Attention please

Recommendation for the Safety assessment of Detergents, Cleaning and Maintenance Products

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Industrieverband Körperpflege- und Waschmitel e.V.*
(IKW – German Cosmetic, Toiletry, Perfumery and Detergent Association)

Recommendation for the Safety Assessment of Detergents, Cleaning and Maintenance Products

1. Introduction

For many years, the manufacturers of detergents, cleaning and maintenance products organised within IKW have been sharing with the general public their expert knowledge of the products they manufacture. This is done in the form of quality recommendations. One objective is the development and marketing of products of optimal performance and quality. At least equally important is the obligation to offer products which are safe for consumers under reasonably foreseeable usage conditions. Consistently pursuing the ideal of sustainability, manufacturers of detergents, cleaning and maintenance products want to keep in good shape for the future. In this context and based on the Rio Declaration of 1992, sustainability is defined as a well-balanced combination of economic, social and ecological aspects that meets the needs of the present without compromising the ability of future generations to meet their own needs.
In this meaning, the present Safety Assessment Recommendation firstly serves consumers who expect efficacious products which are safe in terms of health and environment. Secondly, this Recommendation encourages the sense of responsibility for humans and the environment among company staff in product development and manufacture.
In order to adequately address the economic requirements of companies of the detergents, cleaning and maintenance industry, the safety assessment must be an integral part of formulation development. This is possible only in a close cooperation between the safety assessor and the development chemist.
This Recommendation generally describes the steps to be taken for the development and marketing of safe products. The Recommendation was elaborated by the IKW expert committees »Cleaning and Maintenance Products« and »Detergents«. Both committees consist of experts from competing companies. This ensures the neutrality of the committees.
As a follow-up initiative, it is planned to publish, by way of example, safety assessments for specific product categories (e.g. all-purpose cleaners, waterproofing products).

2. Background

For detergents, cleaning and maintenance products, the legislator expressly places product safety responsibility on the manufacturers and distributors of these products. A rule to this effect is laid down in § 30 of the German code on foods, commodities and feedstuffs (Lebensmittel-, Bedarfsgegenstände- und Futtermittelgesetzbuch - LFGB) (1).
Furthermore, the following legislations apply specifically for certain detergents, cleaning and maintenance products:

- Detergents Regulation (EC) No 648/2004 (2)
- Detergents and Cleaning Products Act (3)
- Chemicals Act (4), Dangerous Substances Ordinance (5) in conjunction with the Dangerous Substances Directive (67/548/EEC) (6), Preparations Directive (1999/45/EC) (7) and Biocidal Products Directive (98/8/EC) (8); Chemicals Ban Ordinance (9) in conjunction with the Restrictions Directive (76/769/EEC) (10);
- Equipment and Product Safety Act (11)
- Provisions on dangerous goods

The intended or foreseeable use is assessed in particular by resorting to:

- The presentation of the product,
- product labelling,
- instructions for use and disposal, where applicable,
- any other types of information provided, together with the product, by the manufacturer or by the party responsible for placing the product on the market.

Detergents, cleaning and maintenance products must be safe for consumers. This obligation calls for an examination of the product, ranging from the selection of raw materials, manufacture and use to product disposal. In particular, the following points must be taken into consideration:

- Selection of toxicologically and ecotoxicologically well-characterised ingredients, taking into account their

concentrations in the finished product and in the use of the finished product;

- adequate packaging for safe storage, maintaining product quality and avoiding misuse and accidents;
- quality controls regarding microbiological or chemical impurities of ingredients and finished products;
- presentation of the product, including labelling and information on use, disposal and first aid in accidents, where applicable.

3. Ingredients

The careful selection of ingredients has a decisive role in ensuring the safety of the finished product. Assessments of ingredients are based on the following elements:

- Identification of the ingredient
- Physical-chemical characteristics
- Significant impurity (impurities)
- Interactions with other ingredients
- Data on toxicological and eco-toxicological properties, e.g. acute oral toxicity, corrosive or irritant effect, biodegradability, aquatic toxicity

The following types of exposure can be relevant:

1. Skin contact
2. Eye contact
3. Inhalation
4. Ingestion

In all types of exposure, the possibility of resorption – i.e. intake and diffusion of the substance in the body – must be taken into account.
The following potential risks can result from the different types of exposure, so that they must be assessed on the basis of toxicological data:

- Irritant or corrosive reactions of skin, eyes and respiratory system;
- allergic reactions of skin and respiratory system;
- toxic effects after inhalation/ingestion or skin resorption.

3.1 Ingredients to be avoided

Various pieces of legislation must be observed in the selection of ingredients for detergents, cleaning and maintenance products. For example, the following ingredients are excluded:

- Substances which are prohibited under the Chemicals Ban Ordinance (9);
- surfactants of insufficient aerobic biodegradability in detergents, according to the Detergents Regulation (EC) No 648/2004 (2);
- anionic or non-ionic surfactants of insufficient primary degradability in detergents and cleaning products, according to the Detergents and Cleaning Products Act (3), which do not fall under the »detergent« definition of the Detergents Regulation (2);
- substances whose toxicological data are irreconcilable with the intended concentration and use;
- substances for which neither toxicological data nor empirical data are available in sufficient quantities, in respect of safe use.

3.2 Sources of toxicological and eco-toxicological data

These sources are, most importantly, safety data sheets from raw material suppliers. Raw material suppliers must comply with national and EU legislations on chemicals and dangerous preparations (occupational health and safety, transport, packaging, labelling), such as e.g. the Dangerous Substances Directive 67/548/EEC (6). Thus they are under the obligation to carry out a toxicological and eco-toxicological characterisation of chemicals which they place on the market. Further potential sources of (eco-)toxicological data:

- Scientific literature, reports by the Scientific Committee on Consumer Products (SCCP) (12) and the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOX) (13), substance monographs and monographs of the Research Institute for Fragrance Materials (RIFM) (14);
- databases, such as the DIMDI substance database (15) or TOXLINE (16);
- list of the detergents committee (Hauptausschuss Detergenzien/HAD) for assessing the environment properties of certain ingredients of detergents and cleaning products (17);
- in-house empirical data for an ingredient or for detergents, cleaning and maintenance products which contain this ingredient;
- expert opinions based on analogies to similar substances or preparations;
- for fragrances, a compliance statement of the International Fragrance Association (IFRA) (18).

Concerning perfume oils, a product data sheet for fragrances or fragrance mixtures according to **Annex 1** to this Recommendation - should be requested, where relevant information is not provided in the safety data sheet.
According to the Detergents Regulation (EC) No 648/2004 (2), all surfactants used in detergents must be fully biodegradable. Furthermore, manufacturers of detergents must have complete information about the composition of mixtures (preparations) used as ingredients.
Under § 1 subparagraph 1 of the German Detergents and Cleaning Products Act (3), detergents may be placed on the market only in such a way that – after their use – every avoidable adverse effect is prevented regarding the state of waters and especially in respect of the natural balance and drinking water supplies, and that there is no impairment in the operating of sewage works (»*nur so in den Verkehr gebracht werden, dass*

nach ihrem Gebrauch jede vermeidbare Beeinträchtigung der Beschaffenheit der Gewässer, insbesondere im Hinblick auf den Naturhaushalt und die Trinkwasserversorgung, und eine Beeinträchtigung des Betriebs von Abwasseranlagen unterbleibt«).

3.3 Conditions of use and exposure
As previously stated under 3.2, conditions of use of the finished product at a later stage are taken into account in the selection of prerequisite information on ingredients. In particular, the following parameters should be considered:

- Product group (e.g. hand dishwashing product, toilet cleaner, leather care product) in which the ingredient is used;
- concentration of the ingredient in the product;
- application and dosage (e.g. spraying, how to apply, diluting with water);
- exposure per application and application frequency for dermal contact (potential duration of contact and contact area), inhalation and ingestion, where applicable;
- foreseeable misuse, which increases exposure.

4. Safety Assessment of Finished Products

For assessment purposes, not only the toxicological profile of ingredients but also experiences in the use of similarly composed products in connection with humans can be resorted to. New ingredients may be used only where adequate data on the safety of such ingredients are available for the intended field of application. This can be ensured e.g. by way of suitable experimental studies. Only after that can a product be released for marketing.
Ideally, safety assessments of detergents, cleaning and maintenance products are possible exclusively on the basis of data for the individual ingredients.

Where this is not possible – e.g. in case of interactions between the various ingredients, such as antagonisms between different surfactants regarding their irritant effect on skin (19) – there are the following alternatives:

- Comparison with sufficiently similar products for which adequate data are available, e.g. within the IKW Trustee-Expert-Model **(Annex 2)**
- Implementation of additional tests

Validated *in-vitro* tests show whether preparations have corrosive effects or not. Two relevant *in-vitro* methods are stated in Annex V part B no. 40 of the Dangerous Substances Directive (6). The TER test brings false positive results for many aqueous-alkaline formulations and is thus better suited for acidic preparations. In the human skin model test, false positive results were observed rather in the acidic milieu; consequently this test is more suitable for alkaline preparations **(Annex 3)**.
Additionally, results from non-validated *in-vitro* tests can be used in safety assessments **(Annex 4)**.
Control studies in voluntary human test subjects are permissible only if the non occurrence of irritant effects can be predicted with high probability. Clinical trials in humans should follow the principles of Good Clinical Practice (GCP) (20) of the EU. The following tests can be carried out:

- Open epicutaneous application (single or repeated);
- closed epicutaneous application (single or repeated);
- controlled application tests.

Some dermatological tests are described, by way of example, in **Annex 5**.

5. Advertising Claims with Relevance to Health

Where health-related advertising claims – such as e.g. »dermatologically tested« – are worded for a product, it must be possible to substantiate such claims with suitable data of good informative value. Regarding scientific requirements, tests involving detergents, cleaning and maintenance products are performed, as a matter of principle, in humans. Such tests in voluntary subjects must fulfil all relevant scientific and ethical criteria. One of these criteria is that – prior to testing – a safety assessment of the finished product is performed by a qualified person.

6. Role of the Safety Assessor

The safety assessor's position in the company must be tailored to his special function and responsibilities. The responsibility for the safe use of products must be delegated in compliance with legal requirements; the safety assessor must be free in delegation decisions. Furthermore, it is in the corporate interest to appoint as safety assessors only persons with the prerequisite professional qualification and sense of responsibility.
The following particular activities are integral elements of safety assessments of detergents, cleaning and maintenance products:

- Examination of the absence of banned ingredients;
- examination of conformity with requirements (quality, maximum concentration, field of application) for raw materials subject to restrictions, e.g. under the Chemicals Ban Ordinance (9);
- examination of available data regarding relevance and completeness (e.g. is sufficient information available on toxicological endpoints of the various ingredients);
- examination of the safe usability of all raw materials, taking into account their use concentrations and the conditions of use of the finished product;
- appraisal of potential interactions between individual ingredients;
- appraisal of the microbiological status of the individual raw materials

and of the finished product, including the preservation of the finished product;

- examination of the finished product, including product packaging and presentation, as well as of required instructions for use, danger warnings and safety advice.

In order to fulfil their tasks, persons responsible for safety assessments must have the following authorities:

- Access to all information of relevance to consumer safety, beyond purely toxicological/dermatological data (e.g. analytical-chemical data on quality, purity and impurity profile, as well as stability of raw materials and finished products).

- Access to the organisation of quality control measures for incoming raw materials and for the production of finished products, as well as access to results obtained within this framework.

- Adequate resources (budget, working hours, staff) for obtaining lacking information (e.g. by way of literature research or by initiating additional studies).

- Access to health-related complaints regarding detergents, cleaning and maintenance products of the company, as well as access to query results at poison information centres.

At the end of the process, one of the following conclusions can be drawn as final outcome of the safety assessment:

- The product is safe without any specific warnings or other precautions.

- The product is safe, on condition that the packaging meets certain requirements, and/or one or several warnings are given, and/or the product application is regulated precisely and with restrictions.

- Available data are not sufficient for a correct safety assessment; further information must be obtained or experimental studies must be carried out.

- The product is not safe in respect of the intended use.

Where one of the two last-mentioned conclusions applies, the product in question must not be placed on the market. Recommendations – e.g. regarding the concrete form of instructions for use or danger warnings/safety advice – are part of the safety assessment. It is recommended that the responsible person documents in writing the progress of the safety assessment, including the possible conditions previously mentioned and the conclusion, and signs the documentation. On request, this documentation should be submitted to the competent monitoring authorities.

Annex 1

Prerequisite items of information on fragrances/fragrance mixtures for use in detergents, cleaning and maintenance products – to be stated in the product data sheet

On request, the party placing fragrances/fragrance mixtures on the market provides customers with the following items of information on fragrances. This is done in the form of a product data sheet.

1. Name and/or article no. of the fragrance/fragrance mixture
2. Party placing the fragrance/fragrance mixture on the market
3. Statement of all names and percentages (referred to 100% of the fragrance/ fragrance mixture) - where these percentages are so high that they can be relevant for the labelling of the finished product – of
   a) ingredients of the fragrance/fragrance mixture classified as dangerous
      and/or
   b) ingredients contained in the natural constituents of the fragrance/fragrance mixture (e.g. lime in orange oil)

Substances mentioned under 3a) and 3b) are generally *) relevant from the following concentrtions for the labelling of detergents, cleaning and maintenance products:

Dangerous properties (danger warnings)	Concentration relevant vor labelling	Consideration threshold**, if lower
Sensitising substances (R42, R43)	from 0.1%	
Substances dangerous for the environment (R50/53)	from 0.25%	0.1%
Substances dangerous for the environment (R51/53)	from 2.5%	0.1%
Very toxic substances (R26, R27, R28)	from 0.1%	
Toxic substances (R23, R24, R25)	from 3%	0.1%
Corrosive substances (R35)	from 1%	
Carcinogenic and/or mutagenic substances cat. 1 or 2 (R45, R 46, R49)	from 0.1%	
Carcinogenic and/or mutagenic substances cat. 3 (R40, R68)	from 1%	
Substances toxic for reproduction cat. 1 oder 2 (R60, R61)	from 0.5%	0.1%
Substances toxic for reproduction cat. 3 (R62, R63)	from 5%	1%

* Other, usually lower limit values may apply according to Annex I to the Dangerous Substances Directive (6) or for substances of very high aquatic toxicity according to the Preparations Directive (7).

** According to Article 3 no. 3 of the Preparations Directive (7) the consideration threshold is the value from which a relevantly classified substance needs to be taken into consideration for classification and possibly also for labelling.

4. Statement of percentages of substances in fragrances/fragrance mixtures – substances as listed in Opinion SCCNFP/0017/98 of the Scientific Committee on Cosmetic and Non-Food Products (SCCNFP) - where these percentages are relevant for the labelling of finished products: Such fragrances must be stated on the packaging of detergents if they are contained in the finished product in volumes of over 0.01%.
5. Declaration that the fragrance/fragrance mixture does not contain any further ingredients relevant for the labelling of detergents, cleaning and maintenance products. Where fragrances/fragrance mixtures do not contain any ingredients – even as constituents of natural raw materials (e.g. essential oils) - in volumes which are relevant to the labelling of detergents, cleaning and maintenance products, this should be expressly stated.
6. Place and date of issue.
7. Name and signature of the person responsible for the product data sheet.

Annex 2

A Trustee-Expert-Model

The Trustee-Expert-Model for the classification and labelling of detergents, hand dishwashing products and cleaning products:

For detergents and cleaning products, which are classified as **irritant** when applying the calculation method, there is the possibility of reviewing this classification based on the so-called **Trustee-Expert-Model**. This Model is followed where there is reason to believe that the calculation method results in »over-labelling« regarding the irritant potential. The Model is based on conclusions by analogy to comparable formulations which proved to be »not irritant« in testing. For this purpose, an opinion is given by an independent expert.

On request, competent monitoring authorities are given access to all data connected with the labelling of a product according to the Trustee-Expert-Model. Such data are summed up in a so-called **product dossier**.

A stepwise approach is taken in the application of the Trustee-Expert-Model:

1. The manufacturing company finds out whether a classification as irritant is necessary according to the calculation method.
2. If the calculation method results in a classification as irritant, the manufacturing company finds out whether there is a sufficient number of similar comparable formulations. For this purpose, the catalogue of comparable formulations can be requested from IKW. In order to ensure confidentiality, comparable formulations are simplified and anonymised. The original formulations and test protocols, which serve as a basis, are available to the trustee. The concerned company selects one or several sufficiently similar comparable formulations for the implementation of the Trustee-Expert-Model procedure.
3. If a sufficient number of similar formulations are available and the manufacturing company wants an opinion on its own formulation, all documents relevant for the opinion (e.g. exact formulation, pH value, result of classification according to the conventional method, safety data sheets of all input raw materials, possibly also determination of the alkaline or acidic reserve according to *Young* et al. (21)) must be addressed – in a closed and sealed envelope, which is marked **confidential/personal** – to:

   Industrieverband Körperpflege- und Waschmittel e.V. (IKW)
   Attention Dr *Bernd Glassl*
   Mainzer Landstr. 55
   60329 Frankfurt am Main, Germany

   The IKW trustee confirms in writing the receipt of the documents to the enquiring manufacturing company and makes arrangements for consulting the scientific expert.
4. Next, the scientific expert performs a comparison between the product to be examined on the one side and the original comparable formulations and relevant original test protocols on the other. The expert returns his opinion – together with all documents provided by IKW – to the IKW trustee.
5. The IKW trustee sends the expert opinion - together with all documents made available to IKW - to the manufacturing company. This is done in a closed and sealed envelope, which is marked confidential/personal. The invoice for the expert opinion is also enclosed.

   The confidential treatment of all documents made available to the IKW trustee is ensured.
6. In a final step, the manufacturing company classifies and labels the product on the basis of the expert opinion. The expert opinion is an essential part of the information or product dossier mentioned in the introductory statement.

B Extended Trustee-Expert-Model (ETGM)

The Trustee-Expert-Model is extended for detergents and cleaning products with a pH value of over 11.5 or under 2 which, according to manufacturer's knowledge, have no corrosive effect on skin.

Where a manufacturing company wants an expert opinion under the Extended Trustee-Expert-Model, the detailed formulation must be submitted openly to the IKW trustee, so that the trustee can identify comparable formulations. A further prerequisite for an expert opinion under the Extended Trustee-Expert-Model is that the formulation is not deemed corrosive, in the light of the determination of the alkaline or acidic reserve of the formulation according to *Young* et al. (21).

As for the rest, the procedure described under A., points 3 to 6, is followed.

Annex 3

Examples of false positive results in *in-vitro* testing of the dangerous property »corrosive to skin«

The following table gives some examples of false positive results of the TER test or the human skin model test according to Annex V part B. no. 40 of the Dangerous Substances Directive 67/548/EEC (6).

			Results of *in-vitro* testing	
Substance	**Result of *in-vivo* testing**	**TER Test**	**EPISKIN® (human skin model)**	**EpiDerm® (human skin model)**
10-undecenoic acid	not corrosive	not corrosive	R34	- / -
Sodium carbonate (50%)	not corrosive	R34	not corrosive	not corrosive
Sodium hydrogencarbonate	not corrosive	R34	not corrosive	- / -
Sodium undecylenate (33%)	not corrosive	R35	R34	- / -
Sodium lauryl sulfate (20%)	not corrosive	R35	not corrosive	not corrosive

These examples are based on table 6 of the s*ummary report of the EpiDerm In Vitro Assay for Assessing Dermal Corrosivity*, which was compiled on 31 March 2001 within the *National Toxicology Program* (NTP) by Dr *Raymond Tice* for the *National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods* (NICEATM) and revised on 24 July 2001.

Annex 4

Further examples of IN-VITRO MODELs

***In vitro* irritation tests in recombinant skin cultures (organotypic skin model)**

Multilayered skin cultures are grown from (epidermal) human keratinocytes and dermal fibroblasts (co-cultures). The uptake of the vital dye neutral red and measuring of mitochondrial enzyme activities (MTT) show the degree of the harmful effect (irritant potential). The advantage over the neutral red test lies in the improved possibility of applying finished formulations, which can be tested also as poorly soluble or water-insoluble formulations and taking into account the barrier function of an artificial stratum corneum.

EPISKIN test: Testing of irritant effect in humans
The EPISKIN test uses human skin models, in order to differentiate between »not irritant«, »irritant« and »corrosive«. There is the possibility of this test providing false positive results.

The validity of the EPISKIN test is currently being examined by the European Centre for the Validation of Alternative Methods (ECVAM). The outcome is expected for 2007.

Literature:

Gueniche, A., Ponec, M.:
Use of human skin cell cultures for the estimation of potential skin irritants
Toxic. in Vitro, 7, 15 - 24 (1993)

Osborne, R., Perkins, M. A.:
In vitro skin irritation testing with human skin cell cultures
Toxic in Vitro, 5/6, 563 - 567, (1991)

Vanghan, F. L.:
Use of an epidermal culture for cutaneous toxicity studies AN
Drug Pharm., Sci, 42, 271-297 (1990)

***In vitro* testing of irritant potential in isolated skin (organ culture)**

Excised and *in vitro* cultivated pieces of skin from different species (human, pig, mouse) form the basis for testing. The irritant effect – which causes membrane damage – can be identified through analysis of intracellular enzymes (lactate dehydrogenase LDH, glutamate oxalacetate transaminase GOT) released to the culture medium, glucose consumption as vitality parameter, and morphological-histological examinations. Advantages of skin explant cultures are easier cultivation and high vitality. Insoluble substances or formulations can be applied directly, and additional parameters can be included in measuring.

Note: The methods can cause an overestimation of impacts of acids and bases, i.e. they can be unsuitable for preparations with high or low pH values.

Literature:

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Bewertung der lokalen Verträglichkeit von Tensiden mittels *in vitro*-Methoden
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Bartnik, F., Pittermann, W., Mendorf, N., Tillmann, U., Künstler, K.:
Skin organ culture for the study of skin irritancy
Toxic in Vitro Vol. 4, No. 4/5, 293-301

Kao, J., Hall, J., Holland, J.:
Quantification of cutaneous toxicity: An *in vitro* approach using skin organ culture
Toxicol. Appl. Pharmacol. 68, 206 - 217 (1988)

Kao, J., Patterson, F., Hall, J.:
Skin penetration and metabolism of topically applied chemicals in six mammalian species, including man: An *in vitro* study with benzo(a)pyrene and testosterone
Toxicology and Applied Pharmacology 81, 502 - 516 (1985)

Testing of cutaneous permeation in excised skin models

Fresh, excised skin specimens from different species (human, pig, rat) – reduced to stratum corneum and epidermis – form the basis for testing. Punched out, round pieces of skin are clamped in suitable chambers and bathed with receptor liquid, on the epidermis side. Integrity of the skin is ensured with tritiated water, prior to testing. Test substances are applied either as gels or as liquids. Typical application conditions can be included. The measuring of the test substance – from starting material, washing water and permeation liquid to the determination of residual contents in skin – results in an overall balance, which allows a monitoring of the progress of experimentation. The models enable work with radioactively labelled substances as well as analysis with HPLC or gas chromatograph.

Literature:

Bracher, M., Faller, C., Noser, F. K.:
Evaluation of an *in vitro* percutaneous permeation model with two oxidative hair dyes
Int. J. Cosmet, Scl 9, 223 - 236 (1987)

Bronaugh, R. L. et al.:
Methods for *in vitro* percutaneous absorption studies II: Animal models for human skin
Toxicol. Appl. Pharmacol. 62, 481 - 488 (1982)

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J. Pharm. Sci. 74, 64 - 67 (1985 a)

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In vitro permeation with pig skin: Instrumentation and comparisen of flow-through versus static-diffusion protocol.
J. Appl. cosmetol. 6, 111 - 122 (1988)

Scott, R.C. et al.:
Permeability of abnormal rat skin
J. Invest. Dermatol. 86, 201 - 207 (1986)

Annex 5
Examples of dermatological testing in humans

Open epicutaneous test

Undiluted finished products or application-relevant diluted products can be tested in an open epicutaneous test, with application times ranging from 15 to 60 minutes (standard application time 30 minutes).

Permanent contact throughout a testing time of 15 (30, 60) minutes enables the observation and evaluation both of objective changes to skin and of the subjective sensation of test persons.

The test serves as a safety test for concentrated finished products, whose skin tolerance in unwanted contact with concentrated product can be assessed. Furthermore, for products applications, which do not exceed the application time under foreseeable conditions, there is the possibility of a realistic compatibility assessment in use. The test is altogether suitable for identifying highly irritant formulations. It is less suitable for identifying or differentiating mildly irritant formulations.

Literature:

Björnberg, A.:
Skin reactions to primary irritants in patients with hand eczema
Gothenburg 1968, Isacsons

Burckhardt, W., Schmid R., Schmid P.:
Die Epicutanprobe durch wiederholte Benetzung
(Translates into: Epicutaneous test through repeated wetting)
XIII. Congressus Internationalis Dermatologie,
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On epicutaneous tests (patch test, contact test, wetting test, combined test, resistance to alkali),
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(Translates into: On the dependency of the non-carrying out of epicutaneous skin tests on localisation and state of the eczema)
Derm. Wschr. 112, S. 237 - 246 (1941)

Carrié, C. und Kühl, M.:
Leitfaden der beruflichen Hautkrankheiten
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2. Auflage, Stuttgart 1969, Thieme-Verlag

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Test strategies for development of cosmetic products using dermatological test models,
Seifen - Öle - Fette - Wachse, Jg. 117,2, S. 42 - 43 (1991)

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Dermatologische Methoden zur Prüfung der Hautverträglichkeit von Handgeschirrspülmittel unter Berücksichtigung der Kennzeichnungs-Verordnung
(Translates into: Dermatological methods for the testing of skin tolerance of hand dishwashing products, taking into account the labelling regulation)
Seifen - Öle - Fette - Wachse, 119, S. 922 - 928 (1993).

Miescher, G.:
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(Translates into: The skin as defence organ)
Hautarzt 8, S. 88 - 93 (1957)

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Zum Nachweis der Ursachen des Kontaktekzems mit der Benetzungsprobe
(Translates into: Regarding the substantiation of causes of contact eczema through the wetting test)
Dermatologie (Basel) 136, 219 (1968)

Schmid, R.:
Die Erfahrung mit einer Epicutanprobe durch wiederholte Benetzung beim Kontaktekzem
(Translates into: Experience with an epicutaneous specimen through repeated wetting in contact eczema)
Med. Diss., Zürich (1963)

Closed epicutaneous test

The closed epicutaneous test – where diluted or undiluted finished products are applied over 24 (48) hours with the help of occlusive chambers – clearly intensifies exposure. The occlusive effect of a test chamber promotes the penetration of applied substances, so that also usually weakly irritant or non-irritant substances or substance mixtures can cause irritation.

The test is suitable for the comparative testing of substances or products. It can also serve to confirm product safety, if the tested product caused no skin reactions under intensified test conditions and would be applied only over shorter periods of time under foreseeable conditions of use.

Where skin reactions are observed, no transfer to the application situation is possible, because no exact transfer factor can be stated regarding the changed barrier function and regarding cumulative effects after multiple applications. Then, controlled application tests or use tests must be resorted to.

With simultaneous use of UV radiation, also photodynamic processes (phototoxic effects) can be studied in the epicutaneous test. Usually, this test does not enable any derivation of statements on photosensitising potential.

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Manual of Contact Dermatitis, 2nd Edition
Munksgaard, Copenhagen, Chicago (1986)

Bandmann, H. J., Fregert S.:
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Springer, Berlin, Heidelberg, New York (1973)

Braun-Falco, O.:
Leserzuschrift: Test am Menschen
(Translates into: Letter to the editor: Testing in humans)
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Seifen - Öle - Fette - Wachse, Jg. 117,2, S. 42 - 43 (1991)

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Repetitive closed epicutaneous test

In the repetitive closed epicutaneous test, applications are made between once and five times per week over a period of 1 to 5 weeks for toxicological issues, and with 1 further application after a free interval after additionally 1 to 3 weeks for allergological issues. As for the rest, the test is implemented as described above.

Literature:

Frosch, P. J. and Kligman, A. M.:
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Sequential order of skin responses during a soap chamber test
Contact Dermatitits 25, S. 242 - 249 (1991)

Controlled application test

Controlled application tests are tests where the intended conditions of use are controlled and simulated repeatedly. Members of a representative group of test persons are to perform the applications under medical supervision, with the possibility of applications going further than intended. This enables the obtaining of objective and subjective tolerance parameters and the im-

plementation of safety assessments for conditions of use at a later stage. For this test, it is necessary to develop – depending on product type – different, specific courses of action and forms of application. Therefore, the following literature is stated only by way of example.

Literature:

Finkey, M. B.:
Evaluation of subjective irritation induced by soap materials
J. Soc. Cosm. Chem., 153 - 161 (1987)

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Hautirritaion und empfindliche Haut
(Translates into: Skin irritation and sensitive skin)
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Irritant effects of a detergent in wash, chamber and repeated open application tests
Contact Dermatitis 34, S. 134 - 137 (1996)

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(Translates into: Safety assessment of cosmetic products from a dermatological viewpoint)
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The controlled use test in a cosmetic product safety substantiation program
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Comparison of exaggerated and normal use techniques for assessing the mildness of personal cleansers
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Koehler, P. B.:
Clinical aspects of safety testing cosmetic products in the nineteen-eighties
J. Soc. Cosmet. Chem. 31, S. 213 - 218 (1980)

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(Translates into: Dermatological methods for the testing of skin tolerance of hand dishwashing products, taking into account the labelling regulation)
Seifen - Öle - Fette - Wachse, 119, S. 922 - 928 (1993)

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Anwendungstest mit parfümierten Kosmetika bei Patienten mit positivem Epikutantest auf Duftstoff-Mischung
(Translates into: Application test with perfumed cosmetics in patients with positive epicutaneous test to fragrance mixture)
Dermatosen 41, S. 237 - 241 (1983)

Tronnier, H., Heinrich, U., Herling, M., Schipp, B.:
Durchführung und Auswertung von »In-use«-Tests
(Translates into: Implementation and evaluation of »in-use« tests)
Parfümerie u. Kosmetik 75, S. 876 - 881 (1994)

Use test

The primary goal of the use test is to examine the fitness for use of detergents, cleaning and maintenance products. This is a test in the typical intended use, involving a larger number of test persons (≥ 50).

Furthermore, this test is a good opportunity to obtain additional information on potential intolerances.

Literature:

Gloxhuber, Ch., Schulz, K. H.:
Test methodes in dermatology, in detergency, theory and test methods, Part II
Marcel Dekker New York, S. 695 - 706 (1975)

Greaves, M. W.:
Topical α-hydroxy acid derivative for relieving dry itching skin
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(Translates into: Testing of safety in terms of health of cosmetic finished products)
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Dermatologische Prüfungen von kosmetischen Mitteln
(Translates into: Dermatological testing of cosmetic products)
Ärztliche Kosmetologie 18, S. 368 - 371 (1988)

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Prüfung der Hautverträglichkeit am Menschen zur Sicherheitsbewertung von Kosmetika
(Translates into: Testing of skin tolerance in humans for the safety assessment of cosmetic products)
Parfümerie u. Kosmetik 76, S. 314 - 322 (1995)

Tronnier, H., Heinrich, U., Herling, M., Schipp, B.:
Durchführung und Auswertung von »In-use«-Tests
(Translates into: Implementation and evaluation of »in-use« tests)
Parfümerie u. Kosmetik 75, S. 876 - 881 (1994)

Market observation

Even with the most thorough pre-tests, isolated cases of complaints regarding the safety for health of products cannot always be avoided. Therefore, it is important to critically observe new detergents, cleaning and maintenance products during their market introduction. All health-related complaints must be recorded and critically questioned, in order to complete the overall strategy for the safety assessment of detergents, cleaning and maintenance products.

Literature:

Matthies, W.:
Der Deutsche Dermatologe, 4, S. 398 - 401 (1993)

< Content

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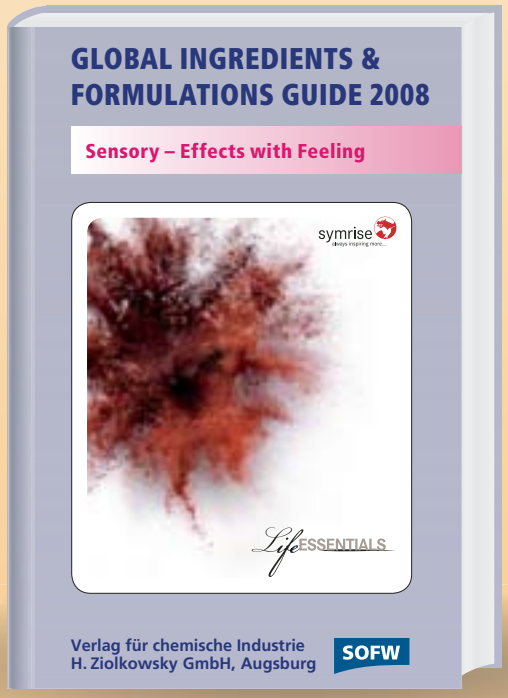

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7. Notes

(1) Lebensmittel-, Bedarfsgegenstände und Futtermittelgesetzbuch, Neufassung vom 26. April 2006 (BGBl. I S. 945)
(German code on foods, commodities and feedstuffs, revised version of 26 April 2006 (federal law gazette I p. 945)

(2) Regulation (EC) Nr. 648/2004 of 31 March 2004 on detergents (Official Journal of the European Union No L 104/1 of 8.4.2004), as last amended by Regulation (EC) Nr. 907/2006 of 20 June 2006 (OJ of the EU No L 168/5 of 21.6.2006)

(3) Wasch- und Reinigungsmittelgesetz (WRMG) vom 29.04.2007 (BGBl. I p. 600)
(German Detergents and Cleaning Products Act of 29.04.2007 (federal law gazette I p. 600))

(4) Chemikaliengesetz (ChemG) Neufassung vom 20.06.2002 (BGBl. I S. 2090), zuletzt geändert § 4 Abs. 6 des Gesetzes vom 1.9.2005 (BGBl. I S. 2655)
(German Chemicals Act, revised version of 20.06.2002 (federal law gazette I p. 2090), last amended § 4 subpara 6 of the act of 1.9.2005 (federal law gazette I p. 2655))

(5) Verordnung zum Schutz vor Gefahrstoffen (Gefahrstoffverordnung-GefStoffV) i.d. Fassung vom 23. Dezember 2004 (BGBl. I S. 3855), geändert durch Art. 2 der Verordnung vom 23.12.2004 (BGBl.I S. 3855)
(German ordinance for the protection against dangerous substances (Dangerous Substances Ordinance), in the version of 23 December 2004 (federal law gazette I, p. 3855), amended by article 2 of the ordinance of 23.12.2004 (federal law gazette I p. 3855))

(6) Directive on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances (67/548/EEC) (Dangerous Substances Directive) of 27.6.1967 (EC OJ 196 of 16.8.1967), as last amended by the 29th Adaptation of 29.4.2004 (2004/73) – EC OJ L 236 of 7.7.2004

(7) Directive (1999/45/EC) of 31 May 1999 relating to the classification, packaging and labelling of dangerous substances, as last amended by Regulation 2006/8/EC of 23.1.2006 (EC OJ L 19/12 of 24.1.2006)

(8) Directive (98/8/EC) of 16 February 1998 concerning the placing of biocidal products on the market (published in the Official Journal of the EC No L 123/1 of 24.4.1998), including Corrigendum (published in the EC OJ No L 150/71 of 8.6.2002)

(9) Chemikalienverbotsverordnung (ChemVerbotsV) (Neufassung vom 13. Juni 2003), zuletzt geändert durch Art. 4 des Gesetzes vom 21.6.2005 (BGBl I S. 1667)
(German Chemicals Ban Ordinance (revised version of 13 June 2003), as last amended by Art. 4 of the act of 21.6.2005 (federal law gazette I p. 1667))

(10) EC Directive relating to restrictions on the marketing and use of certain dangerous substances and preparations (76/769/EEC) of 27.7.1976 (OJ L 262/201 of 27.09.1976) (Restrictions Directive), as last amended by Directive 2005/59/EC of 26.10.2005 (OJ L 306/13 of 25.11.2005)

(11) Gesetz über technische Arbeitsmittel und Verbraucherprodukte (Geräte- und Produktsicherheitsgesetz – GPSG) vom 6.1.2004 (BGBl. 2004 Teil I Nr. 1, S. 2)
(German act on technical work equipment and consumer products (equipment and product safety act) of 6.1.2004 (federal law gazette 2004 part I no. 1 p. 2))

(12) Scientific Committee for Consumer Products, Beratungsgremium der Europäischen Union (http://ec.europa.eu/health/ph_risk/committees/04_sccp/04_sccp_/04_sccp_en.htm)

(13) European Centre for Ecotoxicology and Toxicology of Chemicals (www.ecetoc.org)

(14) Research Institute for Fragrance Materials (www.rifm.org)

(15) German Institute of Medical Documentation and Information (DIMDI), possibility for research in some 70 databases, inter alia on toxicology (www.dimdi.de)

(16) TOXLINE is the toxicology database of the National Library of Medicine's (NLM) of the USA (www.nlm.nih. gov/databases/databases_ toxline.html)

(17) Ecological key values of detergent ingredients for calculation of the Critical Dilution Volume (CDV) of detergent products – HAD list (www.gdch.de/strukturen/ fg/wasch/had/dokumentationen.htm)

(18) International Fragrance Association (www.ifraorg.org)

(19) *M. Payé, C. Block, N. Hamaide, G.-E. Hüttmann, S. Kirkwood, C. Lally, S. Lloyd, P. Makela, H. Razenberg, R. Young*, Antagonisms between surfactants: The Case of Laundry Detergents; Tenside, Surf., Det., 43, S. 290-294 (2006)

(20) CPMP Working Party, Good Clinical Practice for trials on medicinal products in the European Community, Pharmacology and Toxicology, 67, pp. 367-372

(21) *J. R. Young, M. J. How, A. P. Walker W. M. H. Worth*, Classification as Corrosive or Irritant to Skin of Preparations Containing Acidic or Alkaline Substances, without Testing on Animals, Toxic. in Vitro, 2, S. 19-26 (1988)

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