Environmental Research Plan
of the Federal Ministry for the Environment,
Nature Conservation and Nuclear Safety

Action Program "Environment and Health“

Project Funding Number (UFOPLAN) 204 61 218/05

Health risks from biocide-containing products and articles of daily use

by

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ON BEHALF OF THE
GERMAN FEDERAL ENVIRONMENTAL AGENCY

Hannover, November 2005

5 Executive summary

5.1 Introduction, objective and approach

In many areas of our daily life, biocidal active substances are used in consumer products, e.g. 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.

Under this project, the overall exposure to individual biocidal active substances from consumer products was to be modelled and resulting health risks were to be assessed. Information on biocide-containing products of daily use and on their biocidal ingredients was therefore collected by researching the market. A screening was subsequently performed to estimate exposures, and the hazardous properties of the biocidal substances were researched.

Figure 1 schematically shows the selected approach in detail.

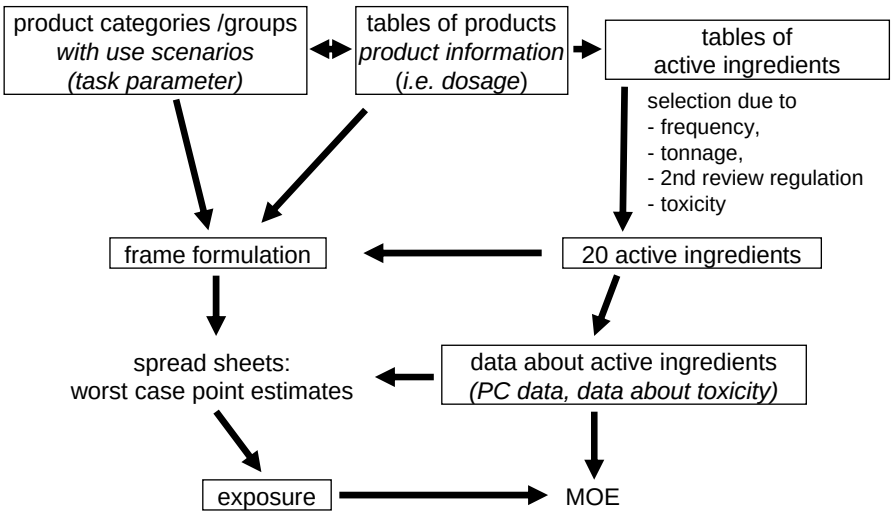

Figure 1 Approach selected for screening potential health risks from biocide-containing products of daily use

5.2 Market research

To make an exposure assessment, data must be available regarding the identification and concentration of the active substance, the type of application and the recommended use of biocidal products. These data were obtained from different sources. For example, product information (market research) was collected in supermarkets and home improvement stores ("on site") and via the Internet. In addition, databases and lists of active substances, such as the register of detergents and cleaning agents of the Germany federal environmental agency, the German drug directory "Rote Liste" etc., were used.

The different household sources of biocides for the most part still need to be identified by laborious on-site 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.

In addition to the actual biocidal products that are relevant indoors in private homes, in particular disinfectants (product types PTs 1, 2), wood preservatives (PT 8) and insecticides, repellents and attractants (PTs 18 and 19), we also investigated preservatives (PTs 6 and 7) in preparations as well as other sources of exposure to biocidal substances. This included e.g. preservatives in cosmetics, human and veterinary drugs, and antimicrobially finished materials, which do not (or only partly) fall under the Biocidal Products Directive.

By on-site research in department stores, superstores, groceries and retail shops, information could be obtained in particular on biocidal products of the PTs 1, 2, 18 and 19. Application concentrations of preservatives in cosmetics, home improvement products and in washing and cleaning products were obtained by researching the Internet and through inquiries directly to the manufacturing companies.

An important source of information was the database of the German federal environmental agency for detergents and cleaning agents (WRM), which provided (product-independent) summary analyses. The analyses also allowed for conclusions to be drawn on the consumption of active substances

in certain application areas, which, however, served only as an initial guideline for the selection of active substances, due to the classification of concentrations of active substances and consumption quantities into rough classes.

These analyses revealed the following as main application areas of biocidal substances in washing and cleaning products: surface disinfection and removal of moulds and films using sodium hypochlorite (NaOCl), alcohols, quaternary ammonium compounds (QAC) and hydrogen peroxide, besides laundry disinfection using NaOCl and QAC. In addition, there are those substances that are used primarily as bleaching agents, such as dichloroisocyanurates and trichloroisocyanuric acid in machine dishwashing products or again sodium hypochlorite and hydrogen peroxide for cleaning clothes. The two latter substances are also used for water purification in private swimming pools.

Preservatives used in liquid washing and cleaning products include isothiazolinones, benzoic acid, phenoxyethanol, chloroacetamide, bronopol and triclosan. Benzalkoniumchloride, glutardialdehyde and formaldehyde 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 Guideline. Our market research showed furthermore that the use of preservatives in toys such as finger paint or plasticine also follows the Cosmetics Guideline. 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. prallethrin) and organophosphates (e.g. chlorpyrifos, dichlorvos and

phoxim). Among the repellents, the active substances researched were Icaridin, IR3535 and DEET.

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, carbendazine, 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.

5.3 Selection of active substances, product classification and frame formulations

Although more than 200 active ingredients have been notified for product types 1, 2 and 6 and more than 100 active ingredients for product types 18 and 19, our market research has shown that only a limited number of active substances are used in several products. In addition, the active substances can be subsumed by chemical groups.

Under 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 (see Table 1). 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 products. 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 gnat repellents, were additionally taken into account.

Products containing the selected active substances were classified by range of application (in a total of 50 scenarios, see Table 2), and frame formulations (e.g. commonly used concentrations of the active ingredients) for each of these scenarios were prepared. The data were complemented by the maximum concentrations usable according to the Cosmetics Guideline, by data provided by the manufacturers of preservatives, and by relevant literature on the ingredients of washing and cleaning agents. This resulted in a total of about 220 frame formulations.

Table 1 **Selected biocidal active ingredient attributed to field of application, and information on notified product types, (3rd Review Regulation: Regulation (EC) No 1048/2005 of 13 June 2005 amending Regulation (EC) No 2032/2003)**

CAS	EC	name	disin-fec-tants	preser-vatives	insec-ticides, repel-lents	MG 1 disin-fectants	MG 2 preservatives	MG 3 pest control	MG 4 other biocidal products
67-63-0	200-661-7	2-Propanol	x			1 2 3 4 5	6 9 10 11 12	18 19	
68391-01-5	269-919-4	Alkyl dimethyl benzyl ammonium chlorides (QAC)	x	x		1 2 3 4 5	6 7 9 10 11 12 13	16 17 18 19	21 22
7681-52-9	231-668-3	Sodium hypochlorite	x			1 2 3 4 5	6 11 12		
2893-78-9	220-767-7	Sodium dichloroisocyanurate	x			1 2 3 4 5	6 9 11 12		
87-90-1	201-782-8	Trichloroisocyanuric acid	x			2 3 4 5	6 7 9 11 12		
7722-84-1	231-765-0	Hydrogen peroxide	x			1 2 3 4 5	6 11 12		
3380-34-5	222-182-2	Triclosan	x	x		1 2 3	7 9		
50-00-0	200-001-8	Formaldehyde	x	x		1 2 3 4 5	6 9 11 12 13	18	20 21 22 23
111-30-8	203-856-5	Glutardialdehyde	x	x		1 2 3 4 5	6 7 9 10 11 12 13		22
65-85-0	200-618-2	Benzoic acid	x	x		1 2 3 4	6 11		20
55965-84-9	mixture	Kathon (CIT/MIT)	x	x		2 3 4	6 7 9 10 11 12 13		
2634-33-5	220-120-9	1,2-Benzisothiazolin-3-one	x	x		2	6 7 9 10 11 12 13		22
52-51-7	200-143-0	Bronopol	x	x		1 2 3 4	6 7 9 10 11 12 13		22
122-99-6	204-589-7	2-Phenoxyethanol	x	x		1 2 3 4	6 7 10 11 13		
79-07-2	201-174-2	Chloroacetamide	x	x		3	6 7 9 10 11 13		
119515-38-7	423-210-8	Icaridin			x			19	
23031-36-9	245-387-9	Prallethrin			x			18	
2921-88-2	220-864-4	Chlorpyrifos			x			18	
62-73-7	200-547-7	Dichlorvos			x			18	
14816-18-3	238-887-3	Phoxim			x			18	

Table 2 Product categories, product groups and exposure scenarios

product category	product group	typical product/scenario	scenario no.
cleaning & washing/ disinfectants	cleaning: all-purpose cleaner, disinfectant cleaner, special cleaner	cleaning (wiping) of small surfaces with concentrate	1
		mixing, cleaning (wiping) of small surfaces	2
		mixing, cleaning (wiping) of large surfaces; floor cleaner	3
	spray: disinfectant spray, cleaning spray	spraying small surfaces; hygiene spray, algae remover	4
		shoe spray	5
		textile spray	6
		mixing, spraying large surfaces; algae remover	7
		spraying + wiping; mould remover, algae remover, window cleaner	8
		spraying + washing-up; mould remover	9
	disinfectant wipe	wiping small surface (in sanitary, kitchen)	10
	toilet (bowl) cleaner	toilet cleaner (spraying under toilet edge, waiting for the product to react, rinsing)	11
	drain cleaner	drain cleaner (pouring in drains)	12
	swimming pool water treatment		13
	laundry products	machine wash using laundry compact	14
		machine wash using laundry additives, hygiene laundry rinse	14b
		hand wash using laundry compact	15
		hand wash using laundry additives, hygiene laundry rinse	15b
	antimicrobially finished textiles		16
	dishwashing products	machine, solid	17
		machine liquid	17b
		hand liquid	17c

product category	product group	typical product/scenario	scenario no.
personal care (cosmetics hygiene articles, disinfectants, special products for babies)	whole body rinse-off	shampoo, shower gel, soap	18, children as 2nd users
	whole body leave-on	moisturiser, body lotion	19, children as 2nd users
	head leave-on	hair gel, make-up	20
	hands leave-on	hand crème, hand disinfection	21
	spray	hair spray, deodorant spray	22
	toilet paper (moist)		23, children as 2nd users
	foot/hand spray	athlete's foot spray	24
	toothpaste		25, children as 2nd users
	mouth wash		25b, children as 2nd users
	lipsticks		25c, children as 2nd users
products for home improvement, handicrafts	latex paint	painting walls	26
	additive for latex paints	mixing, painting walls	26b
	varnish (water-based)	varnishing furniture, window frame, radiator	27
	additive for wallpaper paste	mixing, wallpapering	28
	floor adhesive	laying floors; latex adhesive, tile adhesive	29
	finger paint		30, children as 2nd users
	plasticine		no scenario

product category	product group	typical product/scenario	scenario no.
pest control	repellents	insect milk, crème, -stick; e.g. Autan®	31, children as 2nd users
		spray, e.g. Autan®	32, children as 2nd users
	spray	living room, e.g. Paral® insect spray	33
		targeted spot, spray against wasps, plant louses	33b
		crack & crevice, ant spray	33c
	liquid, crack and crevice treatment	ant killer (pouring)	34
	powder, crack and crevice treatment	ant killer (spreading + pouring)	35 (spreading), 35b (pouring)
	evaporators	indoors, e.g. electrical evaporator	36
		wardrobe, strips against moths	36b
		dustbin	36c
	strips/stickers	strips/stickers against flying insects	37
	bait traps		38

5.4 Exposures

For preparation of the frame formulations, potential exposures for each application were calculated by first estimating the possible load using a worst-case approach. The models proposed in the Technical Guidance Document (TGD) were used for this. In a second step, one relevant scenario each was determined for the selected substances 2-propanol, formaldehyde and chlorpyrifos, and the exposure was refined with the help of computer models such as ConsExpo and SprayExpo. Notably, the variability of physiological default values (e.g. body weight) has less impact on the exposure than the task parameters (application frequency and amount used of the product) and the substance-specific data (e.g. vapor pressure). The worst-case approach was used in order to identify relevant scenarios, active substances and combinations of these. These can then be subject to a detailed analysis of health risks.

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 due to the gas phase is negligible in most cases.

In contrast, there can be massive inhalation exposure through aerosols during spray application, so that for active ingredients whose efficacy potential by inhalation is considered to be of minor importance, this may in fact become the decisive route of intake (e.g. chlorpyrifos). Furthermore, high acute inhalation exposures to formaldehyde are to be expected from home improvement products. Inhalation exposure is also relevant in particular for the insecticide dichlorvos.

Looking at preservatives, there is such a wide range of applications and at the same time a limited number of active substances used (in cleaning products, in cosmetics, in home improvement products etc.), so that the additive exposure from all products is at the focus of interest. In addition, a high potential exposure (both dermal and inhalation) is possible in particular with leave-on cosmetics.

In general, the overall potential inhalation exposure is smaller than the overall dermal exposure. Exceptions are possible if the time and surface of skin contact results in relatively low dermal absorption. As a rule, the overall potential exposure for children (9-11 months) is maximally by a factor of 10 higher than for an adult user.

5.5 Characterisation of active substances

The toxicological data for the substances were analysed on the basis of reviews, supplemented by original literature, and summarised in substance dossiers. Except for the two substances sodium dichloroisocyanurate and trichloroisocyanuric acid, there is sufficient data available, 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, is very varied. 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. The most relevant effect endpoints of the substances and, as far as possible, the NOAELs (no observed adverse effect levels) for the oral, inhalational and dermal routes of intake have been comparatively summarised (see Table 3). 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. Based on the NOAEL values, the MOE (margin of exposure, see below) was calculated.

Table 3 Overview of the toxicity of selected active substances

active substance	skin irritation	mucous membrane irritation	sensitising	mutagenicity	carcinogenicity	toxicity * on reproduction	NOAEL dermal systemic [mg/kg/d]	NOAEL inhalation [mg/m³]	NOAEL oral [mg/kg/d]	ADI / TDI etc. [mg/kg/d]	TRGS 900 / OEL [mg/m³]
2-Propanol	no / slight	slight	no / ?	no	no	yes, at maternal Tox. (D)	n.u.	LOAEL 1230	100	2.4	500
Alkyl dimethyl benzyl ammonium chlorides (QAC)	strong / NOAEL 0.1% aqueous solution	strong	?	no	no	no	LOAEL 10 (subchronic)	n.i.	LOAEL 25	n.s.	n.s.
Sodium hypochlorite	strong (corrosive) / NOAEL < 0.1% aqueous solution	strong (corrosive)	yes	?	no	no / ?	n.i.	n.i.	3	n.s.	n.s.
Sodium dichloro-isocyanurate	medium	strong	n.i.	no / n.i.	n.i.	yes, at maternal Tox. (D)	n.i.	LOAEL 0.1 - 38	50 - 130	0 - 2	n.s.
Trichloroiso-cyanuric acid	strong / ?	strong / ?	n.i.	n.i.	n.i.	n.i.	n.i.	0.5 ?	50 - 130	n.s.	n.s.
Hydrogen peroxide	slight/ LOAEL 10%	strong / LOAEL 0.1%	nein / ?	?	?	?	n.i.	0.7	26	n.s.	1.4
Triclosan	medium / LOAEL 0.5%	medium / NOAEL 1%	yes, slight	no	no	yes, at maternal Tox. (D)	> 80	n.i.	LOAEL 25	n.s.	n.s.

active substance	skin irritation	mucous membrane irritation	sensi-tising	muta-gen-icity	carci-nogen icity	toxicity * on repro-duction	NOAEL dermal systemic [mg/kg/d]	NOAEL inhala-tion [mg/m³]	NOAEL oral [mg/kg/d]	ADI / TDI etc. [mg/kg/d]	TRGS 900 / OEL [mg/m³]
Formaldehyde	strong / LOAEL 0.1%	strong	yes / LOAEL 5% (LLNA)	yes	yes	yes, at maternal toxicity (D)	> 25	0.4	15	0.2	0.37
Glutardialdehyde	strong / NOAEL 0.1%	strong / NOAEL 0.1%	yes / LOAEL 0.25% (LLNA)	no / ?	no / ?	yes, at maternal toxicity (D)	LOAEL 50	0.088	4 - 6	n.s.	0.42
Benzoic acid	slight	slight	no	no	no	no	n.i.	n.i.	250 - 500	0 - 5 and/or 4	n.s.
Kathon (CIT/MIT)	stark / NOAEL 0.056% a.i.	stark / NOAEL 0.056% a.i.	strong / LOAEL 7.5 mg/l	no	no	yes, at maternal toxicity (D)	NOAEL 0.4	0.34	LOAEL 1.5	n.s.	n.s.
1,2-Benzisothia-zolin-3-one	strong / NOAEL 0.05 %	strong	yes / LOAEL 0.005 – 0.05%	no / ?	no / n.i.	yes, at maternal toxicity (D)	n.i.	n.i.	8.4	n.s.	n.s.
Bronopol	strong / NOAEL 0.1%	medium / NOAEL 0.5%	yes / LOAEL 1.5%	no	no	yes, at maternal toxicity (D)	20	n.i.	10	0.1	n.s.
2-Phenoxyethanol	slight	slight	?	no	n.i.	yes (D) (T)	500	n.i.	80	3	110
Chloroacetamide	slight/ LOAEL 9%	slight/ LOAEL 5%	yes / LOAEL unklar (0.003%?)	no	n.i.	yes (T)	35	n.i.	10	n.s.	n.s.

active substance	skin irritation	mucous membrane irritation	sensitising	mutagenicity	carcinogenicity	toxicity * on reproduction	NOAEL dermal systemic [mg/kg/d]	NOAEL inhalation [mg/m³]	NOAEL oral [mg/kg/d]	ADI / TDI etc. [mg/kg/d]	TRGS 900 / OEL [mg/m³]
Icaridin	no	slight	no	no	no	no	100	n.u.	80	n.s.	n.s.
Prallethrin	slight	slight	no	no	no	slight (D)	30	1	2.5	0.025	n.s.
Chlorpyrifos	no / slight	no / slight	?	no	no	yes, at maternal toxicity (D)	5	0.3	0.03	0.01 and/or 0.003	0.2
Dichlorvos	?	?	yes / LOAEL 0.5%?	yes	yes	yes (T)	n.i.	0.05 ?	0.04	0.004 and/or 0.0005	1
Phoxim	slight	slight	yes	no	no	yes (T)	LOAEL 0.5	n.i.	0.38	0.004	n.s.

a.i. active ingredient
? contradictory information, weak indication or observations that can not be interpreted
n.i. not investigated
n.s. not specified
* Differentiation of effects on reproduction toxicity: (D): developmental toxicity, (T): teratogenicity

5.6 Assessment

In addition to systemic effects, irritant effects on the skin and mucous membranes as well as skin-sensitising effects 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 (Kathon and 1,2-benzisothiazolin-3-one), glutardialdehyde and formaldehyde, di- and trichloroisocyanurates, hydrogen peroxide, bronopol and triclosan belong to this group. Regarding non-specific irritations, an additive effect must be assumed if different products containing these active substances are used in parallel or consecutively within a short time. The irritant effect is also relevant for inhalation exposure during spraying. This holds true in particular for formaldehyde and glutardialdehyde.

For 10 of the active substances investigated, there is fairly clear evidence that they have a sensitising effect. These are the isothiazolinones (Kathon and 1,2-benzisothiazolin-3-one), glutardialdehyde and formaldehyde, chloroacetamide, dichlorvos, phoxim, bronopol, triclosan as well as sodium hypochlorite. Di- and trichloroisocyanurates have not been investigated for skin sensitising effects. This broad range of effects and at the same time the substantial importance of dermal contact with objects of daily use, underline the relevance of this endpoint. For some substances, the concentrations which induced sensitization in humans or in the local lymph node assay in mice were compared to the application concentrations in products of daily use (see Table 4). With the exception of bronopol, there seem to be only minor differences between the effect concentrations and application concentrations of these substances. Formaldehyde, 2-phenoxyethanol and Kathon are generally considered to be important allergens. The sensitisation prevalence of these three biocides was 2-4% in studies performed in dermatological hospitals. A detailed assessment and risk characterization is needed for these.

Table 4 **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	references
Kathon (CIT/MIT)	12.5 ppm, (effective conc. 12.5 ppm)	75 ppm (EC_3)	cleaning & washing: 60 ppm cosmetics: 2.5 -7.5 ppm (15 ppm allowed according to cosmetics directive)	HRIPT: Cardin et al., 1986 LLNA: Warbrick et al., 1999
Glutar-dialdehyde	5% (effective conc. 0.5%)	0.1% (EC_3)	cleaning & washing: 0.01 -0.5% cosmetics: ≤ 0.1% (allowed according to cosmetics directive)	HRIPT: Marzulli und Maibach, 1974 LLNA: Basketter, unveröffentlichte Daten, berichtet in Akkan et al., 2004
Formaldehyde	1% (effective conc. 1%)	0.35% (EC_3)	cleaning & washing: 0.05% home improvement: ≤ 0.1% cosmetics: ≤ 0.2% (allowed according to cosmetics directive)	HRIPT: Marzulli und Maibach, 1974 LLNA: Basketter et al., 2001
Bronopol	5% (effective conc. 2.5%)		cleaning & washing as well as home improvement: 0.0011-0.035% cosmetics: 0.01-0.1% (0.1% allowed according to cosmetics directive)	HRIPT: Marzulli und Maibach, 1974
Chloro-acetamide	0.5% (effective conc. 0.5%)		cleaning & washing:0.1 -0.3% home improvement: 0.1- 0.3 % cosmetics: 0.3% (allowed according to cosmetics directive)	HRIPT: Jordan und King, 1977

HRIPT: Human Repeat Insult Patch test
LLNA: Local lymph node assay
EC_3: concentration leading to a triplicate proliferation rate in the Local lymph node assay.

To assess the systemic effects of biocide exposure, MOEs (margins of exposure), i.e. the ratio of NOAEL and exposure concentration (as body dose), were calculated. MOEs were calculated on the one hand for the individual scenarios, and on the other hand for the total of all exposures from all scenarios (for additive exposure, see Table 5). As these MOEs are based on the calculated exposures (screening), they can be only a rough guide for assessing the health risks. The modelled data from the screening are normally at least by a factor of 10-100 higher than the actual exposures. An underestimation of the additive exposure can in general be ruled out. The worst-case approach, however, is very useful to identify relevant scenarios, active substances and combinations of these, which can then be subject to a detailed analysis of health risks. Probabilistic calculations make only sense to differentiate the exposure distribution across the groups of consumers and children after the parameters have been refined. For MOE assessment, the following rule applies: the higher the MOE, the lower the risk.

Overall MOEs 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, Kathon 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, Kathon), 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.

Table 5 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 dichloro-isocyanurate	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
Kathon	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

In summary, further scenarios are not relevant for additive exposure. By summing up all scenarios the exposure increases only on average by a factor of 3 as compared to the highest exposure in a single scenario. On average 11 scenarios per substance were summed. 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. When assessing overall exposure to 2-propanol, it must be taken into account that this biocide is also used e.g. as a solvent. For this application area, our market research did not yield any detailed information, so that it was not considered any further.

Comparing the MOEs for different biocides within one scenario, marked differences are observed between the different biocidal substances. Extremely negative in this respect are the results for the airway-irritant

biocides hydrogen peroxide, formaldehyde and glutardialdehyde regarding inhalation exposure to sprays and concentrates, MOEs being lowest for glutardialdehyde because of the particularly low NOAELs. Remarkable differences between MOEs also exist for 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 analyses have been carried out, since considerably lower and more realistic values (as demonstrated for dyes) can be achieved by refinement of the exposure. Preservatives in cosmetics are thus likely to be sufficiently regulated for health protection. 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.

For indoor use of chlorpyrifos and dichlorvos, risk assessments in the literature provide contradictory results, so that detailed investigations into the risks from indoor exposure to organophosphate-containing insecticides and risk reduction measures are deemed appropriate.