

Aan de Staatssecretaris van Sociale Zaken en Werkgelegenheid

Onderwerp : Aanbieding adviezen herevaluatie bestuurlijke MAC-waarden
Uw kenmerk : ARBO/AMIL/97/00648
Ons kenmerk : U 2706/CB/MP/563-O3
Bijlagen : 18
Datum : 14 december 2000

Mijnheer de staatssecretaris,

Op verzoek van uw ambtsvoorganger bied ik u hierbij de eerste adviezen aan van een reeks over de gezondheidkundige basis van uit het buitenland overgenomen grenswaarden voor beroepsmatige blootstelling aan stoffen. Het verzoek om deze adviezen is in algemene zin vervat in brief nr ARBO/AMIL/97/00648 en in latere stadia door uw departement toegespitst op afzonderlijke stoffen. De adviezen zijn opgesteld door een daartoe door mij geformeerde internationale commissie van de Gezondheidsraad en beoordeeld door de Beraadsgroep Gezondheid en Omgeving.

De beoogde reeks van in het Engels gestelde adviezen zal losbladig worden gepubliceerd onder ons publicatienummer 2000/15OSH en, conform de aan de Gezondheidsraad voorgelegde toespitsingen van de adviesaanvraag, betrekking hebben op 168 stoffen. Het u thans aangeboden eerste pakket bestaat uit een Algemene Inleiding (publicatienummer 2000/15OSH/000) en uit de adviezen genummerd 2000/15OSH/001 tot en met 2000/15OSH/017, respectievelijk betrekking hebbend op:

cesiumhydroxide, cyclopentaan, diboraan, dimethoxymethaan, dipropylketon, fenylfosfine, germaniumtetrahydride, hexachloornaftaleen, methaanthiol, methylcyclohexanol, methylisopropylketon, mica, natriumhydroxide, octachloornaftaleen, silaan, tetrachloornaftaleen, en yttrium en yttriumverbindingen.

Bij afronding van de werkzaamheden van de hierboven bedoelde commissie ontvangt u een Nederlandstalige samenvatting van de in de gehele reeks van adviezen neergelegde bevindingen.

Gezondheidsraad

Health Council of the Netherlands

Onderwerp : Herevaluatie uit het buitenland overgenomen grenswaarden
Ons kenmerk : U
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Datum : 14 december 2000

De u thans aangeboden adviezen heb ik vandaag ter informatie doen toekomen aan de Minister van Volksgezondheid, Welzijn en Sport en aan de Minister van Volkshuisvesting, Ruimtelijke Ordening en Milieubeheer.

Hoogachtend,

prof. dr JJ Sixma

Health-based Reassessment of Administrative Occupational Exposure Limits

Health-based Reassessment of Administrative Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

No. 2000/15OSH, The Hague, 14 December 2000

The Health Council of the Netherlands, established in 1902, is an independent scientific advisory body. Its remit is “to advise the government and Parliament on the current level of knowledge with respect to public health issues...” (Section 21, Health Act).

The Health Council receives most requests for advice from the Ministers of Health, Welfare & Sport, Housing, Spatial Planning & the Environment, Social Affairs & Employment, and Agriculture, Nature Preservation & Fisheries. The Council can publish advisory reports on its own initiative. It usually does this in order to ask attention for developments or trends that are thought to be relevant to government policy.

Most Health Council reports are prepared by multidisciplinary committees of Dutch or, sometimes, foreign experts, appointed in a personal capacity. The reports are available to the public.

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ammonium chloride (fume) [12125-02-9]
benomyl [17804-35-2]
benzenethiol (phenyl mercaptan) [108-98-5]
biphenyl/diphenyl ether mixture [92-52-4; 101-84-8; 8004-13-5]
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zirconium and zirconium compounds [7440-67-7]

These reports were presented to the State Secretary of Social Affairs and
Employment by the President of the Health Council of the Netherlands

General remarks

Health-based Reassessment of Administrative
Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

No. 2000/15OSH/000, The Hague, 14 December 2000

General introduction

1.1 Background of the project

In September 1995, TNO Nutrition and Food Research Institute (Zeist, the Netherlands) reported the Minister of Social Affairs and Employment about the degree of health protection of the administrative occupational exposure limits (OELs) in the list of Maximal Accepted Concentrations (MAC) of 1994. The major part of these OELs were adopted from the American Conference of Governmental Industrial Hygienists' list of Threshold Limit Values in the 1970s. For the purpose of the evaluation concise toxicity profiles were prepared based on the documentation of the ACGIH and European criteria documents on almost 300 substances. TNO concluded that for 109 substances the current OEL was suspected to be too high from a health protection point of view, with deviations ranging from a factor of 2 to 250. For another 106 substances the toxicological data base was judged to be too poor to recommend a health-based OEL.

On September 24, 1996 the State Secretary of Social Affairs and Employment presented a plan to re-evaluate the administrative OELs to the Social and Economic Council. After the Social and Economic Council had given a positive reaction the State Secretary requested the Health Council on April 16, 1997, to re-evaluate these substances in a condensed procedure and to recommend health-based OELs. Given the international character of the

request and in view of the European harmonization, the State Secretary requested the Health Council to invite scientists from outside the Netherlands to participate in the project.

1.2 Setting OELs in the Netherlands

In the Netherlands the legally-binding occupational exposure limits for chemical substances are set using a three-step procedure. In the first step a scientific evaluation of the data on the toxicity of the substance is made by the Dutch Expert Committee on Occupational Standards (DECOS), a committee of the Health Council, on request of the State Secretary of Social Affairs and Employment. This evaluation should lead to a health-based recommended occupational exposure limit for the concentration of the substance in workroom air.*

In the next phase of the three-step procedure the Social and Economic Council advises the State Secretary on the feasibility of using the health-based value as a legally-binding OEL, or recommends a different OEL. In the final step of the procedure the State Secretary sets the regulatory OEL.

The three-step procedure will also be followed for health-based OELs derived in the present re-evaluation project.

1.3 Committee

As a first step the Health Council requested several regulatory authorities of European countries to nominate internationally acknowledged experts in toxicology, epidemiology or occupational medicine with experience in setting OELs. All nominees were requested to send a brief curriculum vitae and a list of publications. The committee was selected from the list of nominees using the following criteria: one member from each foreign country, the expertise within the committee should cover all aspects of hazard assessment of chemical substances, and good spread in (former) affiliation of the members (academia, national institutes and industry). All members were invited on a personal title, except for the corresponding member representing ACGIH. The members of the Committee on Updating of occupational exposure limits are listed in Chapter 2.

* For genotoxic carcinogens DECOS does not derive an OEL but presents an exposure-response relationship.

1.4 Procedure

Under the authority of the Ministry of Social Affairs and Employment, for each substance a short document is prepared by a toxicologist at a research institute in the Netherlands. The requirements for the contents of these short documents were established by the committee during a trial phase*. The documents should be based on a full literature search including at least the data bases Medline, Toxline and Chemical Abstracts. From the published literature a key study is identified serving as the basis for deriving a health-based OEL. For extrapolation of the data (from the key study) to the occupational exposure situation an overall assessment factor is applied covering the aspects inter- and intraspecies variation, differences in duration and pattern of exposure between the key study and the situation of the worker, type of the critical effect, dose-effect relationship and quality of the total data base. In deriving the overall assessment factor the committee uses a check list of the different aspects, adopted from a TNO-report, to discuss and thoroughly weigh all available data. In each case the committee considers the appropriateness of applying default values, see Chapter 3. In case the key study refers to an oral animal experiment, scaling to humans is based on caloric demand (body weight to the power 0.75) rather than on body weight. For the recommendation of a health-based OEL the committee decided to make use of the preferred value system** given the inherent uncertainty of any OEL.

To derive a health-based OEL for a substance at least data on acute toxicity, including irritation (and sensitization), and on repeated-dose toxicity are required. The committee considers as a minimum the availability of a multi-dose study in which a relevant animal species was exposed via a relevant exposure route for a relevant exposure time and in which relevant toxicological endpoints were studied (preferably including body weight gain, haematology, clinical biochemistry, gross and microscopic pathology). Preferably the study provides information about the target organ and critical effect, and produces a no observed adverse effect level.

* The aims of this phase were to determine the requirements for the documents, to develop and test the procedure, and to judge the feasibility of the project. The fourteen substances under consideration during this phase were selected by the Ministry of Social Affairs and Employment in consultation with regulatory authorities in the participating countries.

** The preferred value system implies that OELs are rounded up or down to 'preferred values', e.g. 0.1, 0.2, 0.5, 1, 2, 5, 10 mg/m³ etc.

In case the data base is insufficient to recommend a health-based OEL the committee will strive to judge in a semi-quantitative way whether or not the current administrative limit is health-protective.

Carcinogenic substances are not taken into consideration by the committee. When the data base of a substance indicates carcinogenic and/or genotoxic potential, the committee recommends an evaluation and classification of the substance by DECOS. For substances tested for and proven to be toxic to fertility or development, the committee ascertains that the recommended health-based OEL protects against these effects as well. For quite a number of substances, however, these data were not available.

A draft of each document was released for public review during a period of six weeks and comments received were taken into account in the final version of the document.

The Hague, 14 December 2000,
for the committee

dr CA Bouwman,
scientific secretary

prof. dr J Noordhoek
chairman

The committee

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- J Noordhoek, *chairman*
professor of toxicology; University of Nijmegen, Nijmegen, The Netherlands
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senior scientist; International Programme on Chemical Safety, World Health Organization, Switzerland
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Health Council of the Netherlands, The Hague, The Netherlands
-

Default values

Adopted from the report 'Methods for establishment of Health-based Recommended Occupational Exposure Limits for existing substances', V96.463, 4 July 1996, by TNO Nutrition and Food Research Institute, Zeist, the Netherlands (see also De Raat *et al*, Reg. Toxiol. Pharmacol. 25, 1997: 204-210).

aspects	default value
interspecies differences	3
intraspecies differences	3
differences between experimental conditions and exposure pattern of the worker	1-10
type of critical effect	1
dose-response curve	1
confidence of the data base	1

000-10 Health-based Reassessment of Administrative Occupational Exposure Limits

Abbreviations

Organisations and occupational exposure limits

<i>ACGIH</i>	American Conference of Governmental Industrial Hygienists
<i>DECOS</i>	Dutch Expert Committee on Occupational Standards
<i>DFG</i>	Deutsche Forschungsgemeinschaft
<i>EPA</i>	Environmental Protection Agency (USA)
<i>FDA</i>	Food and Drug Administration (USA)
<i>HBR-OEL</i>	health based recommended occupational exposure limit
<i>HSE</i>	Health and Safety Executive (UK)
<i>IARC</i>	International Agency for Research on Cancer (WHO)
<i>IPCS</i>	International Programme for Chemical Safety
<i>MAC</i>	maximaal aanvaarde concentratie (maximal accepted concentration)
<i>MAK</i>	Maximale Arbeitsplatz Konzentration
<i>MEL</i>	maximum exposure limit
<i>NIOSH</i>	National Institute for Occupational Safety and Health (USA)
<i>NTP</i>	National Toxicology Programme (USA)
<i>OECD</i>	Organisation for Economic Cooperation and Development
<i>OEL</i>	occupational exposure limit
<i>OES</i>	occupational exposure standard
<i>OSHA</i>	Occupational Safety and Health Association (USA)
<i>PEL</i>	permissible exposure limit
<i>REL</i>	recommended exposure limit
<i>RTECS</i>	Registry of Toxic Effects of Chemical Substances
<i>SCOEL</i>	Scientific Committee for Occupational Exposure Limits
<i>SER</i>	Social and Economic Council (Sociaal-Economische Raad NL)
<i>STEL</i>	short term exposure limit
<i>TLV</i>	threshold limit value
<i>TWA</i>	time weighted average
<i>WHO</i>	World Health Organisation

Toxicological terms

<i>BALF</i>	bronchio-alveolar lavage fluid
<i>bw</i>	body weight
<i>CNS</i>	central nervous system
<i>EC₅₀</i>	concentration at which a described effect is found in 50% of the exposed animals or at which the effect is decreased up to 50% of the control value
<i>FCA</i>	Freunds Complete Adjuvans
<i>FEV</i>	forced expiratory volume
<i>FVC</i>	forced vital capacity
<i>GD</i>	gestation day(s)
<i>GPMT</i>	guinea pig maximisation test
<i>GSH</i>	glutathione
<i>h</i>	hour
<i>IC₅₀</i>	concentration at which inhibition of a certain function is found up to 50% of the control value
<i>im</i>	intramuscular
<i>ip</i>	intraperitoneal
<i>it</i>	intratracheal
<i>iv</i>	intravenous
<i>LC₅₀</i>	lethal concentration for 50% of the exposed animals
<i>LC₁₀</i>	lowest lethal concentration
<i>LD₅₀</i>	lethal dose for 50% of the exposed animals
<i>LD₁₀</i>	lowest lethal dose
<i>LDH</i>	lactate dehydrogenase
<i>LOAEL</i>	lowest observed adverse effect level
<i>MAIvC</i>	minimal alveolar concentration
<i>MFO</i>	mixed function oxidase
<i>MMAD</i>	mass median aerodynamic diameter
<i>MOAEL</i>	minimal observed adverse effect level
<i>NOAEL</i>	no observed adverse effect level
<i>n</i>	number
<i>ppb</i>	parts per billion (v/v)10 ⁻⁹
<i>ppm</i>	parts per million (v/v)10 ⁻⁶
<i>PNS</i>	peripheral nervous system
<i>po</i>	<i>per os</i> (= oral)
<i>RBC</i>	red blood cells
<i>RD₅₀</i>	concentration at which a 50% decrease of respiratory rate is observed
<i>SCE</i>	sister chromatid exchange
<i>sc</i>	subcutaneous
<i>UDS</i>	unscheduled DNA-synthesis
<i>V_{max}</i>	maximal reaction velocity of an enzyme
<i>w</i>	week

Statistical terms

<i>CL</i>	confidence limits
<i>GM</i>	geometric mean
<i>OR</i>	odds ratio
<i>RR</i>	relative risk
<i>SD</i>	standard deviation
<i>SEM</i>	standard error of mean
<i>SMR</i>	standard mortality ratio

Analytical methods

<i>BEI</i>	biological exposure index
<i>GC</i>	gas chromatography
<i>HPLC</i>	high performance liquid chromatography
<i>MS</i>	mass spectrometry
<i>NMR</i>	nuclear magnetic resonance
<i>PAS</i>	personal air sampling
<i>TLC</i>	thin layer chromatography

