Executive summary

Health Council of the Netherlands: Standards for dermal exposure at the workplace. The Hague: Health Council of the Netherlands, 2001; publication no. 2001/28

Background and request for an opinion

Standards for occupational exposure to hazardous substances currently apply only to exposure via respiration. The standard is a numeric al one in the form of a Maximum Allowable Concentration: the MAC value. The scientific basis for the MAC value is a risk assessment for the substance in question which leads to a recommended health limit, the *Health Based Recommended Occupational Exposure Limit* (HBR-OEL). If the risk assessment shows that exposure via the skin might also be important, a general warning is added to the MAC value to avoid contact in the form of the so-called "H" indication, also known as skin notation. This form has been chosen because the role of dermal exposure and protective measures to be taken depend to a large extent on the actual situation at the workplace and thus can best be assessed on site. Of the more than 650 MAC values, a quarter have a skin notation.

Improvement in understanding of the toxicity of substances has led to the fine-tuning of MAC values, and generally to a reduction. Concentrations in air consequently decrease, as a result of which the dermal exposure element of the total toxic load increases proportionately. The dermal exposure aspect, which is usually secondary to exposure via respiration in the assessment of toxicological risks, therefore increasingly calls for specific attention. TNO has recently reported on scope for laying down a limit value for dermal exposure, the *Dermal Occupational Exposure Limit*. This variable can be expressed as the limit for the concentration of a substance in a bodily fluid or as the

limit for the amount of substance per unit of skin surface area. These developments had prompted the State Secretary for Social Affairs and Employment to seek an opinion on the matter from the Health Council of the Netherlands. The Secretary is asking the Council to examine the desirability and feasibility of standardising dermal exposure. To answer the questions, the President of the Health Council of the Netherlands set up a special committee.

Dermal load

Various cases of injudicious use and accidents show that, as a result of dermal exposure to various kinds of substances, damage can arise in the body (systemic toxicity). With these case reports, verdicts on the relationship between the level of exposure ('dose') and the impact on health are not possible because reconstruction of the exposure conditions is too imprecise. However, these cases provide general pointers for a policy for limiting or preventing dermal exposure to hazardous substances. In the case of certain substances, these findings prompted the addition of a skin notation to the MAC value.

However, the occupational risk of skin contamination has yet to be fully charted. Depending on the nature of the substance and the working conditions, dermal exposure may contribute to the total internal toxic load. Under certain conditions, the contribution via the skin to the total toxic load may be greater than via other forms of exposure. The Committee considers that, with the general risk assessment of hazardous substances, more attention than ever before must be paid to the risks of dermal absorption. This approach must be geared to, on the one hand, the identification of toxic substances readily absorbed by the skin and, on the other, to their significance for the work situation.

Determination of dermal absorption

In recent decades, a great deal of attention has been paid to scientific clarification of the dermal absorption of chemicals, for example in the case of medicinal products, cosmetics and pesticides. This absorption is being studied in separate areas, namely penetration of the skin, permeation via the skin and absorption from the skin in the underlying tissues and their bloodstream. Thus, coefficients have been determined for various substances which describe the distribution of the substance on the skin and in the horny layer of the epidermis (*stratum corneum*; the outermost layer of the epidermis). Flow through the skin as a whole, the quantity of substance that passes through the skin per unit of time and per unit of surface area, is a measure of dermal

absorption and primarily depends on the reduction in concentration in the horny layer. As the distribution coefficient referred to has been determined for only a few substances, the distribution coefficient of a substance between octanol and water (log *Ko/w*) is instead used. However, this is well-known for most substances. The physicochemical models for estimating dermal absorption make use of this distribution coefficient and various other simple physicochemical characteristics.

Various methods for a more direct determination of dermal absorption are described in the literature. These range from *in-vivo* trials with volunteers to *in-vitro* research with skin preparations. The most reliable basis for risk assessment is provided by data from research with volunteers, but this kind of research is often problematic. One alternative is *in-vivo* research on laboratory animals. This type of research, too, is socially contentious. A great deal of attention has therefore been paid to *in-vitro* research, in which animal or human skin preparations are used. The results of such research are, however, usable to only a limited extent. Among the *in-vitro* methods, those that involve human skin are the most highly recommended in the literature.

Standards

There are various possible ways of limiting dermal exposure via standards. The DOEL value (*dermal occupational exposure limit*) sets a direct limit for dermal exposure, while the BL value (*biological exposure index* or biological limit value) sets this limit for the total internal toxic load. Both limit values are examples of numerical standards. These are supplemented by the above-mentioned skin notation, which can be added to the MAC value and is intended as a general warning of the harmful effects in the case of skin contact. The MAC value, the concentration limit in ambient air, is the numerical standard here.

The Committee discusses the advantages and disadvantages of the various standards. It has also formulated a guide, in the form of a step plan, for the way in which the dermal exposure aspect can be examined. This step plan takes account of currently limited understanding and makes proposals on setting priorities in risk assessment, particularly with reference to dermal exposure and its effects.

Conclusions

The skin is not an impregnable barrier for toxic substances and provides a pathway for the absorption of these substances into the body. Scope for regulating dermal exposure is not as great as is sometimes suggested. In the case of many substances, the necessary

epidemiological and toxicological data for deriving a standard are lacking, while the analytical and monitoring methods are often inadequate. A general warning in the form of skin notation has a preventive effect, but does not lead to further research on dermal absorption and its consequences. This means that the consequences of dermal exposure must be examined for each substance and, if necessary, a scope for numerical standardardisation.

The Commission would answer the questions asked by the State Secretary as follows:

Question 1: Is standardisation of skin contamination by systemically acting substances possible and desirable?

The Committee considers that it is generally speaking desirable to have scope to standardise dermal contamination. In view of question 2, the State Secretary's thinking on this is first of all for numerical standardisation. The Committee has not confined itself to numerical standards, and has discussed the following three forms of standardisation:

- standardisation via a limit for external dermal exposure, i.e. a limit on the quantity of substance on the skin and thus on potential absorption via the skin (the dermal exposure limit or DOEL value)
- standardisation via a limit value for internal toxic contamination, i.e. a limit on the total quantity of a substance absorbed by the body (the biological limit or BL value)
- the (existing) addition of a warning to prevent dermal exposure to the standard concerning exposure via the airways at the workplace (the MAC value with skin notation).

The DOEL value and the BL value are numerical standards. The skin notation for the MAC value is not, but functions as a general warning which will in practice have to lead to protective measures. The DOEL value and the BL value can only be applied if there are suitable measuring and monitoring methods.

The choice between the various options depends on the nature of the substance, the way in which the substance can come into contact with the skin and the existence of reliable methods for sampling, (bio)chemical analysis, biological monitoring (BN) or biological effect monitoring (BEM). The DOEL value is of interest for practical reasons. The BL value seems ideal from the health point of view. The number of BL values available is, however, limited. The German *MAK-Kommission* and the American *ACGIH*, committees which have paid attention over the last decade to the development

of BL values, have been able to lay down a value of this kind for only several dozen substances. Sufficiently reliable monitoring techniques must be available for both the BL value and the DOEL value. Such techniques are generally specific to a particular substance. They also call for the active involvement of the individual worker. The Committee considers that no general judgements can be made concerning the choice of one standard or another. Experts will need to assess for each substance which standard is the most suitable. The Committee prefers the BL value to the DOEL value, but the choice can work out differently in practice. The necessary data are often lacking, and an MAC value with skin notation will be resorted to. Even if an MAC value does not exist, a skin notation may be appropriate.

Question 2: Can this standardisation be shaped via the concept of a dermal limit value developed by TNO?

The TNO proposal for a dermal limit value matches the DOEL value referred to above. This applies, in the Committee's view, if it is certain that a substance is primarily absorbed via the skin and methods are not available for adequate biological monitoring (BM) or biological effect monitoring (BEM). If the BM and BEM are indeed available, the Committee prefers, as indicated above, a BL value as this places a limit on total exposure.

Question 3: For which substances (physicochemical properties, toxicological profile) does the Health Council of the Netherlands consider it desirable that dermal standards be drawn up and applied?

The Committee proposes a step plan leading to a judgement on the setting of priorities for assessing the risks of dermal exposure posed by a substance. The step plan is tailored to existing standardisation procedures in the Netherlands in which experts play an important role. The physicochemical and toxicological parameters specified in the step plan can also be used by those responsible for occupational health in practice to ascertain the dangers of dermal exposure to the substance or substances used and investigate whether measures are needed. The Committee's thinking on this is in the first place for measures to protect the skin. The adoption of a numerical standard, and thus allowing a certain degree of skin contact, calls for a general consensus and is only possible if monitoring techniques are available for the substance(s).