Toxicology and tolerance of euxyl® PE 9010

euxyl® K PE 9010 is a preservative concentrate, which is used in cosmetic preparations in a recommended use-concentration of 0.5 % to 1.0 %.

As active substances euxyl® PE 9010 contains phenoxyethanol which is listed in Appendix V of the EU Cosmetic Products Regulation 1223/2009/EC or in Appendix VI of EU Cosmetics Directive 76/768/EC[i] respectively and approved for safe use throughout the EU. As auxiliary substances euxyl® PE 9010 contains ethylhexylglycerin.

On the basis of the results of toxicological tests and on the condition that no over-additive effects occur, the following assessment and evaluation of toxicology, tolerability and use was carried out. In the focus of evaluation are skin and mucosa irritant or corrosive effects.

Toxicity

The acute toxicity of the formulation is at both oral and dermal application rather low. The oral LD_{50} of the undiluted product is expected in the range of 1300 mg/kg. The toxicity at use concentrations is expected even less.

The intake of toxicological problematic concentrations by inhalation is not expected at standard procedures.

Irritation

Based on the ingredients skin and mucosa irritant effects are expected with the undiluted product at local skin exposure. Irritation effects are not expected with the diluted product.

At direct eye contact irritations are expected with the undiluted product. A thorough rinsing with water is recommended in such cases.

In general the active ingredients are non-volatile substances that do not result in toxicological relevant concentrations in the compartment air at the recommended use concentration. Nevertheless an irritant effect on mucosa of the respiratory tract cannot be excluded.

At the use of phenoxyethanol in products for sensitive areas (e.g. face) a sujective burning was reported sporadically. Own studies to the „Stinging Potenzial“ of a frame formulation allow the conclusion that at use on sensitive skin areas (e.g. Make-Up-Remover) subjective paraesthesia can occur in single cases. This possibility should be excluded with a suitable test if applicable.

Sensitising potential

In terms of the possibility of sensitisation it should be noticed that biological active substances in general have a certain potential.

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Sensitising effects in the meaning of contactallergical reactions at skin contact or chronic effects of the personnel are extremely seldom expected with appropriate contact.

If ethylhexylglycerin influences the skin compatibility of the component phenoxyethanol in euxyl® PE 9010 was tested with skin compatibility epicutan tests.

- Concentrations of 1,1 % euxyl® PE 9010 and 1% phenoxyethanol in water and in glyceryl stearate were applied for 24 hours at the forearms of 40 Caucasian test persons with healthy skin. After 24, 48 und 72 h no skin reactions were observed.
- Concentrations of 1,1 % euxyl® PE 9010 and 1% phenoxyethanol in water and in glyceryl stearate were applied for 24 hours at the forearms of 40 Japanese test persons with healthy skin. After 24 and 48 h no skin reactions were observed.
- Concentrations of 1,1 % euxyl® PE 9010 and 1% phenoxyethanol in water and in glyceryl stearate were applied for 24 hours at the forearms of 30 Chinese test persons with healthy skin. After 24 and 48 h no skin reactions were observed.

The product should not be used if a proven hypersensitivity to one of the ingredients exists.

Mutagenicity

Based on the ingredients mutagen effects are not expected.

Labelling

The product needs labelling in accordance with the Dangerous Substances Directive. Please see MSDS for details.

Safe Use

According to the EU Cosmetic Products Regulation 1223/2009/EC or EU Cosmetics Directive 76/768/EC[i] respectively all components may be used in concentrations of max. 1.0 % (phenoxyethanol), which are considered safe up to these concentrations.

These concentration limits are equivalent to a maximum use concentration of 1.1 % euxyl® PE 9010. With the recommended use concentration the euxyl® PE 9010 concentration used is less than this permissible concentration.

Relating to safety the Cosmetic Ingredients Review (CIR) in the USA draws the same or even higher safe concentrations for these active ingredients.

The „No Observed Adverse Effect Level“ (NOAEL) describes the hazard potential of a substance as it is the highest dosage (normally in an animal test) at which no harmful side effects or adverse reactions are caused by the substance. The NOAEL is used to evaluate the “Acceptable Exposure Levels” (AEL) for human applications. Within the estimation of human exposition is provides a basis for the definition of a “Margin of Safety” (MoS).

For cosmetic preservatives the NOAEL value is in principle not relevant as the safe level is already evaluated within the annex V of the EU Cosmetic Products Regulation 1223/2009/EC. Nevertheless sometimes also a NOAEL value for preservatives is required. The NOAEL of the product is calculated on the basis of the lowest NOAEL of the single ingredients taking into consideration the concentration of the

ingredients in the product. For euxyl® PE 9010 the overall NOAEL is calculated as 444 mg/kg/d for oral applications.

This recommendation is subject to the required safety assessment that has to be performed for the individual cosmetic formulations according to the EU Cosmetic Products Regulation 1223/2009/EC. Especially for the use with children under the age of three a detailed safety assessment should be made.

Conclusion

Altogether euxyl® PE 9010 with the given upper concentration limits can be regarded as safe for its application from the toxicological point of view. Skin and mucosa irritant effect are expected with the undiluted product. The inhalation of atomized sprays must be avoided. When the above-mentioned use-concentrations are adhered to, neither local skin or mucous membrane irritation nor systemic side effects as a result of dermal absorption of the substances are expected.

Adequate protection measures are recommended particularly with regard to the rules of Employer's Liability Insurance Associations or government safety organisations.

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For further information we refer to the following publications:

Ethylhexylglycerin:

- Toxicology and Tolerance of Sensiva SC 50, Schülke & Mayr GmbH

Phenoxyethanol

- OECD SIDS, 2004
- BIBRA, toxicity profile, 1988
- Anonymous: Final Report on the safety assessments of phenoxyethanol. J. Am. Coll. Toxicol. 9 (2): 259-288 (1990)
- ECETOC Working Group: The toxicology of glycol ethers and its relevance to man. ECETOC Technical Teport 64: 348 p. (1995)
- Howes, D.: Absorption and Metabolism of 2-Phenoxyethanol in rat and man. 15th IFSCC Int. Congress 26.-29.09.1988.
- Miller, R.R.: Metabolism and Disposition of Glykol Ethers. Drug Metabolism Rev. 18: 1-22 (1987)
- Morton, W.E.: Occupational Phenoxyethanol neurotoxicity: a report of three cases. J. Occupat. Med. 32 (1): 42-45.
- Toxicology and Tolerance of Phenoxyethanol, Schülke & Mayr GmbH

[i] In the transitional period of the EU Cosmetic Products Regulation 1223/2009/EC til 2013 the appendixes of the EU Cosmetics Directive 76/768/EC are still valid for harmonisation reasons.