Hydrogen sulfide

[7783-06-4]	
Supplement 2010	
MAK value (2006)	**5 ml/m³ (ppm) ≙ 7.07 mg/m³**
Peak limitation (2006)	**Category I, excursion factor 2**
Absorption through the skin	**–**
Sensitization	**–**
Carcinogenicity	**–**
Prenatal toxicity (2006)	**Pregnancy Risk Group C**
Germ cell mutagenicity	**–**
BAT value	**–**

MAK value and peak limitation

The MAK value of 5 ml/m³ for hydrogen sulfide was based on avoiding neurotoxic effects on the olfactory epithelium and considerable odour annoyance. Although a NOAEC (no observed adverse effect concentration) of 10 ml/m³ could be derived from several sub-chronic studies in rats and mice for damage to the epithelium (2007 documentation, published in English translation in 2013; documentation "Hydrogen sulfide" 2013), the evaluation of odour annoyance was extrapolated from an earlier study with humans that only investigated concentrations up to 0.15 ml/m³. Odour annoyance was significantly increased at this concentration (Winneke 1992). It was evident from the extrapolation of these results that considerable odour annoyance can be expected with exposure levels of 5 ml/m³. It was not possible at the time to evaluate conclusively whether this odour annoyance interferes with occupational activities or in some other way results in adverse effects (documentation "Hydrogen sulfide" 2013).

When the MAK value was established, the only available human data for sensory or cognitive effects of hydrogen sulfide after short-term exposure in the range of 5 to 10 ml/m³ were published only as an abstract reporting the preliminary results of a volunteer study with exposure to maximum concentrations of 5 ml/m³ (Fiedler

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et al. 2004). These data were based on a sub-sample of 40 volunteers who had been exposed to hydrogen sulfide concentrations of 0.05, 0.5 and 5 ml/m^3 for 2 hours. In a continuous performance test, the reaction times of the volunteers were increased after exposure to 5 ml/m^3. At that time, the study could not be evaluated conclusively as the targeted sample size had not yet been reached and no details of the test method were known.

Following publication of the study (Fiedler et al. 2008), the MAK value could be re-evaluated, as was announced in the 2007 documentation.

The final results of the experimental exposure study are now available. They are based on a random sample of 74 healthy, non-smoking volunteers consisting of 35 women and 39 men with a mean age of 24.7 years (± 4.2 years). The study design included repeated exposure sessions with different conditions; the order of the three exposure conditions (0.05, 0.5 and 5 ml/m^3) was completely permutated, and the volunteers were assigned randomly to one of six possible exposure sequences. The entire investigation lasted 3 hours with an exposure period of 2 hours. All tests were carried out in the morning. The participants of the study rated acute symptoms, various aspects of chemosensory perception (odour and irritation) and ambient air quality, measured parameters of postural sway and contrast sensitivity, and carried out tests evaluating cognitive performance to detect any effects of this short-term exposure. Nasal lavage was carried out before and after exposure. However, the authors did not describe any biochemical variables that might have been obtained from these samples and that could have been used to objectify sensory irritation.

All the dependent variables were first determined during the exposure-free control phase prior to each exposure. This was done to correct for any inter-individual differences during the baseline situations. The ratings were recorded six times (chemosensory perception) or five times (symptoms) during the exposure phase; the other variables were determined once during the influence of each of the hydrogen sulfide concentrations. Variance analysis was used for the statistical evaluation; the level of significance was adjusted by means of Bonferroni correction to allow for pairwise comparisons of the individual conditions at specific times.

Statistical analyses showed that the ratings for odour and irritation intensity and hedonic odour quality (pleasantness or unpleasantness) increased with concentration. The pairwise comparisons of the conditions differed significantly for these three ratings, particularly at the beginning of exposure. Thus, all three pair comparisons differed significantly in terms of odour intensity almost 5 and 15 minutes after the beginning of exposure. This corresponds to a definite, concentration-dependent increase in these ratings. The odour intensity ratings decreased under all conditions in the course of the 2-hour exposure phase (habituation). At the earliest time of determination, the irritation intensity ratings differed only when exposure to 5 ml/m^3 and 0.5 ml/m^3 was compared with exposure to 0.05 ml/m^3; however, when compared with each other, the two higher exposures were not significantly different. At later time points (after 15 minutes), only the ratings for exposure to 5 ml/m^3 and 0.05 ml/m^3 differed. The authors did not report whether the irritation in-

tensity ratings likewise decreased. This seems likely as only the pairwise comparisons for the first two measurements differed significantly.

In general, it is difficult to evaluate these effects. Although the ratings were determined using the Labelled Magnitude Scale (LMS; scale from 0–100; Green et al. 1996), which is considered to be a valid method for the quantitative assessment of sensory estimations, the publication did not include the means and standard deviations of these ratings. Therefore, the intensity of chemosensory perception during the exposure to 5 ml/m^3 cannot be assessed.

Statistical analysis of the sum of the 33 recorded acute symptoms and individual groups of symptoms (for example, eye irritation) did not reveal any general concentration-dependent increase in the ratings in the sense of an increasing trend over the three investigated concentration conditions. A significant interaction between the three concentration conditions and exposure time was detected only for the "anxiety" symptom group, which included symptoms such as "worried" or "feel tense". The individual comparisons showed that the ratings for the "anxiety symptoms" were significantly greater at the beginning of the exposure to 5 ml/m^3 than for exposure to 0.05 ml/m^3. This difference likewise decreased during the 2-hour exposure period. However, some of the ratings for the three conditions continued to differ significantly from each other even at later time points. The ratings reached a maximum mean of just 4 on the LMS used, which corresponds to "weak".

Immediately after the beginning of exposure, further differences were found when the low and high concentrations were compared for "symptoms of the lower respiratory tract" (for example, coughing) and "cognitive symptoms" (for example, concentration difficulties). These differences were no longer significant at later measurements. Almost 90 minutes after the beginning of exposure, the ratings for "symptoms of the upper respiratory tract" (for example, sneezing) were significantly higher for 5 ml/m^3 than for 0.05 ml/m^3.

The dependent variables postural sway and contrast sensitivity were generally not significantly affected by the concentration of hydrogen sulfide in the ambient air. Significant effects on postural sway were, however, observed under all three conditions in some individuals.

There were no statistically significant differences between the three exposure conditions for performance in the motor tapping test or the four cognitive tests (simple reaction time, symbol digit substitution, auditory verbal learning test and continuous performance test). The authors reported trends ($p \leq 0.10$) for some exposure-related differences in performance in the continuous performance test and auditory verbal learning test.

In the continuous performance test, reaction times were significantly increased during exposure compared with during the control phase, and the authors reported that the reaction time tended to differ ($p = 0.06$) between the 0.5 and 5 ml/m^3 conditions. The authors did not give any further details concerning this trend or the extent of these differences. Thus, the publication does not clarify whether the increase in reaction time was greatest during exposure to 5 ml/m^3. A trend was observed also for the verbal learning test in so far as the decrease in verbal memory

performance during exposure relative to the control ratings differed for the three exposure conditions. The smallest decline in performance (fewer recalled words during exposure than before exposure) was observed at 5 ml/m^3. At 0.05 and 0.5 ml/m^3, this decline in performance was considerably greater; however, the performance of the volunteers during the control phase for exposure to 5 ml/m^3 was already lower compared with the performance of the volunteers during the control phase for exposure to the two low concentrations.

Manifesto (MAK value, classification)

MAK value. In accordance with the authors it can be stated that there were no concentration-dependent effects on the examined cognitive, sensory and motor performances. No adverse neurobehavioural toxicity resulted from short-term exposure to hydrogen sulfide in the range of the MAK value. Therefore, acute neurotoxic effects are unlikely to occur after occupational exposure to 5 ml/m^3.

It is difficult to draw conclusions from this study for the evaluation of the irritating effects of hydrogen sulfide and the odour annoyance because the authors did not include any descriptive statistics for the rating scales for chemosensory perception and the groups of symptoms that were examined. Although odour and irritation intensity ratings increased in relation to the concentration, there was a decreasing trend for odour intensity over the 2-hour exposure phase, suggesting habituation to the unpleasant odour of hydrogen sulfide.

The significant differences found for the other symptom domains were not stable over time and were recorded mainly at the beginning of the exposure period. Even if the authors did not provide explicit data for the symptoms over the course of time, these results showed that the investigated concentrations did not lead to a permanent significant increase in acute symptom ratings. This evidence of an "adaptive" time course of symptoms may generally be interpreted as showing that the acute effects of the odour are more relevant after exposure to hydrogen sulfide than sensory irritation. On the basis of the study results now available, it is still difficult to evaluate the extent of odour annoyance, as the exact ratings are not given. Indirectly, however, the results of neuropsychological tests showed there not to be a reduction in performance that could be interpreted as adverse distractive effects of the odour (Rohlman et al. 2008).

In the light of these results, the MAK value of 5 ml/m^3 can be regarded as sufficient to avoid also unreasonable annoyance at the workplace.

Peak limitation. The critical effect caused by hydrogen sulfide is damage to the olfactory epithelium, which is a local effect. Therefore, hydrogen sulfide was classified in Peak Limitation Category I in 2006. Based on the provisional results of the volunteer study (Fiedler et al. 2004), an excursion factor of 2 was established, because no increased markers were found for nasal irritation in 40 of 100 volunteers. The study has meanwhile been published (Fiedler et al. 2008), but does not describe

the results of nasal lavage. However, this study confirms the excursion factor of 2 when the restrictions mentioned above are taken into account. At 5 ml/m^3, the ratings for acute symptoms were not permanently increased (adaptive course) and were relatively weak. Somewhat severer acute symptoms are therefore to be expected at 15-minute exposure peaks of 10 ml/m^3. However, the excursion factor is substantiated by the results from another volunteer study with 15-minute exposure to 10 ml/m^3, in which none of the volunteers reported throat irritation (Bhambhani et al. 1996), and by the NOAEC of 10 ml/m^3 derived from animal studies (see documentation "Hydrogen sulfide" 2013).

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