days.
It should be kept in mind, though that for some applications, this time frame may be less suitable. For example, when results of a PACEM assessment are used to be combined or compared with biomonitoring data of a substance with a short elimination half-life, the one-day granularity may not be able to capture the short time fluctuations in a biomarker. Also, if toxicological responses are in fact the result of a build-up in exposure over multiple days (e.g. result of a prolonged inflammatory response) the time frame of one day may be too short to adequately describe the inter-day correlations in exposure, essential for relating exposure to this type of effect.

7.2 Exposure time frame

For the different exposure metrics (chapter 4) calculated in PACEM, a short term daily exposure and a long term average daily exposure can be derived.
Short term daily exposure is a measure of acute exposure, and is, in PACEM defined as the maximum daily exposure that each individual experiences in the simulation period. To calculate the maximum daily exposure, for each individual the day with on which the aggregate exposure is highest is identified and taken as a measure of the daily exposure.
The long term daily dose is evaluated by determining the average daily dose. For each individual the average (arithmetic mean) of the aggregate daily exposures in the simulation period is derived. The average daily dose is expected to represent the average exposure experience by each individual over a long period in his/her lifetime.

8 Simulation settings PACEMweb

PACEM requires user input on case specific information. This includes information on the exposure per use event (exposure fractions) and the concentration of the substance in the products available on the market. This data is input per product as a probability distribution, accounting for variability in the factors. In addition to providing values for input parameters, the user has to select settings of the analysis.

Analysing exposure with PACEMweb is done by sequentially specifying input on data and simulation settings in a series of input windows. Starting with the input window 'assessment settings', each subsequent window is entered after pressing the 'next' button at the bottom of the window. Currently, input is a one-way process. One can review previous input but not adjust it.
To begin a new assessment: go to PACEMweb (www.pacemweb.nl) and press the 'PACEMweb' link in the title bar :

After an analysis has been executed, results may be analysed, creating different views on the analysis results. This process is adaptable, different views can be generated sequentially by going back and forth between the 'analysis settings' and 'output' windows.

8.1 Running an exposure assessment in PACEMweb

Input for a particular assessment features two aspects:

a. input on general settings of the assessment
b. product specific settings

PACEMweb provides two different sections in the input for these aspects, the 'Assessment Settings' and the 'Product Settings' sections. The content of the 'Product settings' section depends on the selections made in the 'Assessment Settings'. Input in the 'Assessment Settings' and the 'Product Settings' sections need to be provided sequentially.

8.2 Assessment settings

In the assessment settings, selections are made on which product group to include in the assessment, for which country the population is modelled, and the exposure metric. Also, if a systemic dose estimate is made, input on absorption of the substance via different routes (inhalation, dermal, oral) should be provided. If an external exposure is assessed, the absorption fractions should be set at 1. It should be noted that in this case, only dose estimates for each route separately should

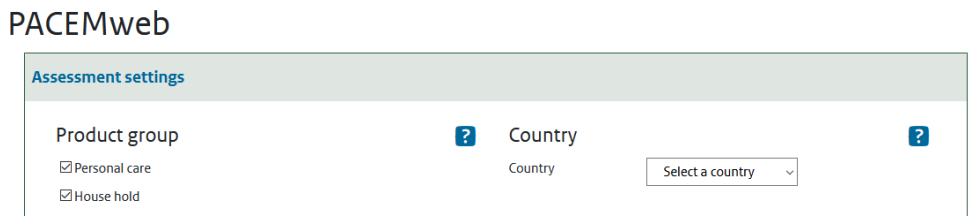
be considered. The total dose, calculated by adding the dose via all routes, is meaningless in the case of external exposure.

8.2.1 *Product group*

PACEMweb includes product use information on two product groups:

- Personal Care Products (PCPs)
- Household Cleaning Products (HCPs)

An assessment can be done for PCPs only, HCPs only, or for PCPs and HCPs combined.



8.2.2 *Country*

The target population nationality is selected via the 'Country' drop-down. Product usage information on both PCPs and HCPs is available for Germany, Spain, UK and France.

PCP data for The Netherlands has been collected in a separate survey. If 'The Netherlands' are selected in a combined PCP and HCP assessment, the HCP usage data for Germany are selected from the HCP data set and combined with the PCP usage data for The Netherlands.

The option 'All available' will combine usage information on Germany, France, United Kingdom and Spain into one assessment. The combined data are not scaled to the actual population sizes of these countries to provide an accurate representation of the European population.

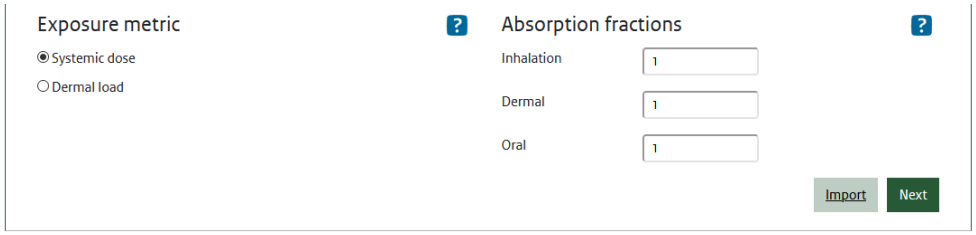
See also chapter 3.

8.2.3 *Exposure Metric*

Two different metrics of exposure are supported as an end point of an assessment in PACEM Web:

- systemic dose: the daily amount of substance absorbed into the body per kg body weight of the exposed individual
- dermal load: the amount of substance per cm^2 of exposed skin. Dermal load is associated with the risk of sensitization of sensitizing substances. PACEM determines daily dermal load for all body parts, but reports ultimately only the body part with the highest dermal load for each person in the population.

See also chapter 4.



8.2.4 *Import previous assessment*

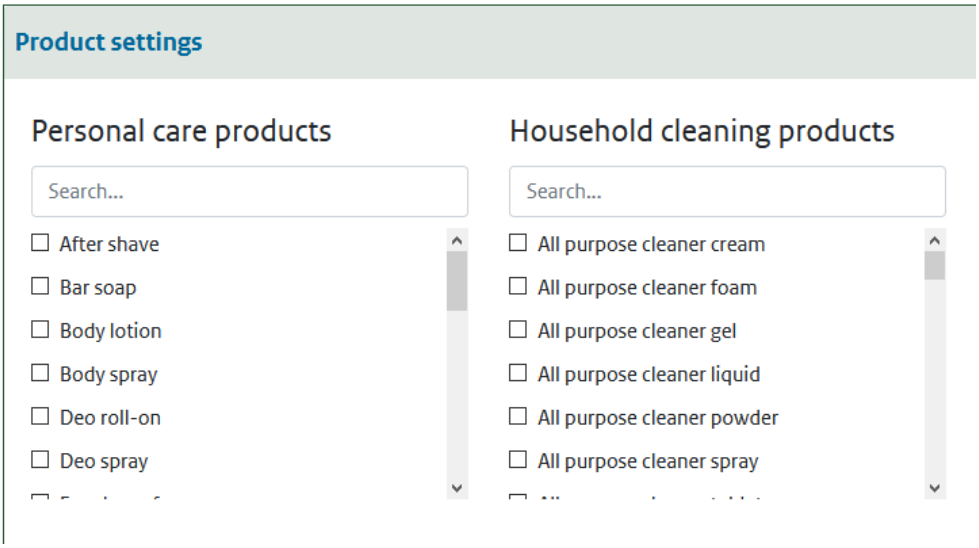
With the ‘Import’ button a previous assessment (pcm-file) that has been stored in a local file can be reopened (see 9.5). All assessment and product settings from this imported analysis are used, and the user can press ‘next’ in at the bottom of the product settings tab to continue to the simulation settings.

8.3 Product settings

In this section, the assessor selects products to be included in the assessment. For all the selected products, details about the concentration of the substance in the product and exposure evaluation of the product are specified. After products have been selected and their exposure parameters have been specified, pressing ‘next’ will advance the assessment to the ‘simulation settings’ window, from where the analysis can be started.

8.3.1 *Product selection*

For each product group (i.e. PCPs or HCPs) included in the assessment, a list of available products in the survey is given. From the list, the user may select products to be included. The survey on PCP product usage in The Netherlands contains a different set of products than that of the other surveyed countries. See also section 8.2.2.



8.3.2 *Concentration data*

The concentration data columns comprise two aspects:

- the occurrence of the substance in products, quantified as the percentage of products (brands) on the market that contain the substance. A value ranging from 0% to 100% is required. The occurrence is accounted for in the calculations, by adding products with zero concentration to the simulations.

- the concentration of the substance in products that do contain the substance. The concentration is specified as [mass/mass], the user selects the appropriate units. By default the user can enter a point value concentration. When a concentration distribution is desired, click on the button to open the *Distribution settings* window.

See also chapter 6.

8.3.3 *Exposure fractions or retention factor*

The exposure fraction or retention factor describes the external exposure per use of the product per gram of substance used, i.e. the fraction of the substance that actually comes into contact with the consumer. Exposure fractions are user input and need to be evaluated outside PACEM. For details on how to evaluate exposure fractions or retention factors, see chapter 5. A value ranging from 0 to 1 is required for each product and route. By default the user can enter a point value concentration. When a concentration distribution is desired, click on the button to open the *Distribution settings* window.

Product settings table. Specify product concentration and exposure fractions for the products selected in the assessment

Product settings

Selected Products	Concentration data		Exposure fractions (g/g substance used)			
	% Products with substance	Concentration in product mg/g	Inhalation	Dermal	Oral	Paste values
Body spray	100		1	1	1	ConsExpo

8.3.4 *Absorption fractions*

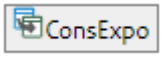
The absorption fractions can only be entered when systemic dose is the exposure metric. When selecting dermal load, this option is not displayed. The absorption fraction is the fraction of a substance that transfers over the body's barriers in the lungs, GI tract or skin into the body. Absorption into the body is assumed to depend on the route of exposure only and not on the product. A value ranging from 0 to 1 is required for each route. See also section 4.1.

8.3.5 *Using ConsExpo to estimate exposure fractions.*

To assist in the development of exposure fractions, RIVM's consumer exposure assessment tool ConsExpo (www.consexpoweb) has, from version 1.1 on, been equipped with a method to calculate exposure fractions.
In ConsExpo, an exposure assessment and scenario can be defined for a product/substance combination (see the ConsExpo manual, www.rivm.nl/bibliotheek/rapporten/2017-0197.pdf). As one of the outputs of a ConsExpo simulation, exposure fractions for PACEM are provided. These are available via ConsExpo 'output-> exposure fractions' window.

In the Exposure Fractions output window, the calculated exposure fractions can be copied to the Windows clipboard by pressing the ‘copy values for PACEMweb’ button:

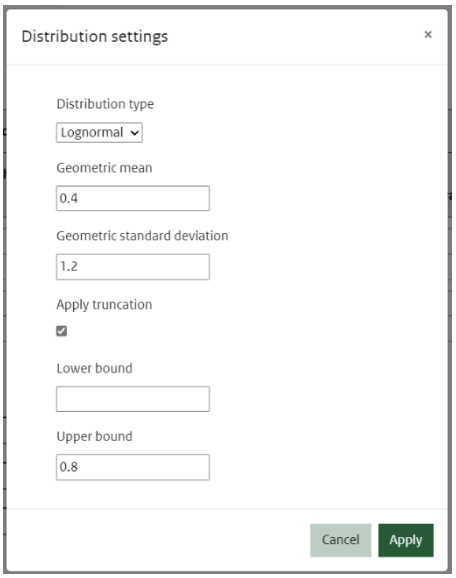
In PACEM’s product settings window, exposure fractions copied in ConsExpo can be pasted into the exposure fraction fields of a specific product by pressing the ‘ConsExpo’ button:



in the last column of the product settings table.

8.3.6 *Distribution settings*

A distribution type needs to be selected. Depending on the selected distribution type, enter the required distribution characteristics. When a distribution is selected, input values are sampled randomly from the specified distribution in a Monte Carlo scheme.



In PACEMweb, input values for exposure fractions and concentration information of the substance in products are specified as probability distributions. Deterministic evaluations are supported as well. The ‘point’ distribution is treated as a special case of distribution where the value can take on only one value.
PACEMweb supports the following distributions:

Distribution name	Parameters		Description & notes
Point	Value	the value the parameter takes on	Parameter takes on only one value. Use for deterministic evaluations
Uniform	Min	Lower bound of parameter's value	Parameter takes on values in the range of [min, max]. All intermediate values are equally likely.
	Max	Upper bound of parameter's value	
Normal	Mean		A lognormal distribution allows negative values. When negative values occur during sampling, they are replaced by positive values.
	Standard deviation		
	Truncation	Allows to specify upper and lower bounds on the distribution. This limits sampling to a smaller domain of the normal distribution function.	Both lower and upper bound may be specified, or only one of the bounds.
Lognormal	Geometric mean		
	Geometric standard deviation		
	Truncation	Allows to specify upper and lower bounds on the distribution. This limits sampling to a smaller domain of the lognormal distribution function.	Both lower and upper bound may be specified, or only one of the bounds.
Triangular	Location (minimum)	Lowest value of the parameter	Samples are between min and max with the highest probable value
	Mode	Most probable value of the parameter	

Distribution name	Parameters		Description & notes
	Scale (maximum)	Highest value of the parameter	at the 'mode'. Probability decreases linearly from the mode down to min and max, where it is zero.
Trapezoidal	Minimum	Lowest value of the parameter	Samples are between the minimum and maximum. Probability rises linearly to a constant level between the lower and upper modes.
	Lower mode	Level starts	
	Upper mode	Level ends	
	Maximum	Highest value of the parameter	
Beta	Alpha		Beta distribution samples values from 0 to 1 (incl. 0 and 1). Can thus only be used for parameters within a fixed range.
	Beta		

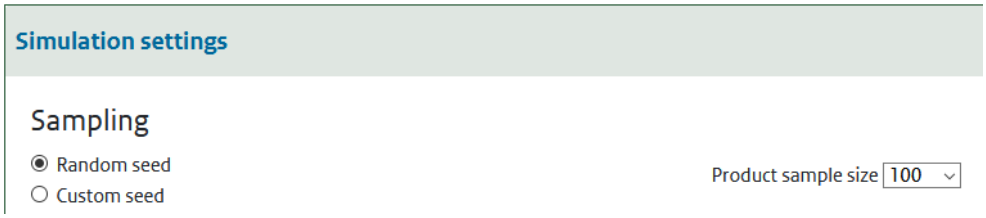
8.4 Simulation settings

8.4.1 *Sampling*

Here, details on the 'sampling' need to be given. These consist of:

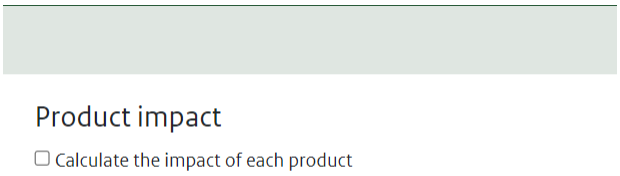
- sampling: the randomization of the sampling. Either a new random seed is used to generate the simulation (option 'random simulation') or the random seed of a previous assessment is used (option custom seed') to be able to reproduce exact results for a simulation. In that case, the a simulation should be run after providing an integer seed. Results of this simulation may then always exactly be reproduced later by using the exact same value for the seed.
- product sample size per simulated individual: the number of products that is used to represent the distribution (if one is specified) of product properties such as concentrations and exposure fractions in the analysis. In a probabilistic assessment, a distinct product sample of this size is assigned to each individual in the model population. A model population of e.g. 5000 persons combined with a product sample size of 100 will lead to 500 000 different exposure diaries. The sample size is restricted to the set {1, 10, 100, 1000}. Larger sample sizes will

generate a larger set of calculations. This increases the stability of the results but also execution time of an analysis.



8.4.2 *Product impact*

By selecting 'calculate the impact of each product', PACEM evaluates the impact of the exposure of each product on the exposure of the population. This is done by evaluating 1) the distribution of exposure of all products combined, and 2) the exposure of population to all products minus the product for which the impact is considered and reporting the difference. The impact will generally be different for different segments in the population. Therefore, the product impact is calculated at different percentiles of the population and reported as two distributions. The difference between these distributions, at each percentile is a measure of the product impact.

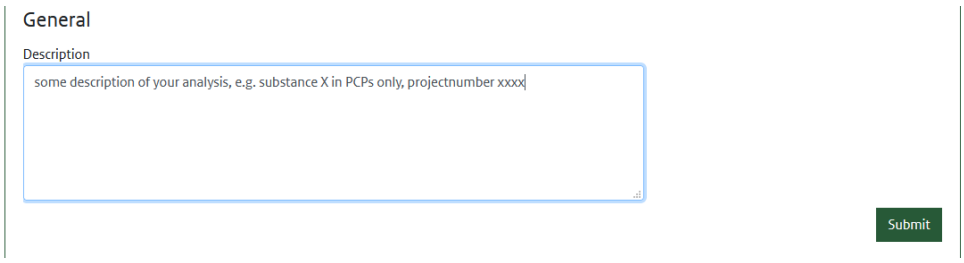


Including product impact in the simulation adds significantly to the computational burden and will lead to longer simulation times.

8.4.3 *General*

In this optional field a description of the analysis can be entered. When saving the analysis settings and input using the export button on the *Simulation status* tab, this description facilitates the identification of a saved analysis.

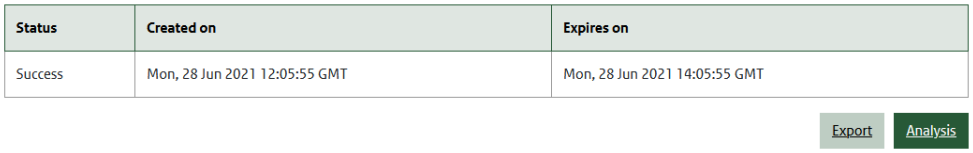
Pressing the 'submit' button, queues the analysis on the server, where it awaits execution.



8.5 Simulation status

The status of the analysis is displayed in the ‘simulation status’ window. Statuses distinguished are:

- ‘queued’ : awaiting execution on the server
- ‘in progress’: analysis being executed on the server
- ‘success/failure’: result of the analysis after execution



Results of an analysis will be kept on the server for a limited time. The date and time on which the analysis will expire is shown in the last column.
During this time it is possible to return to the analysis and re-analyse its results.
Pressing the button ‘export’ allows the user to locally save the (assessment and product) settings of the current analysis as an pcm-file, which can be uploaded to repeat the same analysis (see 9.2.5).
Pressing ‘Analysis’ brings up the analysis settings window (see next chapter).

9 Output PACEMweb

9.1 Analysis settings

Results of the analysis are stored on the server. After the analysis is successfully finished, the assessor may construct different views on the simulation data. These include:

9.1.1 *Exposure time frame*

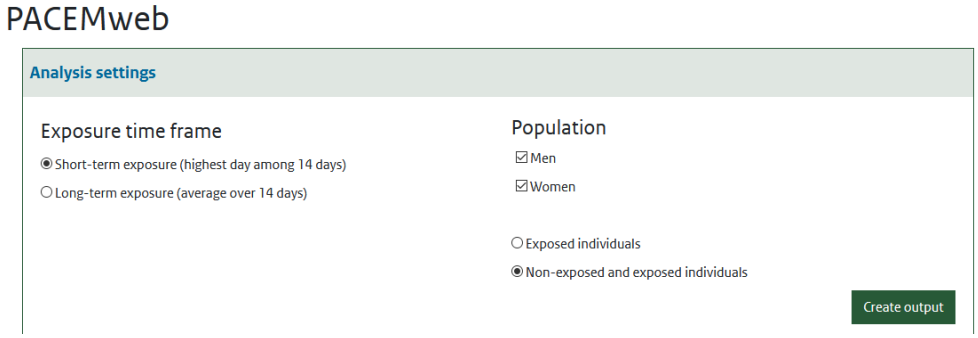
Acute or chronic exposures are available for review.

- For acute exposure ‘highest day’ of exposure in the simulated time frame of 14 days is selected for each simulated individual and its distribution in the population is presented
- ‘Average’ displays the distribution of the average daily aggregate exposure over 14 days among all simulated individuals

9.1.2 *Population*

Allows for the analysis of sub-populations. Stratification of the population may be according to sex : options are to review exposure for men, women separately and combined. Additionally, it is possible to review resulting population exposure for the entire population (exposed as well as non-exposed; option ‘All’), and for the exposed individuals only.
Non-exposed individuals in the population represent persons that either do not use the selected products or persons that do use one or more of the selected products but their products do not contain the substance. Currently, only the ‘exposed only’ option is supported.

Pressing ‘create output’ creates output for the selected view on the results in a new tab called ‘Analysis results’. The user can click on the ‘Analysis settings’ tab to change the settings. After clicking the ‘create output’ button the previous output will be replaced.



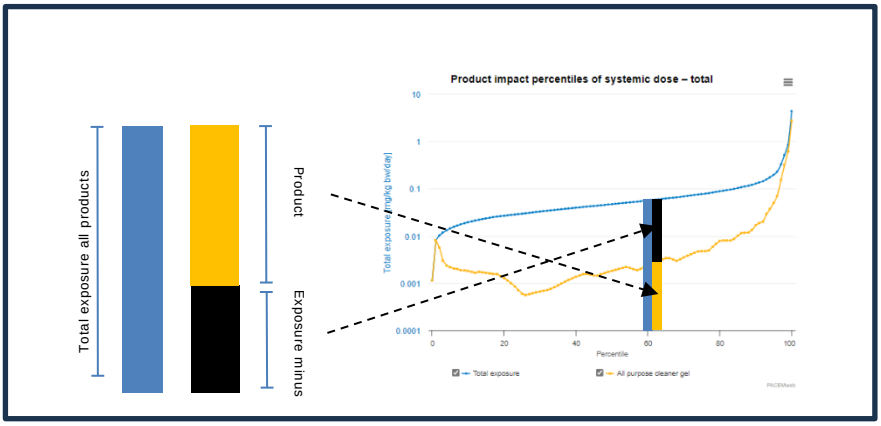
9.2 Analysis results

Results of the analysis are presented in different formats:

- As a percentiles table, giving exposure at different, pre-defined percentiles of the population. For routes separately as well as for the total exposure.

- As a plot, displaying both a histogram of the frequencies as well as the cumulative distribution function. A dropdown list next to the plot allows the selection of the route for which to display the information. Plots can be exported by pressing the ≡ icon in the right-hand upper corner of the plot.

If Product Impact has been simulated, a plot of the impact of each product on the exposure distribution is shown. Product impact is evaluated at each percentile of the exposure distribution. Referring to the figure below, product impact (yellow bar/line) is determined as the difference between, on the one hand, the aggregate exposure from all products (blue bar/line) at the percentile of the population and, on the other hand the aggregate exposure from all products except the considered product (black bar) at that same percentile of the population.

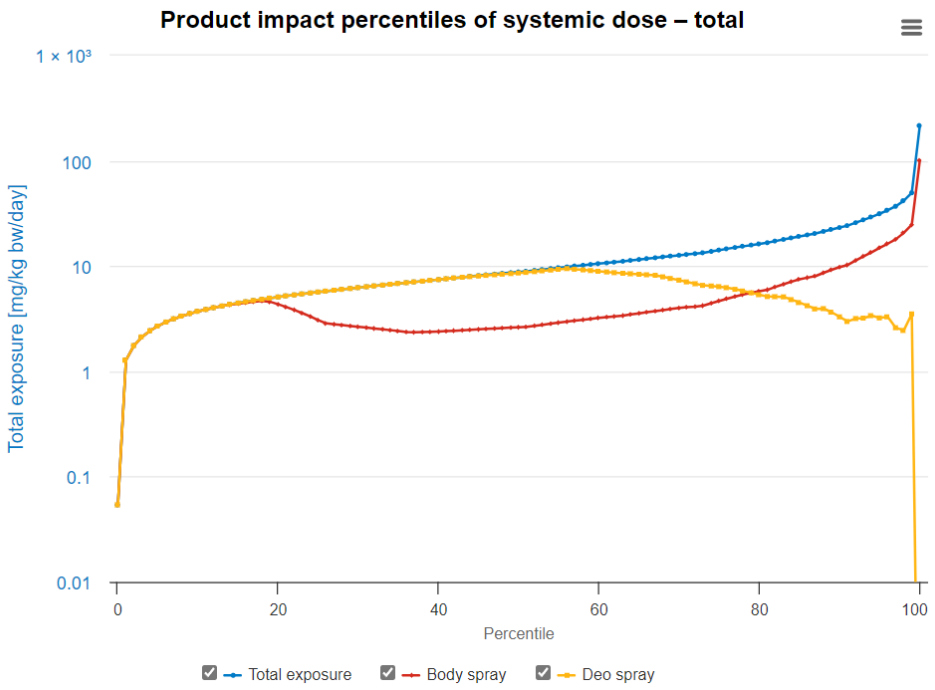


In the plot of the product impact that PACEM generates, the total aggregate exposure (blue bar/line) in the population is plotted, together with the product impact of all products in the simulation (yellow bar/line). Only the impact for one product is shown in this case. The product impact describes how much the exposure at a specific percentile increases if the product is included in the assessment. Conversely, the product impact provides direct insight in how much the exposure of the population would be reduced when the use of a substance in a particular product would be restricted. The metric of product impact was designed to answer one policy-relevant question as clearly as possible: how much will the exposure at a given percentile decrease if the use of the substance was eliminated from this product?

Product impact plots of individual products can be switched off and on using the checkboxes in the legend below the graph.

In the (artificial) example below, the total exposure is from two products: a body spray and a deodorant spray. For the deodorant spray, the impact is high up to roughly the 60th percentile. For this portion of the population, exposure is almost exclusively from this product. However, for higher percentiles, the impact of deodorant spray decreases. For the highest exposed persons in the population, the contribution of this product to the total exposure is even negligible. For body spray, on the other hand, the impact is significant over the entire range of exposure in the population.

(Note, as an aside, that exposure is plotted on a logarithmic axis in this example).



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Annex I: PCPs in the Dutch and European PCP surveys

Products surveyed in PCP surveys

Dutch PCP survey	European PCP survey		
	ETCD-1 (France, Germany, UK, Spain)	**ISC (Scotland)**	**Alba (Scotland)**
General hygiene			
Deodorant	Deodorant Spray	Deodorant Spray	
	Deodorant Roll On	Deodorant Roll On	
Perfume or Eau de toilette	Eau de Toilette		
	Eau de Parfum		
Shower gel	Shower Gel		Shower gel
Bathing foam/oil			
Toothpaste	Toothpaste	toothpaste	
	Mouthwash		Mouth rinse
	Liquid Soap		
	Bar Soap		
Shaving products			
Shaving foam/gel/oil/soap			
Aftershave	After Shave		
Hair care			
Shampoo	Shampoo	Shampoo	
Conditioner	Rinse off Conditioner		
Hairspray	Hair Spray		
Other (gel, lotion, foam, wax)	Hair Styling Excl. Spray		Hairstyling
Hair dye			
Skin care			
Body lotion	Body Lotion Mass	Body lotion	
	Body Lotion Prestige		
	Body Spray		
Hand cream	Hand Cream		Hand cream
Day cream	Face Moisturiser	Face Moisturiser	
Night cream			
Facial cleaning lotion or tonic			
Cosmetics			
Foundation	Liquid/Makeup Foundation		Liquid foundation
Make-up remover			
Powder or rouge			
Eye shadow			
Mascara			

Dutch PCP survey	European PCP survey		
	ETCD-1 (France, Germany, UK, Spain)	**ISC (Scotland)**	**Alba (Scotland)**
Eye pencil			
Eyebrow pencil			
Lip pencil			
Lipstick or lip gloss	Lipstick	Lipstick	
Lip balm			
Nail care			
Nail polish			
Nail polish remover			
Tanning products			
Bronzers			
Sunscreen			
After sun			

Annex II: HCPs included in PACEM

The following HCPs are included in the PACEM database. Each HCP is further specified by its formulation, i.e. spray, liquid, foam/crème, tablet or wipe/tissue.

- All purpose cleaners - cleaning products that can be used on almost any hard surface i.e. stainless steel, ceramics, wood, glass etc.
- Kitchen cleaners - products used for cleaning and/or degreasing different surfaces in the kitchen, i.e. oven cleaner, water softener, stainless steel cleaner etc.
- Floor cleaners - products specially designed for cleaning different types of flooring such as hardwood, linoleum or tile. This is not to be confused with floor polish (see below).
- Glass and window cleaners - cleaning products specially designed for surfaces such as glass, windows and mirrors.
- Bathroom cleaners - products specially designed for cleaning different surfaces in bathrooms, such as bathtubs, sinks, faucets, shower cabins etc.
- Furniture polish - products used on furniture in order to give it a smooth and shiny surface.
- Floor polish - products which are used on non-carpeted floors such as hardwood and tile in order to give them a smooth and shiny surface. This is not to be confused with floor cleaners (see above).

Annex III: Conversion of the Dutch PCP data to PACEM format

Amounts

Biesterbos et al. (2013) used photographs to visualize the amount of product used in the following product categories: general hygiene, shaving products, hair care, skin care and tanning products. The photographs contained three images displaying an increasing amount of product. The weight of the amount of product shown in each of the images was recorded. This information was used to transform the categorical data provided by the respondents to the amount (g).

For the following PCPs the visual display of amounts was not meaningful: deodorant spray, perfume or eau de toilette, aftershave spray, hair spray, eye shadow, mascara, eye pencil, eyebrow pencil, lip pencil, lipstick, lip balm and nail polish. For these products the used amount was assessed by asking alternative questions to describe the amounts used such as: ‘‘how often did you spray?’’ (spray products), ‘‘where exactly did you apply the product?’’ (eye shadow, eye pencil and lip pencil), ‘‘how many layers did you apply?’’ (mascara, eyebrow pencil, lip pencil, lipstick, lip balm and nail polish). A small experimental study was performed and the mean amounts used were calculated by weighing before and after application of the product.

The amounts calculated by Biesterbos et al. (2013) from the pictures and questionnaire were included in the Dutch PCP use data in PACEM.

Frequency

The product-use database contains a list of PCPs applied by each questionnaire respondent . The product use amounts and use frequencies had to be specified by the questionnaire respondents as value ranges. For these quantities uniform uncertainty distributions in the respective ranges were defined, e.g. the product use frequency of “2–3 times per week” was translated into a uniform distribution with minimum = 2/7 and maximum = 3/7 times per day.

Annex IV: Conversion European HCP data

Amounts

Measures from survey

spray	number of sprays	1-2 g per spray	taken from spray report (Delmaar and Bremmer, 2009). Pump spray 1-1.7 g/spray. Maximum value for a plant spray of 2.2 g/spray.
liquids	caps	40 g/cap	Measurement of 2 all purpose cleaners: 390 resp 400 mL/ 10 caps. Assume density of 1 g/mL
foams, crèmes, etc.	tablespoon	5 g	Wikipedia: 15 mL, assuming ~1g/mL
tablets	tablet	5-6 g/tablet	estimate
wipes and tissues	wipe	5 g/wipe	estimated from Wallmart product info (shipping weight) of 'Clorox disinfectant wipes' and 'DYMON Stainless Steal Cleaner Wipes'

Further assumptions
Uniform (U) distributions between the specified ranges
Amounts for 'more than X' have been assigned a range of [X – 2X]

Conversion of amounts

measure	**value**	**number**	**distribution**	**parameter 1 (g)**	**parameter 2 (g)**
spray	1	1 x	uniform	1	2
	2	2 x	"	2	4
	3	3 x	"	3	6
	4	4 x	"	4	8
	5	5 x	"	5	10
	6	> 6 x	"	6	12
cap	1	< 0.5	uniform	0	20
	2	0.5-1.0	"	20	40
	3	1.0-1.5	"	40	60
	4	1.5-2.0	"	60	80
	5	2.0-2.5	"	80	100
	6	2.5-3.0	"	100	120
	7	3.5-4	"	140	160
	8	4 - 4.5	"	160g	180
	9	4.5 - 5	"	180g	200
	7 (kitchen and	3 caps or more	"	120	240

measure	value	number	distribution	parameter 1 (g)	parameter 2 (g)
	bathroom cleaner)				
	10 (floor cleaner)	5 caps or more	“	200	400
tablespoon	1	<0.5	uniform	0	2.5
	2	0.5-1	“	2.5	5.0
	3	1-1.5	“	5	7.5
	4	1.5-2	“	7.5	10
	5	2-2.5	“	10	12.5
	6	2.5-3	“	12.5	15
	7	>3	“	15	17.5
wipes	1	1	point	5	0
	2	2	“	10	0
	3	3	“	15	0
	4	4	“	20	0
	5	5	“	25	0
	6	>5	“	30	0
tablets	1	1	uniform	5	6
	2	2	“	10	12
	3	3	“	15	18
	4	4	“	20	24
	5	5	“	25	30
	6	>5	“	30	36

Frequency

The data is specified as a use frequency per product category (all-purpose cleaner, kitchen cleaner etc.) and the number of products used in the particular category (e.g. all-purpose spray, all-purpose liquid). The use frequency per specific product is not specified. For the conversion it is assumed that if multiple products are used in a specific category, the products are used with an equal frequency.
Thus, the use frequency for a product becomes:

$$\frac{use\ frequency\ category}{number\ of\ products\ in\ the\ category}$$

For the conversion of the use frequency from the questionnaire, the following conversion factors have been used:

Possible answers in survey	frequency	distribution	parameter 1	parameter 2
At least once a day	1 per day	point	1	0
Several times a week	2 - 6 per week	uniform	0.285	0.857

Possible answers in survey	frequency	distribution	parameter 1	parameter 2
Once a week	1 per week	point	0.1428	0
Once every two weeks	1 per 2 weeks	point	0.0714	0
Once per month	1 per month	point	0.0333	0
Less than once a month	1 – 12 per year	uniform	0.00277	0.0333
Do not know	unknown	point	0	0

Annex V: Retention factors

Retention factors listed by the SCCS (2018, tables 2A and 2B)

Products	**Retention factor (%)**
Body lotion	100
Deodorant (spray and non-spray)	100
Douche gel	1
Eye shadow	100
Eyeliner	100
Face cream	100
Hair conditioner	1
Hair dyes	1
Hair styling products	10
Hand cream	100
Lipstick / lip salve	100
Liquid foundation	100
Make-up remover	10
mascara	100
Mouthwash	10
Shampoo	1
Toothpaste (adult)	5

Retention factors (%) of several PCPs for each exposed body part as used in the assessment of geraniol (Nijkamp et al. 2015). Empty fields indicate that it is assumed that the body part is not exposed when using the particular product. Note that assessing other substances may require retention factors for other products as well, when the substance occurs in other products. In addition, substance chemical properties may also result in different retention factors.

Body part / **Product**	**Trunk**	**Head**	**Arms (exl. hands)**	**Hands**	**Legs**	**feet**
Aftershave balsam		100				
Aftershave spray		100				
Aftersun cream	100	100	100	100	100	100
Bathing foam	1	1	1	1	1	1
Bathing oil	1	1	1	1	1	1
Body lotion milk	100	100	100	100	100	100
Bronzing cream	100	100	100	100	100	100
Conditioner		1		1		
Deo cream	100		100			
Deo roller stick	100		100			
Deo spray	100		100			
Deo tissue	100		100			
Douche gel foam scrub	1	1	1	1	1	1
Face day cream		100		100		
Face night cream		100		100		
Hair foam		100		100		

Body part / Product	Trunk	Head	Arms (exl. hands)	Hands	Legs	feet
Hair gel		100		100		
Hair lotion		100		100		
Hair wax		100		100		
Hand cream				100		
Liquid foundation		100				
Makeup remover		100				
Perfume eau de toilette spray		100				
Shampoo		1		1		
Shaving foam		10				
Shaving gel		10				
Shaving oil		10				
Sunscreen cream	100	100	100	100	100	100

Retention factors (%) of several HCPs for each exposed body part as used in the assessment of geraniol (Nijkamp et al. 2015). Empty fields indicate that it is assumed that the body part is not exposed when using the particular product. In general, it was assumed that trunk, head, legs and feet are not exposed to HCPs Note that assessing other substances may require retention factors for other products as well, when the substance occurs in other products. In addition, substance chemical properties may also result in different retention factors.

Body part / Product	Arms (exl. hands)	Hands
All purpose/kitchen/floor/glass/bathroom cleaner		
liquid	5.2	0.18
spray		5
wipes		30
gel	5.2	0.18
powder	5.2	0.18
cream		5
foam		5
tablets	5.2	0.18

Annex VI: Developing exposure fractions

Exposure fractions summarize exposure that arises on product use. They implicitly comprise information on the exposure duration, the release of the substance from the product, contact between user and product.
Exposure fractions may be developed by defining a standard scenario of exposure for each product use. This scenario needs to be evaluated by making assumptions on exposure duration, personal behaviour, substance and product properties. Using such a parametrized scenario, exposure D may be calculated for a specific amount (e.g. 1 g) of product. This may be done using custom models or dedicated exposure tools such as, for example, ConsExpo Web [3]. The exposure fraction is obtained by dividing the dose D in g by the used amount of product (e.g. 1 g). Note that the concept of an exposure fraction assumes that exposure is linear in the amount used. This assumption will not generally be correct. E.g. in cases where saturation phenomena will occur as in evaporation or dermal absorption relative exposure will decrease with increasing amount used.

Example 1
Inhalation exposure of a volatile cleaning agent in a liquid cleaner is considered. As a scenario we consider the application of 1 g of cleaning agent in a small, low ventilated room (room volume: 20 m^3; ventilation rate q: 0.5 air changes/hour). We assume the agent evaporates immediately and disperses through the room. The user of the product remains in the room for 1 hour and inhales the evaporated agent with an inhalation rate of 1 m^3/h.

The amount inhaled follows from:

$$D = \frac{A \times (1 - e^{-q \times T})}{qV} \times Rinhale \approx 0.04g$$

The exposure fraction in this case is then taken to be 0.04/1 = 0.04 [g/g].

Example 2
As an alternative to the method described in example 1, a dedicated consumer exposure assessment tool may be used. In this example, the exposure fraction of an all-purpose liquid cleaner is evaluated using ConsExpo. Additionally, the dependency of the exposure fraction on the substance's volatility is evaluated.
Using ConsExpo, a scenario is created on from the fact sheet database available in the tool. Using the scenario:

Fact sheet	Cleaning and Washing
Product category	All-purpose cleaners
Product	All-purpose cleaner, liquid
Scenario	Application-cleaning

[3] https://www.consexpoweb.nl/ https://www.consexpoweb.nl/

This selects the ConsExpo 'evaporation from liquids' model with default exposure factors as model input.
The following information needs to be provided in addition:

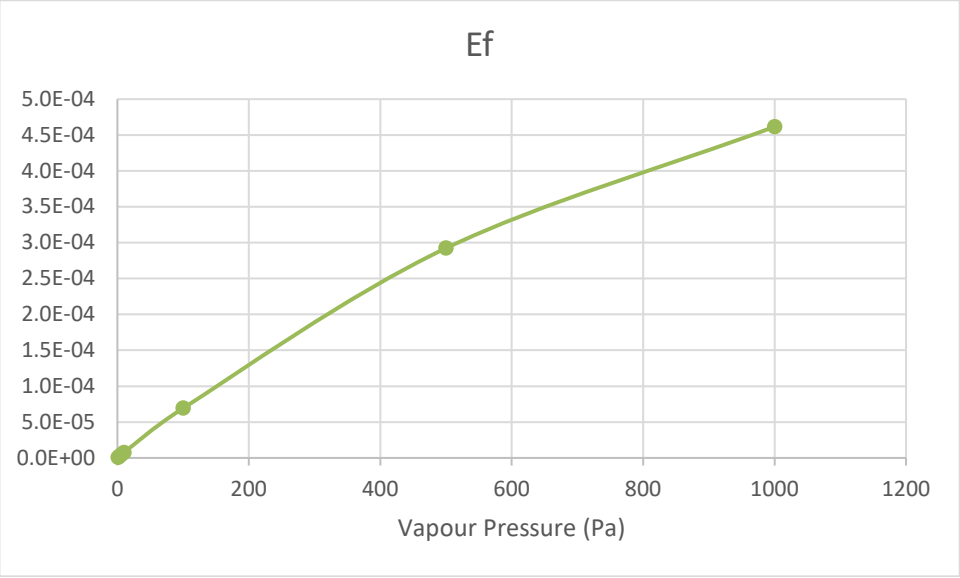
Weight fraction	0.1
Molecular weight substance	100 g/mol
Vapour pressure substance	1 Pa

ConsExpo evaluates the inhalation dose as amount of substance inhaled per kg body weight. In PACEM, normalisation on the body weight is done in a separate step. We need only to estimate the amount inhaled. This is obtained by setting the body weight to (the artificial value) 1 kg in ConsExpo.
Using these settings, ConsExpo evaluates exposure (inhaled dose) as 0.048 mg. From the ConsExpo fact sheet we find that the total amount of all-purpose cleaner was set at 65g. To obtain the exposure fraction the inhaled dose is divided by the amount used:

$Ef = 0.048 \times 10^{-3} / 65 = 7.4 \times 10^{-7}$ (g/g)

This is almost negligible, as expected for a substance of low volatility. Varying the vapour pressure, including values for higher volatility gives the following dependence of the Ef on vapour pressure:

VP(Pa)	1	5	10	100	500	1000
ConsExpo dose (mg/g)	0.048	0.24	0.48	4.5	19	30
Ef	7.38462E-07	3.69E-06	7.38E-06	6.92E-05	0.000292	0.000462



The relationship between Ef and the vapour pressure may be used to propose default exposure fractions for the all-purpose cleaner.

This approach may be generalized to other products.

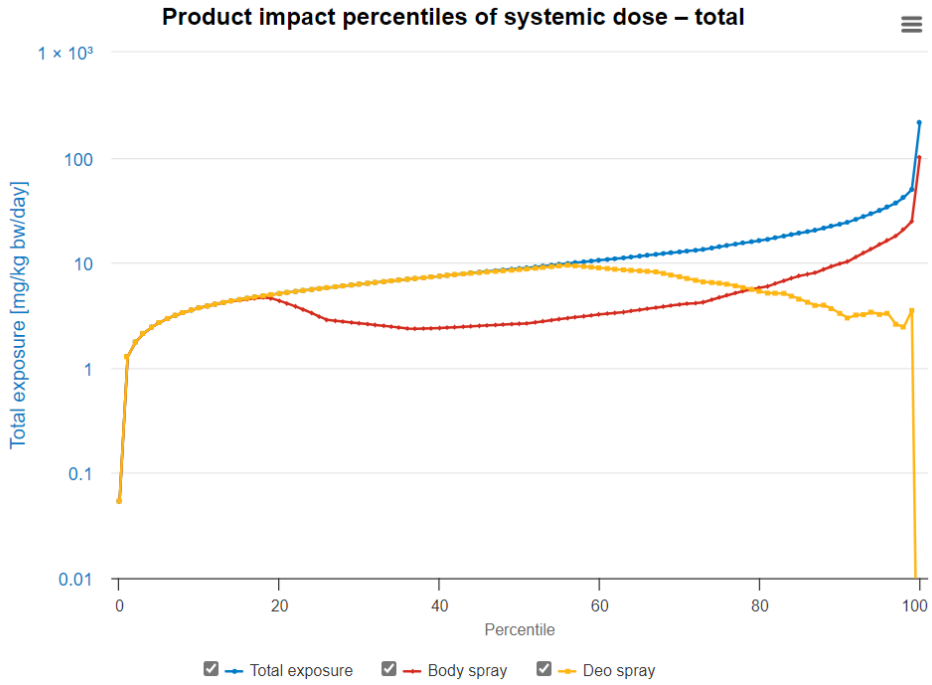
Variance in the single product use exposure
The procedures laid out above derive exposure fractions as single numbers. As discussed before, the Ef summarizes the effects of multiple exposure factors in a single number. In reality, many of these exposure factors will vary from one person and exposure event to another. To account for this variability, exposure fractions could be represented by probability distributions. In an exposure evaluation with PACEM, exposure fractions could be sampled at random from this variability distribution. The evaluated aggregate exposure would, as a result, include an estimate of the (inter- and intra-person) variability.

Example 3
ConsExpo can also be used to evaluate exposure probabilistically. Input parameters representing exposure factors can be specified as a distribution, reflecting variability in its value. Using Monte Carlo simulation, a distribution of exposure in the single product use scenario is estimated. Normalizing the calculated dose with the used amount gives a distribution of the Ef in terms of different statistics such as, e.g. median, standard deviation, 90-percentile. These summary statistics of the calculated Ef can be used to define a parametric probability distribution that can be passed as input to PACEM.

Annex VII: Background information on the product impact evaluation

PACEM version 1.1 introduces a new feature: a characterisation of the Product Impact. As this feature may not be intuitively clear, we provide some more discussion in this annex.

PACEM evaluates the product impact as a contribution of the exposure of a product to the total exposure of the population. Product impact is evaluated at each percentile of the exposure distribution in the population. It is determined as the difference between, on the one hand, the aggregate exposure from all products at the percentile of the population, and on the other hand, the aggregate exposure from all products except the considered product at that same percentile of the population.
The product impact is presented in a graphical form as shown in the example below. The impact of a product may be inferred from two curves: the exposure to all products at each percentile (the blue line) and the product impact curve (red and yellow lines for the two different products 'Body spray' and 'Deo spray'). The closer the product impact curve is to the total exposure curve, the larger the fraction of total exposure due to the product (and hence the product's impact) is. The difference between the total exposure curve (blue) and the product impact curve (red or yellow) equals the exposure at the percentile when leaving out the product in question.



It is important to note that this measure of the impact does not give insight into the impact of a product at the level of the individual. If an individual is exposed at a specific percentile when considering all products combined, this same individual may move, after leaving out a product, to a very different percentile of the population exposure distribution. When the population exposure distributions are compared for these two situations (including or excluding the product) at a specific percentile, we are usually comparing exposures of two different individuals.
To give an example, an individual that uses a very large amount of body lotion, but no other personal care products, might have a very high total exposure and might therefore be located at one of the higher percentiles in the total exposure distribution. However, if body lotion is left out of the analysis, this individual would have zero exposure and would therefore move to the zeroth percentile.
How the individuals' positions change on the percentile scale will in general be different for every product that is being left out. With each left-out product, different individuals are therefore compared. As a consequence, the product impacts of different products at the same percentile do not need to sum to 100% or the total exposure.

To illustrate this further, consider as a simplified example a population of four individuals. Individual 1 has no exposure, individual 2 is exposed to 1 mg/kg bw/day from product A, individual 3 is exposed to 2 mg/kg bw/day from product B, and individual 4 is exposure to 3 mg/kg bw/day from product C. The table below (at the end of this section) shows the percentiles of the total exposure distribution and the product impacts, while illustrating how the individuals move around the percentile scale. Here, the product impacts at the 33rd percentile sum to 300%, while at P100, they sum to 33%.

While the underlying mathematics may seem complicated, the metric of product impact was designed to answer one policy-relevant question as clearly as possible: how much will the exposure at a given percentile decrease if this product no longer contributes any exposure? If, for example, a policy maker has a goal to decrease exposure at the 67th percentile of the above (example) population as much as possible, the product impact reveals that interventions on product B and product C will be interesting to explore. If a complete intervention is possible (e.g. a total ban on the substance in one of these products), then an intervention on either product will decrease the exposure at the 67th percentile by 50%. An intervention on product A, by contrast, will not have any effect on the 67th percentile, because its impact on that percentile is 0%. Note that if a simultaneous intervention on multiple products is considered, the effect of the intervention cannot be quantified by summing the product impacts. Instead, the PACEM simulation can be repeated with one or more products left out.

Table. Example of a calculation of product impact. An artificial example of a population of four individuals, using three products. Individual 1 has no exposure, individual 2 is exposed to 1 mg/kg bw/day from product A, individual 3 is exposed to 2 mg/kg bw/day from product B, and individual 4 is exposure to 3 mg/kg bw/day from product C.

Total exposure			Product impact A					Product impact B					Product impact C				
Percentile	Individual	Exposure (mg/kg bw/day)	Percentile	Individual	Exposure (mg/kg bw/day)	Product impact (mg/kg bw/day)	Product impact (%)	Percentile	Individual	Exposure (mg/kg bw/day)	Product impact (mg/kg bw/day)	Product impact (%)	Percentile	Individual	Exposure (mg/kg bw/day)	Product impact (mg/kg bw/day)	Product impact (%)
P0	#1	0	P0	#1 & #2	0	0	NA	P0	#1 & #3	0	0	NA	P0	#1 & #4	0	0	NA
P33	#2	1	P33			1	100	P33			1	100	P33			1	100
P67	#3	2	P67	#3	2	0	0	P67	#2	1	1	50	P67	#2	1	1	50
P100	#4	3	P100	#4	3	0	0	P100	#4	3	0	0	P100	#3	2	1	33