

# Consumer exposure to biocides – identification of relevant sources and evaluation of possible health effects

Stefan Hahn <sup>1\*</sup>, Klaus Schneider <sup>2</sup>, Stefan Gartiser <sup>3</sup>, Wolfgang Heger <sup>4</sup>, Inge Mangelsdorf <sup>1</sup>

<sup>1</sup>Fraunhofer Institute for Toxicology and Experimental Medicine, Department Chemical Risk Assessment, Nikolai-Fuchs-Str. 1, 30625 Hanover, Germany

<sup>2</sup>Research and Advisory Institute for Hazardous Substances GmbH (FoBiG), Werthmannstr. 16, 79098 Freiburg, Germany

<sup>3</sup>Hydrotox GmbH, Bötzingen Str. 29, 79111 Freiburg, Germany

<sup>4</sup>German Federal Environmental Agency, Corrensplatz 1, 14195 Berlin, Germany

\* Corresponding author

Email addresses:

SH: [stefan.hahn@item.fraunhofer.de](mailto:stefan.hahn@item.fraunhofer.de)

SG: [info@hydrotox.de](mailto:info@hydrotox.de)

KS: [klaus.schneider@fobig.de](mailto:klaus.schneider@fobig.de)

WH: [wolfgang.heger@uba.de](mailto:wolfgang.heger@uba.de)

IM: [inge.mangelsdorf@item.fraunhofer.de](mailto:inge.mangelsdorf@item.fraunhofer.de)

# **Abstract**

## **Background**

Biocide-containing products are used by consumers for various purposes in the home environment. To assess potential health risks, data on biocide-containing products were gathered by a market survey, exposures were estimated by a worst-case approach (screening), and the hazardous properties of active components were evaluated.

## **Methods**

Information on biocide-containing products was collected by "on-site" research, and also by an Internet inquiry as well as databases and lists of active substances. Twenty active substances were selected for detailed investigation. The products containing these substances were subsequently classified by range of application; frame formulations were developed. Potential exposures were then estimated using a worst-case approach according to the TGD. Relevant scenarios, active substances and combinations thereof were identified. The toxicological data for these substances were compiled in substance dossiers. For estimating risks the margins of exposure (MOEs) were determined.

## **Results**

We found that only a limited number of biocidal active substances or groups of biocidal active substances were included in products of daily use. The lowest MOEs for dermal exposure or exposure by inhalation were obtained for the following scenarios and biocides: indoor pest control using sprays, stickers or evaporators (chlorpyrifos, dichlorvos), spraying of disinfectants, cleaning of surfaces with concentrates (hydrogen peroxide, formaldehyde, glutardialdehyde). The risk from additive exposure for the individual biocides from different exposure scenarios was

on average by a factor of 3 higher than the highest single exposure. From the 20 biocides assessed 10 had skin sensitizing properties. The biocides isothiazolinone (mixture of 5-chloro-2-methyl-2H-isothiazolin-3-one and 2-methyl-2H-isothiazolin-3-one, CMI/MI), glutardialdehyde, formaldehyde and chloroacetamide may be used in household products in concentrations which have induced sensitization in experimental studies. Therefore, exposure to biocides from household products may contribute to induction of sensitization in the population.

### **Conclusions**

This project aimed at giving an overview on exposure to and risks from different biocides in the home environment. In several instances a more refined analysis is needed for a detailed health risk assessment which is expected to become available within the framework of the EU Biocides Directive.

### **Background**

In many areas of our daily life, biocidal active substances are used to ensure personal hygiene, disinfect surfaces, control insects and preserve a wide range of non-durable goods. For some application areas, special antibacterial products of daily use (e.g., detergents, textile products, toilet seats) are offered in addition. More than 200 active ingredients have been notified within the scope of the Biocidal Products Directive for applications such as disinfection (for human hygiene or private and public health area) or in-can preservation and more than 100 active ingredients as insecticides or repellents. However, for some of the notified substances complete dossiers have not been submitted (e.g., chlorpyrifos, phoxim), so that the actually available number of biocidal active substances is expected to decrease. Human exposure may occur by inhalation from spraying of products containing biocides or from biocides evaporating from the products. Furthermore, biocides may come into contact with the

skin during use of products containing biocides. Oral exposure is assumed to play a minor role with the exception of mouthing of contaminated objects by children.

Despite the wide uses and possible exposure, little is known about exposure concentrations and no systematic measurements are available for the home environment. Measurements have been taken primarily at workplaces for example to determine exposure to formaldehyde during disinfection in hospitals [1-2] or at workplaces during spraying of biocides [3]. Besides these, few measurements on consumer exposures are available for example on the emission of biocides from emulsion paints [4-6] or on the exposure to insecticides such as dichlorvos or chlorpyrifos [7-9]. Relevant for consumer exposure are also investigations on biocide emission from carpets [10].

As alternative to measurements, exposures can be estimated using appropriate models. For exposure estimates regarding the use of household products, these have been outlined in guidance documents issued by the European Commission for assessing exposure for chemicals and biocidal active substances [11-12], and also in the HERA Guidance Document [13]. Computer-based models are available to calculate these exposure data and to refine calculated worst-case exposure data (e.g., SCIES-CEM (implemented in E-Fast), Consexpo [14], and SprayExpo [15]). However, also for application of exposure models the database is weak, especially typical concentrations in products, use patterns and consumption data are missing.

To get an overview about the relevance of the biocides used in household products, in a project sponsored by the German Federal Agency on the Environment (project period 15.10.2004 – 30.11.2005), the content of biocides in consumer products was investigated, overall exposure to individual biocidal active substances from consumer products was modelled using a worst-case approach, toxicological data

were evaluated and potential health risks were assessed. For more detailed information see the final report of the project [16].

## Methods

The approach taken can be divided roughly into three phases: selecting information, estimating the exposure, assessing and classifying the health hazards. **Figure 1** schematically shows the selected approach in detail.

The following consumer products, which might contain biocides, were taken into consideration: disinfectants, wood preservatives and insecticides, repellents and attractants, also preservatives in preparations (e.g., in washing and cleaning products, in cosmetics, in home improvement products, etc.). Information on the identity of active substances, their concentration and application of biocidal products, was collected in supermarkets and do-it-yourself stores ("on site market research"). The obligation to label biocidal products according to article 20 of the Biocidal Products Directive facilitates this task, as practically all necessary details are printed on the retail package. Additional information was obtained from inquiries to industry and via the Internet. Furthermore, databases and lists of active substances were analysed, such as the register of detergents and cleaning agents of the German Federal Environmental Agency, which provided (product-independent) summary analyses, and the German drug directory "Rote Liste".

In addition to biocides used indoors in private homes, other sources of exposure to biocidal substances were taken into account. These included for example preservatives in cosmetics, human and veterinary drugs, and antimicrobially finished materials, which do not (or only partly) fall under the Biocidal Products Directive. Application concentrations of preservatives were obtained by researching the Internet and by direct inquiries to manufacturing companies. For cosmetics, no information

on the preservatives was available for individual products. Therefore the maximum concentrations according to the Cosmetics Directive [17] were used for the exposure assessment. Finally some information could be obtained from the relevant literature.

The information on products and active substances has been compiled in so-called product tables (containing information on each individual product identified, its biocidal ingredients and concentrations as well as instructions for use) and active substance (biocide) tables which summarized data obtained from the product tables. The individual products have then been assigned to product categories, product groups and typical products or exposure scenarios. Whenever gaps became apparent in the information on scenarios and products, the research was systematically refined (iterative process).

Twenty active substances were selected for detailed investigation. The most important selection criteria were the application quantity (as far as known), a wide range of applications in the household and the personal home environment (e.g. as disinfectants and preservatives in household products, in handicraft materials, in cosmetics), and the use in a variety of household products. Furthermore, the selected active substances should be stated as notified in the Second Review Regulation of the Biocidal Products Directive to guarantee that they will be on the market in future. Active substances of low toxicity, such as citrate or sodium hydrogen carbonate, were excluded. Individual active substances intended for special application scenarios, e.g. mosquito and ant repellents, were additionally taken into account.

Products containing the selected active substances were categorized by types of applications. Then frame formulations (e.g. commonly used concentrations of the active ingredients) for each type of application were developed.

The algorithms proposed in the Technical Guidance Document on Risk Assessment (TGD) [11] were used for the estimation of the exposure (for screening purposes only). In the case of exposure to compounds by evaporation, the exposure concentration was limited to the maximum amount according to the ideal gas law. In addition the fugacity was introduced, to describe the distribution between liquids and gases. This was important for formaldehyde, which despite its high vapour pressure does not quickly evaporate from solutions due to its high water solubility (low Henry coefficient). Default values were taken from the TGD, ConsExpo 4.0, the HERA guidance document [13], the US-EPA Exposure factors handbook [18] and by expert guess. Additionally, specific data were taken from product information (via internet and market research). The exposure calculated for the different routes (inhalation, dermal, oral) was summed up and also the exposure from different sources of the same biocide were summed up to give the overall exposure. For this purpose the exposure was calculated as body dose. For all routes 100% absorption was assumed. Mouthing behaviour of children was not taken into consideration (for details cf. Hahn et al. [16]).

The toxicological data for the substances were analysed on the basis of reviews, supplemented by original literature, and summarised and evaluated with respect to the exposure data (for details cf. Hahn et al. [16]).

To assess the systemic effects of biocide exposure, MOEs (margins of exposure), i.e. the ratio of NOAEL (No Observed Effect Adverse Level) and exposure concentration (as body dose), were calculated. MOEs were calculated for the individual scenarios and for the total of all exposures from all scenarios.

## Results

### Market research

Although more than 200 active ingredients have been notified within the scope of the Biocidal Products Directive for applications like disinfection (for human hygiene or private and public health area) or in-can preservation and more than 100 active ingredients as insecticides or repellents, our market research has shown that only a limited number of active substances are used in most of the products [16]. In addition, the active substances can be subsumed by chemical groups such as formaldehyde and formaldehyde releasers, hydrogen peroxide and hydrogen peroxide releasers, pyrethroids, organophosphates, alcohols.

The market research revealed the following as main application areas of biocidal substances in washing and cleaning products, whereas the intended effect is not always primarily biocidal but possibly bleaching or cleaning: a) surface disinfection (incl. removal of moulds and films) using sodium hypochlorite (NaOCl), alcohols, quaternary ammonium compounds (QAC) and hydrogen peroxide; b) laundry disinfection / cleaning clothes using hydrogen peroxide, NaOCl and QAC; c) machine dishwashing products using dichloroisocyanurates and trichloroisocyanuric acid; d) dichloroisocyanurates, trichloroisocyanuric acid, sodium hypochlorite and hydrogen peroxide are the main biocidal active substances used for water purification in private swimming pools.

Preservatives used in liquid washing and cleaning products include isothiazolinones, benzoic acid, 2-phenoxyethanol, chloroacetamide, bronopol and triclosan. QAC, glutardialdehyde and formaldehyde or formaldehyde releasers are used as disinfectants and preservatives, too. Substances prevailing in the preservation of cosmetics are 2-phenoxyethanol, hydroxybenzoates (parabens), isothiazolinones and bronopol. The concentration range can be estimated fairly well based on the

maximum concentration of active ingredients stipulated in the Cosmetics Directive. Our market research showed furthermore that the use of preservatives in toys such as finger paint or plasticine also follows the Cosmetics Directive. As most relevant active substances used for in-can preservation we identified isothiazolinones, bronopol and formaldehyde releasing agents, while specific fungicides and herbicides such as triazines and carbamates are used for film preservation.

Household insecticides and repellents are used in the form of bait boxes, strips/stickers, powders or liquid preparations to control crawling insects and in the form of sprays and evaporators to control flying insects. The most commonly used active substances belong to the categories of pyrethroids (e.g., tetramethrin, allethrin, prallethrin, etc.) and organophosphates (e.g., chlorpyrifos, dichlorvos, phoxim, etc.). Among the repellents, the most relevant active substances researched were Icaridin, Ethyl 3-(N-butylacetamido)propionate and Diethyltoluamide.

To control ectoparasites on pets, mainly pyrethroids are used (e.g. in impregnated collars, sprays, powders and shampoos). As further sources of biocides in household-related areas, we identified antimicrobially finished textile materials (in particular sportswear, carpets and mattresses). Here, mainly zinc pyrithione, triclosan, carbendazim, different isothiazolinones, permethrin and triclosan are used as storage preservatives, as moth repellents and for odor control. No definite statement can be made at present about the relevance of other antimicrobially finished objects (such as antimicrobial bin liners, toilet seats and carving boards) for the overall exposure. We could find no meaningful data for the active substances used in this domain, which are normally integrated directly into the polymers.

## **Exposure assessment**

Within this project, 20 active substances were selected for detailed investigation, 15 of which are used as disinfectants and preservatives and 5 as insecticides and repellents (**Table 1**). Products containing the selected active substances were classified by range of application. This resulted in a total of 50 scenarios (**see additional file 1: Table 2: Product categories, product groups and exposure scenarios**) and about 220 frame formulations. For all these frame formulations the exposure for the consumer was estimated using the algorithms of the TGD with some modifications. These estimations of the potential exposure are worst-case approaches intended for screening purposes. A refinement probably results in considerably lower and more realistic values.

The results of the exposure calculation are given in **Table 3** for oral exposure, exposure by inhalation and dermal exposure. In addition, the exposure from the three routes was summarized to result in an overall exposure.

For all active substances, there is generally a high degree of dermal exposure if there is direct skin contact with concentrates.

Roughly half of the selected biocidal active substances have a relatively low vapour pressure and/or a low Henry coefficient, so that inhalation exposure via the gas phase is negligible in most cases. Exceptions are dichlorvos and formaldehyde, which could evaporate from insecticide strips and home improvement products, respectively. In contrast, there can be high inhalation exposure through aerosols during spray application. This includes biocides like hydrogen peroxide, glutardialdehyde, formaldehyde, chlorpyrifos.

Looking at preservatives, there is a wide range of applications and at the same time a limited number of active substances used (e.g., in cleaning products, in cosmetics, in home improvement products, etc.), so that the additive exposure from all products is

a matter of interest. In addition, a high potential exposure (both dermal and inhalation) is possible in particular with leave-on cosmetics.

### **Characterisation of biocide toxicity**

Except for the two substances sodium dichloroisocyanurate and trichloroisocyanuric acid, there is sufficient data for all selected biocidal active substances available to characterise the systemic toxicity after long-term exposure, at least for oral exposure, although many of the relevant studies have not been published and are described only in secondary reports.

The profile of toxic effects, in agreement with the different chemical classes represented, varies broadly both in terms of type of effects and of potency [16]. For example, the insecticides belonging to the group of organophosphates (chlorpyrifos, dichlorvos, phoxim) show the known effects on cholinesterases in blood and in the brain, whereas for substances such as hydrogen peroxide, formaldehyde and glutardialdehyde irritant effects are most prominent. NOAEL values after subchronic or chronic oral exposure vary across 4 orders of magnitude: The lowest value is 0.025 (chlorpyrifos), the highest is 500 mg/kg/d (benzoic acid). As expected, the toxicity of pest control agents is substantially higher than that of disinfectants or preservatives. The relevant effects of the substances and, as far as possible, the NOAELs (no observed adverse effect levels) for the oral, inhalational and dermal routes of intake were summarised (see **additional file 2: Table 4: Overview of the toxicity of selected active substances**).

In addition to systemic effects, irritant effects on the skin and mucous membranes deserve special attention. For 11 out of 20 substances, relevant irritation of the skin and mucous membranes was found: sodium hypochlorite, alkyl dimethyl benzyl ammonium chloride (QAC), isothiazolinones (mixture of 5-chloro-2-methyl-2H-

isothiazolin-3-one and 2-methyl-2H-isothiazolin-3-one (CMI/MI), 1,2-benzisothiazolin-3-one), glutardialdehyde and formaldehyde, di- and trichloroisocyanurates, hydrogen peroxide, bronopol and triclosan belong to this group. Regarding irritation, an additive effect must be assumed if different products containing these active substances are used in parallel or consecutively within a short time period. Irritation effects in the respiratory tract may be relevant for inhalation exposure during spraying. This holds true in particular for formaldehyde and glutardialdehyde.

Furthermore, for 10 of the active substances investigated, there is evidence that they may possess skin sensitising properties. These are the isothiazolinones (CMI/MI and 1,2-benzisothiazolin-3-one), glutardialdehyde and formaldehyde, chloroacetamide, dichlorvos, phoxim, bronopol, triclosan as well as sodium hypochlorite. No data are available for skin sensitising effects of di- and trichloroisocyanurates [16]. The substantial importance of dermal contact with objects of daily use, underline the relevance of this endpoint. For some substances, the concentrations which induced sensitisation in humans or in the local lymph node assay in mice were compared to the application concentrations in products of daily use (**Table 5**). With the exception of bronopol, there seem to be only minor differences between the effect concentrations and application concentrations indicating that CMI/MI, glutardialdehyde, formaldehyde and chloroacetamide in household products may induce sensitization.

### **Identification of potential risks**

Comparison of the modelled exposure concentrations with the NOAELs enabled calculation of a margin of exposure (MOE) as a preliminary indication of potential risk. For MOEs > 1 the exposure concentration is lower than the NOAEL, for MOEs

< 1 the exposure concentration is higher than the NOAEL, i.e. the higher the MOE, the lower the potential risk. These MOEs can be used for relative comparison between the biocidal substances. Overall MOEs (**Table 6**) summed up for each individual compound over all exposure scenarios and all routes of exposure ranged from 57 for benzoic acid to 0.0057 for dichlorvos. In all cases, oral exposure has only a minor share in the overall exposure. For the inhalation pathway, MOEs below 1 were obtained for dichlorvos, formaldehyde, hydrogen peroxide, glutardialdehyde, CMI/MI and chlorpyrifos. The low MOEs are in general dominated by only a small number of scenarios: pest control using sprays (chlorpyrifos), stickers or evaporators (dichlorvos), spraying of disinfectants or cleaning of surfaces with concentrates (glutardialdehyde and hydrogen peroxide), application of water-based paints and adhesives (formaldehyde, CMI/MI), and use as preservative in personal hygiene products (formaldehyde). For the dermal pathway, MOEs below 1 were calculated for sodium hypochlorite, hydrogen peroxide, alkyl dimethyl benzyl ammonium chloride (QAC), 2-propanol and phoxim. In this context, similar to inhalation exposure, the focus for sodium hypochlorite, hydrogen peroxide and 2-propanol was on scenarios in which the biocidal substances are applied by spraying or in which concentrates are used.

The influence of additive exposure on the MOE was assessed by comparing the MOE with the highest single exposure with the MOE for the exposure summed up for all scenarios for the same route of exposure [16]. 2 to 24 scenarios were available per substance (average 11 scenarios). The highest additive effect was calculated for bronopol, the maximum factor here being 6.3 for inhalation and 8 for dermal intake, with a total of 24 scenarios. The average factor was 2.7 for inhalation and 3.1 for dermal exposure.

Comparing the MOEs for different biocides within one scenario, marked differences are observed between the different biocidal substances. The results for the airway-irritant biocides hydrogen peroxide, formaldehyde and glutardialdehyde give rise to concern regarding inhalation exposure to sprays (**Table 7**) and concentrates, MOEs being lowest for glutardialdehyde because of the particularly low NOAELs. Remarkable differences between MOEs for the different compounds also exist for the use of the substances as preservatives in cosmetics. This is of minor importance, however, for the assessment of the health hazard, as all MOEs are very high both for inhalation and for dermal exposure. An exception is formaldehyde, which should, however, not be finally assessed until detailed exposure analyses have been carried out, since considerably lower and more realistic values can be achieved by refinement of the exposure assessment [16]. Regarding the use of insecticides as sprays for crack and crevice treatment, the MOE obtained for the organophosphate chlorpyrifos is substantially lower than that for the pyrethroid prallethrin (**Table 8**).

## Discussion

As shown above, in this project, the relevance of different biocides in consumer products was assessed by modelling exposure concentrations and comparing these with NOAELs. The exposure was calculated using a worst-case approach using the algorithms given by the TGD with some modifications. Such worst-case approaches within exposure assessments are often used as a first tier for screening of risks and for comparison of different substances or exposure routes. Due to the preliminary nature of the exposure assessment (screening), the MOEs can, however, be only a rough guide for assessing the health risks. Exposure levels obtained from the worst-case approach might be by a factor of 10-100 higher than the actual exposures [16, 19]. For refining the exposure data the exposure should be modelled with suitable

models (Consexpo [14], Sprayexpo [15]) or even better be measured. In cases, where much information is available and exposure distributions are of importance, in addition probabilistic estimates might be used [20]. These can then be subject to a detailed analysis of health risks.

Usually for defining safe levels in risk assessments a margin of safety of 100 is considered appropriate [21]. However, a refinement of the exposure estimation may reduce the exposure by at least a factor of 10 to 100. Therefore only compounds and scenarios with MOEs < 1 have been highlighted in the results section. These involve mainly the indoor use of organophosphate pesticides. A refined exposure analysis including measured data from the literature for chlorpyrifos (e.g., [9], [22], [23], [24], etc.), and dichlorvos (e.g., [7], etc.) is necessary for assessing the risks from exposure to these organophosphates. To date the application of chlorpyrifos for biocidal purposes is not allowed because industry did not submit a dossier for evaluation while dichlorvos is being evaluated on a community level in the review programme of the Biocidal Product Directive. Other active substances may be considered for future use, as our comparative assessment showed that the exposure to prallethrin (a pyrethroid insecticide) resulted in a much higher MOE indicating a lower potential risk.

Another possible cause for concern was the use of sprays, which contain irritating compounds such as hydrogen peroxide, glutardialdehyde and formaldehyde. Also here a refined exposure analysis is of high priority.

Our analysis showed that the overall risk does not increase significantly if the exposure to a biocide from many uses is considered, because exposure is determined by few relevant scenarios. However, when assessing the overall MOE for 2-propanol, it must be taken into account that this biocide is also used as a solvent,

which might add considerably to overall exposure. For this application area, our market research did not yield any detailed information, so that it could not be considered in a quantitative way.

Furthermore the use of biocides with sensitizing properties deserves further attention and detailed evaluation. For CMI/MI, glutardialdehyde, formaldehyde and chloroacetamide the concentration in the household products was in the same order of magnitude as the concentration which induces sensitization. The sensitisation prevalence of these biocides was 2-3% in studies with 7800 patients from dermatological hospitals [25] and is also high in the general population (0.4% for CMI/MI [25]). A detailed risk characterization for these biocides is therefore needed.

## **Conclusion**

In conclusion, this project aimed at giving an overview on exposure to and risks from different biocides in the home environment. As mentioned above, in several instances a more refined analysis is needed. In the framework of the EU Biocides Directive detailed dossiers on exposure and health effects as well as risk assessments have been submitted to the rapporteur member states. Therefore it is to be expected that a detailed health risk assessment for individual biocides used in household products will become available.

## Abbreviations

CMI/MI	mixture of 5 chloro-2-methyl-2H-isothiazolin-3-one and 2-methyl-2H-isothiazolin-3-one
MOE	Margin of Exposure
NaOCl	Sodium hypochlorite
NOAEL	No observed adverse effect level
QAC	Quaternary ammonium compounds such as alkyldimethyl benzyl ammoniumchlorides
TGD	Technical Guidance Document (cf. [11])
TNsG	Technical Notes for Guidance (cf. [12])

## Competing interests

Some author(s) are involved in the preparation of several dossiers of biocidal active substances and biocidal products which have been submitted within the scope of the Biocidal Products Directive. However, this has not affected the independency of the authors. The authors declare that they have no competing interest.

## Authors' contributions

SH, SG, KS, WH and IM jointly conceived the manuscript. SG carried out the market research and developed the frame formulations together with SH; WH gave general support. SH carried out the exposure estimations and KS the characterisation of the biocide toxicity. WH, IM, SG, SH and KS participated in the selection of relevant biocides. IM and KS evaluated the health risks of the selected biocides in household products. SH wrote the first draft of the manuscript, which all authors revised and updated. All authors read and approved the final manuscript.

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**Figure 1: Approach selected for screening potential health risks from biocide-containing products of daily use**

**Table 1: Selected biocidal active ingredient attributed to field of application**

CAS	EC	Name	Dis-infectants	Preservatives	Insecticides, repellents
67-63-0	200-661-7	2-Propanol	x		
68391-01-5	269-919-4	Alkyl dimethyl benzyl ammonium chlorides (QAC)	x	x	
7681-52-9	231-668-3	Sodium hypochlorite	x		
2893-78-9	220-767-7	Sodium dichloroisocyanurate	x		
87-90-1	201-782-8	Trichloroisocyanuric acid	x		
7722-84-1	231-765-0	Hydrogen peroxide	x		
3380-34-5	222-182-2	Triclosan	x	x	
50-00-0	200-001-8	Formaldehyde	x	x	
111-30-8	203-856-5	Glutardialdehyde	x	x	
65-85-0	200-618-2	Benzoic acid	x	x	
55965-84-9	mixture	mixture of 5 chloro-2-methyl-2H-isothiazolin-3-one and 2-methyl-2H-isothiazolin-3-one (CMI/MI)	x	x	
2634-33-5	220-120-9	1,2-Benzisothiazolin-3-one	x	x	
52-51-7	200-143-0	Bronopol	x	x	
122-99-6	204-589-7	2-Phenoxyethanol	x	x	
79-07-2	201-174-2	Chloroacetamide	x	x	
119515-38-7	423-210-8	Icaridin			x
23031-36-9	245-387-9	Prallethrin			x
2921-88-2	220-864-4	Chlorpyrifos			x
62-73-7	200-547-7	Dichlorvos			x
14816-18-3	238-887-3	Phoxim			x

**Table 3: Worst-case exposure estimates**

<b>Biocide</b>	<b>Exposure in mg/kg/d</b>			
	<b>inhalation</b>	<b>dermal</b>	<b>oral</b>	<b>overall</b>
2-Propanol	82	382	0	387
Alkyl dimethyl benzyl ammonium chloride (QAC)	0.75	42	0.0010	43
Sodium hypochlorite	0.57	76	0.16	76
Sodium dichloroisocyanurate	3.7E-12	5.7	0.0027	5.8
Trichloroisocyanuric acid	4.3E-6	6.0	0.0030	6.0
Hydrogen peroxide	15	127	0.013	134
Triclosan	0.084	2.6	0.011	2.6
Formaldehyde	3.7	2.8	0.085	5.2
Glutardialdehyde	2.5	6.0	0.00025	8.1
Benzoic acid	3.1	4.3	0.0050	4.4
CMI/MI	0.17	0.15	0.000018	0.30
1,2-Benzisothiazolin-3-one	0.058	3.3	0.00013	3.3
Bronopol	0.22	1.9	0.0010	2.0
2-Phenoxyethanol	17	23	0.011	30
Chloroacetamide	4.3	4.6	0.0032	6.9
Icaridin	0.66	6.9	0	6.9
Prallethrin	0.012	0.039	0	0.051
Chlorpyrifos	0.61	2.2	0	2.8
Dichlorvos	7.0	0.096	0	7.0
Phoxim	0.059	1.8	0	1.9

CMI/MI = mixture of 5 chloro-2-methyl-2H-isothiazolin-3-one and 2-methyl-2H-isothiazolin-3-one

**Table 5: Comparison of concentrations with sensitising effects in human (HRIPT) or in mice (LLNA) to the estimated concentrations of application in products of daily use**

active substance	sensitising concentration in human (HRIPT)	sensitising concentration in animal testing (LLNA)	Concentration of application		
			cleaning & washing	cosmetics	home improvement
CMI/MI	12.5 ppm <sup>[26]</sup> (challenge conc. 12.5 ppm)	75 ppm (EC <sub>3</sub> ) <sup>[27]</sup>	≤ 60 ppm	2.5 - 7.5 ppm (15 ppm <sup>a</sup> )	
Glutardialdehyde	5% <sup>[28]</sup> (challenge conc. 0.5%)	0.1% (EC <sub>3</sub> ) <sup>[29]</sup>	0.01 - 0.5%	≤ 0.1% (0.1% <sup>a</sup> )	
Formaldehyde	1% <sup>[28]</sup> (challenge conc. 1%)	0.35% (EC <sub>3</sub> ) <sup>[30]</sup>	≤ 0.05%	≤ 0.2% (0.2% <sup>a</sup> )	≤ 0.1%
Bronopol	5% <sup>[28]</sup> (challenge conc. 2.5%)		0.0011 - 0.035%	0.01 - 0.1% (0.1% <sup>a</sup> )	0.0011 - 0.035%
Chloroacetamide	0.5% <sup>[31]</sup> (challenge conc. 0.5%)		0.1 - 0.3%	≤ 0.3% (0.3% <sup>a</sup> )	0.1 - 0.3 %

CMI/MI = mixture of 5 chloro-2-methyl-2H-isothiazolin-3-one and 2-methyl-2H-isothiazolin-3-one  
HRIPT: Human Repeat Insult Patch test  
LLNA: Local lymph node assay  
EC<sub>3</sub>: concentration leading to a triplicate proliferation rate in the Local lymph node assay.  
a = max. value of cosmetics directive [17]

**Table 6: MOE based on additive exposure in adults (total of all scenarios)**

active substance	MOE			
	inhalation	dermal	oral	total
2-Propanol	1.8	0.26		0.26
Alkyl dimethyl benzyl ammonium chlorides (QAC)	33	0.24	25000	0.59
Sodium hypochlorite	5.2	0.040	18	0.040
Sodium dichloroisocyanurate	1.9e+10	8.7	18637	8.7
Trichloroisocyanuric acid	4122	8.4	16578	8.4
Hydrogen peroxide	0.0052	0.20	1950	0.19
Triclosan	298	31	2273	9.6
Formaldehyde	0.018	5.3	176	2.9
Glutardialdehyde	0.0043	8.3	15903	0.49
Benzoic acid	80	57	50000	57
CMI/MI	0.24	2.7	22200	1.3
1,2-Benzisothiazolin-3-one	144	2.6	66954	2.6
Bronopol	45	10	9827	4.9
2-Phenoxyethanol	4.7	21	7617	2.6
Chloroacetamide	2.3	7.7	3174	1.4
Icaridin	121	14		12
Prallethrin	6.7	761		49
Chlorpyrifos	0.058	2.3		0.011
Dichlorvos	0.00086	4.2		0.0057
Phoxim	6.4	0.27		0.20

CMI/MI = mixture of 5 chloro-2-methyl-2H-isothiazolin-3-one and 2-methyl-2H-isothiazolin-3-one

**Table 7: MOE of different biocides for exposure scenario 8 (spraying and wiping, mould remover, algae remover, window cleaner)**

active substance	MOE			
	inhalation	dermal	oral	total
<i>disinfection</i>				
2-Propanol	12	1.1	accidental	1.1
Hydrogen peroxide	0.012	0.52	accidental	0.52
Sodium hypochlorite	2.4e+12	12	accidental	12
Alkyl dimethyl benzyl ammonium chlorides (QAC)	320	1.3	accidental	3.3
<i>in-can preservative</i>				
CMI/MI	11	13	accidental	13
1,2-Benzisothiazolin-3-one	1018	11	accidental	11
Bronopol	2229	114	accidental	57
Formaldehyde	2.1	60	accidental	60
Glutardialdehyde	0.034	20	accidental	1.6
2-Phenoxyethanol	128	100	accidental	16

CMI/MI = mixture of 5 chloro-2-methyl-2H-isothiazolin-3-one and 2-methyl-2H-isothiazolin-3-one

**Table 8: MOE of different biocides (insecticides) for exposure scenario 33c (sprays for crack and crevice, ant sprays)**

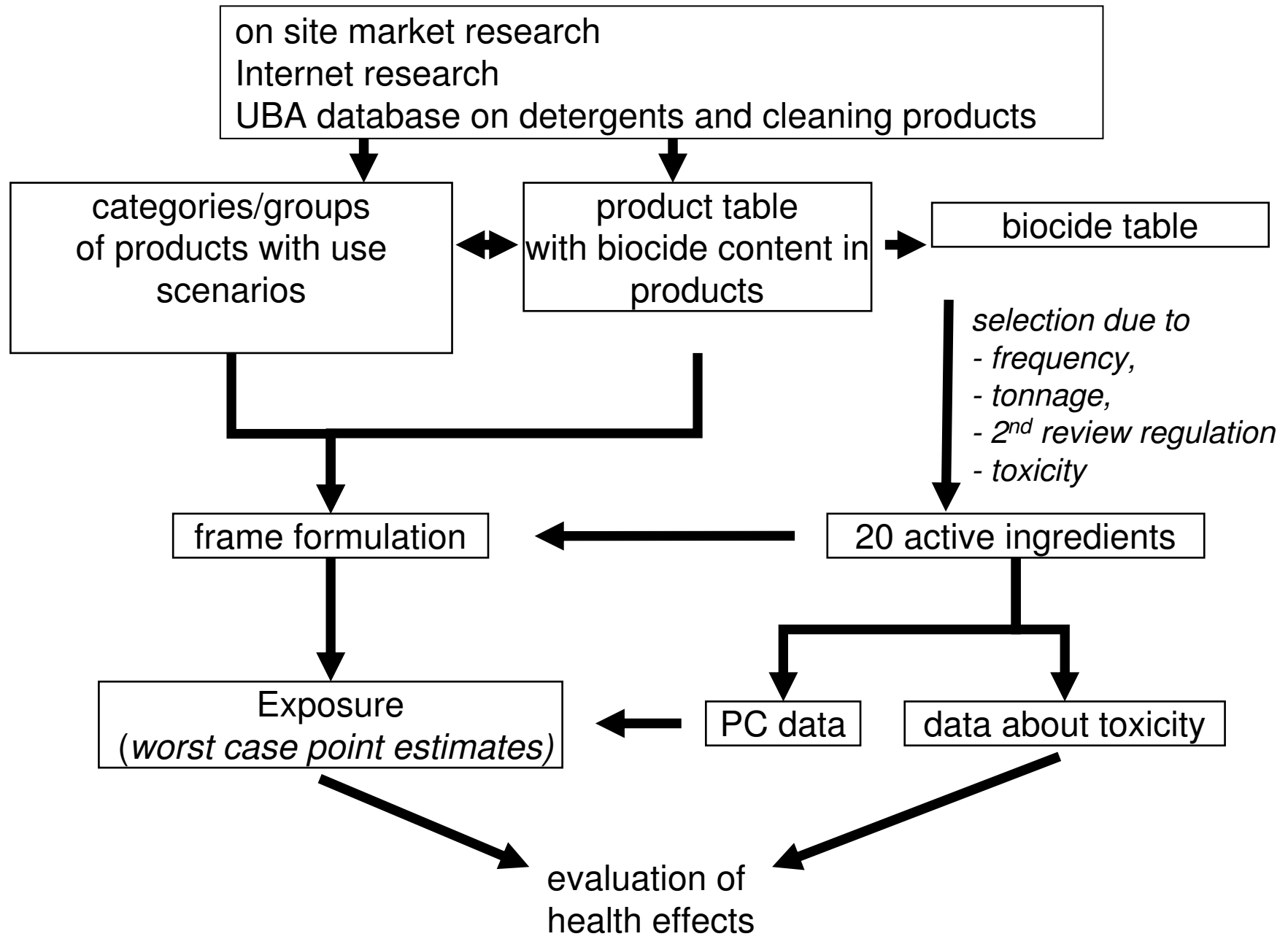
active substance	MOE			
	inhalation	dermal	oral	total
Chlorpyrifos	0.15	6.4	accidental	0.030
Prallethrin	6.8	770	accidental	49

**additional file 1:**

**table 2.xls: Table 2: Product categories, product groups and exposure scenarios**

**additional file 2:**

**table 4.xls: Table 4: Overview of the toxicity of selected active substances**



**Additional files provided with this submission:**

Additional file 1: table 2.xls, 26K

<http://www.ehjournal.net/imedia/1812039699274888/supp1.xls>

Additional file 2: table 4.xls, 22K

<http://www.ehjournal.net/imedia/1105616024274888/supp2.xls>