



To the Minister of Social Affairs and Employment

Subject : Presentation of advisory letter *Comparison of recommended exposure limits for hydrogen sulphide*
Your reference : G&VW/GW/2009/1078
Our reference : 22-09/AvdB/fs/459-V63 Publication no. 2010/06E/OSH
Enclosure(s) : 2
Date : July 15, 2010

Dear Minister,

The Health Council of the Netherlands received a request from the Ministry of Social Affairs and Employment on 22 January 2009 to reassess the health-based occupational exposure limit recommended by the Health Council for five substances based on of the Scientific Committee for Occupational Exposure Limits (SCOEL) recommendation for the substance in question (see annex A). I forwarded this request to the Dutch Expert Committee on Occupational Safety of the Health Council (DECOS) (see annex B). In this advisory letter I will inform you of the Committee's findings with respect to the health-based occupational exposure limit for hydrogen sulphide (H₂S).

Health Council Advisory Report (2006)

In 2006 DECOS assessed the consequences of occupational exposure to hydrogen sulphide and recommended a health-based occupational exposure limit for hydrogen sulphide of 2.3 mg/m³ (1.6 ppm). This Health Council advisory report then served as the basis for the SCOEL recommendation issued early 2007. Although the SCOEL derived its health-based occupational exposure limit from the same critical study and the same health effect (nasal tissue damage), the SCOEL recommended a higher health-based occupational exposure limit than DECOS. This difference may be explained by the fact that the SCOEL deemed a lower extrapolation factor necessary than DECOS in order to compensate for various uncertainties (i.e. 2 vs. 6).



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New data Schroeter *et al.*

A number of new studies have been published since the Health Council and SCOEL recommendations. Two studies are relevant in determining a health-based occupational exposure limit: Schroeter *et al.* 2006¹, and Schroeter *et al.* 2010².

The Schroeter *et al.* 2006 study used pharmacokinetic modelling to elucidate the difference in hydrogen sulphide absorption by the nasal epithelium in humans and rats respectively. The authors conclude that nasal absorption of hydrogen sulphide in humans is half of that in rats.

A Schroeter *et al.* study published in 2010 used a different nasal model. They find this model more effective and accurate than the 2006 model and suggest that the earlier numerical results of the 2006 study should therefore be interpreted with some caution. The authors used the new model to study variation in hydrogen sulphide absorption between humans; they conclude that such variation between humans is limited.

Deriving the health-based occupational exposure limit

DECOS therefore reaffirms its opinion that the Dorman *et al.* 2004, Brenneman *et al.* (2000) and Moulin *et al.* (2002) studies continue to serve as the primary studies for deriving the health-based occupational exposure limit for hydrogen sulphide. At a level of 14 mg/m³, nasal effects are no longer observed in rats. The Committee considers this level therefore to be the no observed adverse effect level (NOAEL).

The NOAEL should then be translated into a health-based occupational exposure limit. Here the Committee takes several uncertainties into account; interspecies variation, interindividual variation (intraspecies variation), variation in exposure duration, dataset quality, etc.

The effect of hydrogen sulphide is localised. In such cases, the DECOS generally does not deem a compensation factor for differences between laboratory animals and humans necessary. However, a pharmacokinetic model showed the amount of hydrogen sulphide that may be absorbed through the nose in humans to be lower than in rats, which may justify the use of a factor lower than 1. Nevertheless, the DECOS is of the opinion that the results of the 2006 Schroeter *et al.* study – though they certainly have merit – should be interpreted somewhat cautiously, as was noted also by Schroeter *et al.* (2010).



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The Committee uses a factor of 2 in order to compensate for (1) differences in exposure duration (from subchronic (6 hours daily) in the animal experiment to chronic occupational exposure, 8 hours daily) and (2) limited pathology data. This is in line with the 2006 Health Council advisory report.

Additionally, the 2006 Health Council advisory report applied an uncertainty factor of 3 to compensate for interindividual differences (intraspecies variation) in *kinetics* and dynamics. However, on the basis of the 2010 Schroeter *et al.* study, the Committee concludes that the interindividual variations in *kinetics* between humans (the absorption of hydrogen sulphide) are only minimal. Reducing the uncertainty factor may therefore be justifiable; however the question is how high the compensation factor for interindividual differences in *dynamics* between humans should then be. The Committee is of the opinion that it remains difficult to express uncertainty in dynamics as substantiated numerical values, and therefore decides, for safety reason, to maintain a factor of 3 to compensate for the interindividual differences.

Conclusion and recommendation

On the basis of the above considerations, the DECOS maintains a health-based occupational exposure limit for hydrogen sulphide of 2.3 mg/m³ (time-weighted average over 8 hours per day); this is the health-based occupational exposure limit proposed by the Committee in 2006. The Committee sees no imperative to amend the health-based occupational exposure limit for hydrogen sulphide on the basis of the SCOEL recommendation and the studies published since 2007.

I endorse the Committee's conclusions and recommendations and trust this information is sufficient.

Yours sincerely,
(signed)
Professor D. Kromhout
Acting President



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Literature

- 1 Schroeter J.D., Kimbell J.S., Andersen M.E., Dorman D.C., Use of a pharmacokinetic-driven computational fluid dynamics model to predict nasal extraction of hydrogen sulfide in rats and humans. *Toxicol. Sciences* 2006; 94(2): 359-367.
- 2 Schroeter J.D., Garcia G.J.M., Kimbell J.S., A computational fluid dynamics approach to assess interhuman variability in hydrogen sulfide nasal dosimetry. *Inhal. Toxicol.* 2010; 22(4): 277-286.

The request for advice

The Health Council of the Netherlands received a request from the Ministry of Social Affairs and Employment on 22 January 2009 to reassess the health-based occupational exposure limit recommended by the Health Council for five substances on the basis of the Scientific Committee for Occupational Exposure Limits (SCOEL) recommendation for the substance in question:

Dear Ms Wijbenga,

By letter of 27 November 2008 (ref ARBO/P&G/2008/33902), the Acting Chief of the Occupational Safety department of my Directorate has asked you to draw up a brief overview. In preparation to a quick scan for the health-based occupational exposure limits for the seven named substances. The context of this request has been explained in the above-mentioned letter. Specifically, this letter asked that you first draw up a brief overview, after which I would provide you with a detailed request for further activities. May I ask that you forward this request to the President of the Health Council of the Netherlands.

I have received the brief overview referred to, for which I thank you; it was discussed recently between the Health Council and Directorate staff. My specific request to you now is as follows.

I ask that you reassess the health-based occupational exposure limits recommended previously by the Health Council, on the basis of the SCOEL recommendation for this substance. As needed, I ask that you include in this reassessment the new studies on which SCOEL has based its advice and which

were not yet available at the time of the Health Council advisory report. Your staff have indicated that a scientific study summary may first need to be prepared, of which I have taken note.

With respect to the substance list, and based on your statement of affairs, you may disregard formaldehyde until future notice.

With respect to scheduling, I would ask that you submit your recommendation no later than 1 July 2010.

Yours sincerely,

Director, Occupational Safety and Health,

(signed)

M.P. Flier

The Committee

Dutch Expert Committee on Occupational Safety (DECOS)

- G.J. Mulder, *chairman*
Emeritus Professor of Toxicology, Leiden University, Leiden
 - R.B. Beems
Toxicologic pathologist, formerly employed at the National Institute for Public Health and the Environment, Bilthoven
 - P.J. Boogaard
Toxicologist, Shell International BV, The Hague
 - J.J.A.M. Brokamp, *advisor*
Social and Economic Council, The Hague
 - D.J.J. Heederik
Professor of Health risk analysis, Institute for Risk Assessment Sciences, Utrecht University, Utrecht
 - R. Houba
Occupational hygienist, Netherlands Expertise Centre for Occupational Respiratory Disorders (NECORD), Utrecht
 - H. van Loveren
Professor of Immunotoxicology, Maastricht University, Maastricht; National Institute for Public Health and the Environment, Bilthoven
 - T.M. Pal
Occupational physician, Netherlands Center for Occupational Diseases, Amsterdam
-

- A.H. Piersma
Professor of Reproductive toxicology, National Institute for Public Health and the Environment, Bilthoven
- H.P.J. te Riele
Professor of Molecular biology, VU University Amsterdam, Amsterdam
- I.M.C.M. Rietjens
Professor of Toxicology, Wageningen University and Research Centre, Wageningen
- H. Roelfzema, *advisor*
Ministry of Health, Welfare and Sport, The Hague
- G.M.H. Swaen
Epidemiologist, Dow Benelux N.V., Terneuzen
- R.C.H. Vermeulen
Epidemiologist, Institute for Risk Assessment Sciences, Utrecht
- R.A. Woutersen
Toxicologic pathologist, TNO Quality of Life, Zeist; Professor of translational toxicology, Wageningen University and Research Centre, Wageningen
- P.B. Wulp
Occupational physician, Labour Inspectorate, Groningen
- A.S.A.M van der Burght, *scientific secretary*
Health Council of the Netherlands, The Hague

The Health Council and interests

Members of Health Council Committees – which also include the members of the Advisory Council on Health Research (RGO) since 1 February 2008 – are appointed in a personal capacity because of their special expertise in the matters to be addressed. Nonetheless, it is precisely because of this expertise that they may also have interests. This in itself does not necessarily present an obstacle for membership of a Health Council Committee. Transparency regarding possible conflicts of interest is nonetheless important, both for the President and members of a Committee and for the President of the Health Council. On being invited to join a Committee, members are asked to submit a form detailing the functions they hold and any other material and immaterial interests which could be relevant for the Committee's work. It is the responsibility of the President of the Health Council to assess whether the interests indicated constitute grounds for non-appointment. An advisorship will then sometimes make it possible to exploit the expertise of the specialist involved. During the establishment meeting the

declarations issued are discussed, so that all members of the Committee are aware of each other's possible interests.