Efforts to Improve the Skin Notation associated with OELs in Switzerland

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Background. Occupational exposure limits provided by most institutions have traditionally been supplemented by skin notations to indicate potential uptake via the skin. However, these notations often vary from institution to institution, indicating variable and sometimes lacking scientifically satisfactory criteria and databases for their establishment. Indeed, Grandjean et al. demonstrated that although most countries have a similar number of chemicals for which a skin notation has been defined (around 30% of the total number of chemicals), the overlap between substances is poor from one country to the next (e.g. only 101 of the 176 substances with a skin notation in Germany own a skin notation in the U.S. [Granjean et al., 2004]). Moreover, skin notations are generally qualitative indicators whilst exposure assessors and risk managers tend to require quantitative indices to properly assess occupational hazards. Together with the recent trends of diminishing inhalation exposures, which increases the relative importance of skin route, these observations led Swiss authorities to undertake a project aimed at re-evaluating the current process used to attribute skin notations.

In Switzerland, the OEL list is composed of 708 substances, of which 232 have a skin notation. The definition of the skin notation in Switzerland is as follows: « intoxication risk by resorption through the skin ». They are attributed according to either clinical experience or workplace studies on a substance by substance basis.

The aim of this project is to improve the skin notation, detailing the different local toxicity of chemicals to the skin, and to treat the absorption potential in a quantitative way. The specific objectives of the project are to suggest qualitative criteria to characterize the local risks of chemicals for the skin, and to develop quantitative criteria for the evaluation of the risk associated with systemic toxicity caused by skin resorption. These should lead to an improved skin notation and will be applied to the entire list of OELs in Switzerland.

Methods. Several approaches are currently being considered by the working group.

Qualitative criteria for local effects : R-phrases may be a way to classify the substances. They describe the nature of particular risks associated with the use of a specific substance as defined by the European community (2001/59/CE). The R-phrases concerning skin hazards comprise R38, R43, R66 that describe local or toxic effect for the skin (R38-Irritating to skin, R43-May cause sensitisation by skin contact, R66-Repeated exposure may cause skin dryness or cracking).

Quantitative criteria for dermal absorption : Several models describe skin absorption using the diffusion model [Fiserova-Bergerova, 1990, McKone et al, 1992, Potts and Guy, 1992], where the flux Fl is described by the Fick's law:

$$Fl = D\frac{dC}{dx} \qquad \text{Eq. 1}$$

where: Fl is the flux through the skin [$mg \cdot cm^{-2} \cdot h^{-1}$], D is the diffusion coefficient through the stratum corneum [$m^2 \cdot s^{-1}$] and dC/dx is the concentration gradient through the stratum corneum [$mg \cdot cm^{-4}$].

From there, either k_p, the permeation coefficient, or Fl_{max}, the maximum flux through the skin of a defined surface area, can be used as a basis for a quantitative classification of substances, and may be systematically applied to the OEL list.

$$Fl_{\max} = k_p \cdot S \qquad \text{Eq.2}$$

where Fl_{max} is the maximum flux through the skin [$mg \cdot cm^{-2} \cdot h^{-1}$], k_p is the permeation coefficient [$cm \cdot h^{-1}$] and S is the water solubility of the chemical [$g \cdot L^{-1}$].

Approaches which combine the cutaneous absorption potential of chemical with a danger index (such as the internal dose corresponding to inhalation of concentrations at the OEL) have also been described in the literature [Fiserova-bersegova, 1990; Johansson, 2003].

Another strategy would be to use the R-phrases for a quantitative classification of dermal absorption potency. The phrases R21, R24, R27 describe systemic toxicity resulting from dermal absorption, based on ranges of dermal LD50 in animals. Using R-phrases as a basis for skin notations therefore implies basing the new notation scheme on dermal LD50 in animals, as it is actually the case in Poland. This has been recommended by some authors, and criticized by others (Czerczak, Kupczewska, 2002, 2003 ; Chen et al., 2003).

The working group intends to compare these approaches in order to evaluate their agreement with the substances found in the Swiss list of OELs and decide on a global procedure for the attribution of skin notations in Switzerland. Comparison between modelised values of permeation coefficients and experimental values found in international databases of inter-laboratories studies [e.g. EDETOX] will be giving important insight about the accuracy, the strength and the weakness of the models.

Results. An Excel spreadsheet is currently being built for the whole Swiss list of OELs with relevant substance information (Name, CAS, OEL, Skin notation, R phrases, molecular weight, melting point, solubility, water-octanol partition coefficient, pKa). The different approaches described above will be implemented and compared with experimental values.

Experimental octanol water partition coefficients and water solubility are not available for every chemical in the OEL list. When missing, these data can be modelled from basic physicochemical information (http://www.syrres.com/eSc/est_kowdemo.htm) [Howard et al, 1995].

Table 1. Numbers of chemicals with a skin notation and R-phrase related to skin in the Swiss OEL list

Chemicals	Skin Notation	R21	R24	R27	R38	R43	R66	OEL list
	232	63	65	27	83	48	18	708

Table 2. Content of the excel spreadsheet in numbers of chemicals

Chemicals	S	K_{ow}	$K_{p\ exp.}$	$J_{max\ exp.}$	OEL list
	249	383	34	24	708

Conclusions. Results obtained in the project should improve the reliability and usefulness of skin notation for practitioners. The OEL Commission is expecting to implement the results in the 2009 edition of the OEL list.

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