



# Recommendation from the Scientific Committee on Occupational Exposure Limits for dimethylsulfamoyl chloride

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## Recommendation from the Scientific Committee on Occupational Exposure Limits for Dimethylsulfamoyl chloride

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|--|--|
| 8-hour TWA:  | not feasible to derive a health-based limit (see Recommendation) |
| STEL (15 min):   | not feasible to derive a health-based limit (see Recommendation) |
| Notation:  | S (skin absorption)  |
| SCOEL carcinogen Group: A (non-threshold carcinogen)<br><i>[provisional assignment because of insufficient data]</i> |  |

### Substance:

Dimethylsulfamoyl chloride

Synonyms: Dimethylaminosulfonyl chloride  
N,N-Dimethylsulfamyl chloride  
N,N-Dimethylsulfamoyl chloride

Structural formula:  $(\text{CH}_3)_2\text{N-SO}_2\text{-Cl}$

CAS No. 13360-57-1

Molecular formula:  $\text{C}_2\text{H}_6\text{NSO}_2\text{Cl}$

Molecular weight: 143.5

Melting point: not specified

Boiling point: 182-184°C

EU Classification: R 45 (carc. cat 2), T; R23, Xn;  
R22; Xi; R36/37/38

Conversion factor: 1 ppm = 5.954 mg/m<sup>3</sup>; 1 mg/m<sup>3</sup> = 0.168 ppm

Dimethylsulfamoyl chloride is a reagent for chemical syntheses (Kevill et al. 2006).



## Health effects

After subcutaneous administration to rats, dimethylsulfamoyl chloride induces malignant tumours at the injection site in a high percentage of animals (Steinhoff and Künstler 1981).

Toxic effects in man have not been described. The structural similarity to the potent carcinogen N,N-dimethylcarbamoyl chloride (Sellakumar et al. 1980) has raised the question of whether dimethylsulfamoyl chloride possesses carcinogenic activity.

The dermal LD50 in rats after 24 h application under local occlusion was 527 and 1620 mg/kg b.w. in two different sets of experiments. Three and 24 h after the beginning of this application, respectively, the animals appeared apathic and dyspnoic for 3-10 days, pointing to a potential of systemic absorption through the skin. Also, local irritation and corrosion was observed (DFG 2003).

In a range-finding carcinogenicity study, groups of 25 male and 25 female Sprague-Dawley rats were administered subcutaneous doses of 100 mg/kg or 10 mg/kg or intratracheal doses of 1 mg/kg once weekly (Steinhoff and Künstler 1981). Since dimethylsulfamoyl chloride is reactive with water it was applied in arachis oil. Correspondingly, groups of 25 male and 25 female rats were treated subcutaneously (s.c.) or intratracheally (i.t.) with arachis oil alone. The subcutaneous dose of 100 mg/kg/week was the maximal applicable dose because of its local irritant effect. The intratracheal dose of 1 mg/kg/ week also approximates the maximum tolerable dose, or is at least very close to it, because the LD50 for single intratracheal instillation was shown to be 13 mg dimethylsulfamoyl chloride/kg body weight.

In the experiment with rats (Steinhoff and Künstler 1981) the subcutaneous injections were given for 40 weeks; at this time the first substance-related tumours were detectable at the injection site. Intratracheal instillation (1 mg/kg weekly) was continued until week 102. After the end of treatment the animals were kept under observation until they died naturally. There were no differences in body weights between the treated groups and the corresponding controls. Survival times after intratracheal treatment were not shorter than in the control group. Survival of both male and female rats administered dimethylsulfamoyl chloride subcutaneously was significantly and dose-dependently reduced in comparison to the controls. This reduction in survival time was caused by the development of malignant tumours at the injection site (s.c., fibrosarcomas). The frequency of such tumours in the groups of 25 male and 25 female rats (1 tumour per animal) is shown in the table below.

| Total tumours | Number of animals with tumours |    | Treatment group | Mean survival in days |     |
|---------------|--------------------------------|----|-----------------|-----------------------|-----|
|               | m                              | f  |                 | m                     | f   |
| 5             | 4                              | 1  | vehicle control | 876                   | 764 |
| 33            | 22                             | 11 | 10 mg/kg/week   | 659                   | 694 |
| 39            | 22                             | 17 | 100 mg/kg/week  | 520                   | 627 |

The number and distribution of the other malignant tumours and that of the benign tumours in the rats treated by subcutaneous injection was not related to the dimethylsulfamoyl chloride treatment. Apart from the local carcinogenic effect, there was no indication of other toxic effects of the dimethylsulfamoyl chloride after subcutaneous administration.



After intratracheal (i.t.) instillation of dimethylsulfamoyl chloride (1 mg/kg/week) to male rats the number of malignant tumours was increased in comparison with the i.t. control from 6 to 13. This could be a chance finding because practically the same number (12) of malignant tumours was found with a similar distribution pattern in the s.c. control after subtraction of the 4 fibrosarcomas at the injection site. Three brain tumours (astrocytomas) were found after the intratracheal treatment with dimethylsulfamoyl chloride; they developed in one male and two female rats. The remaining malignant tumours in the female rats corresponded in number and distribution with those in the control animals. The same was true for the benign tumours in both sexes. There were no other indications of toxic effects of dimethylsulfamoyl chloride after intratracheal instillation at a dose of 1 mg/kg/week.

## Recommendation

Dimethylsulfamoyl chloride is a substance, which is structurally related to the potent carcinogen dimethylcarbamoyl chloride. The compound has a marked local dose-dependent carcinogenic effect upon subcutaneous injection in the rat using at doses of 100 mg/kg/week and 10 mg/kg/week. After intratracheal instillation of 1 mg/kg/week (LD<sub>50</sub>: 13 mg/kg *i.t.*) the carcinogenic effect was not as clear-cut, although the development of astrocytomas of the brain pointed to a systemic carcinogenicity.

The structurally related compound, dimethylcarbamoyl chloride, revealed marked local carcinogenicity in animals after inhalation (Sellakumar et al. 1980), as well as after intratracheal (Steinhoff et al. 1986) or subcutaneous (Steinhoff and Künstler 1981) administration. The carcinogenic effect was most marked after subcutaneous injection.

Dimethylsulfamoyl chloride, compared with dimethylcarbamoyl chloride after subcutaneous and intratracheal administration, also proved to be a local carcinogen after subcutaneous injection, although the effect was weaker than that of dimethylcarbamoyl chloride.

In essence, dimethylsulfamoyl chloride is an experimental carcinogen that has been categorised in category 2 and labelled R45. According to its direct chemical reactivity and to its structural analogy to dimethylcarbamoyl chloride, a genotoxic effect appears almost likely. Accordingly, dimethylsulfamoyl chloride is assigned to the SCOEL carcinogen group A (Bolt and Huici-Montagud 2008) as a non-threshold carcinogen. A health-based OEL cannot be supported. Because of the paucity of available data, this assignment is provisional.

There is insufficient data to perform a quantitative risk assessment. Any occupational contact with the substance must be avoided.

As there are experimental indications of a relevant systemic absorption through the skin, a "skin notation" is applied.



## References

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*Criteria document used: DFG (1991, 2003)*