Rijksinstituut voor Volksgezondheid en Milieu
Ministerie van Volksgezondheid, Welzijn en Sport

Stofdocument deel A

CAS-nr: 7446-09-5 **Zwaveldioxide** **SO_2** **VN-nr: 1079**
GEVI: 268

Synoniemen: geen (Engels: Sulfur dioxide)

Interventiewaarden		10 min.	30 min.	1 uur	2 uur	4 uur	8 uur
Voorlichtingsrichtwaarden	**VRW (mg/m^3)**	2,0	2,0	2,0	2,0	2,0	2,0
Alarmeringsgrenswaarden	**AGW (mg/m^3)**	20	20	20	19	15	7,6
Levensbedreigende waarden	**LBW (mg/m^3)**	440	310	240	190	150	76

Datum vaststelling: 06-10-2016 — 1 mg/m^3 = 0,376 ppm; 1 ppm = 2,66 mg/m^3

Explosiegrens: geen data

Geur: stekend, irriterend
LOA: 36 mg/m^3

Fysisch-chemische eigenschappen

Uiterlijk: kleurloos, onder druk tot vloeistof verdicht gas
Brand: niet brandbaar

Relatieve dichtheid gas (lucht=1): 2,2

Molecuulmassa:	64,0 g/mol
Zuurgraad:	Geen data
LogKow:	Geen data
Wateroplosbaarheid:	11,4 g/100 ml (goed)
Verzadigde dampdruk:	3300 mbar

Overige informatie

Publieke grenswaarde: 0,7 mg/m^3 (15 min)
MAK: 2,7 mg/m^3
TLV-TWA: 5,3 mg/m^3

Toxicologische eigenschappen

Effecten bij inhalatoire blootstelling

Onder VRW: geen effecten

VRW → AGW: irritatie van slijmvliezen van ogen, neus en keel. Astmatici: keelpijn, hoesten, branderig gevoel en slikmoeilijkheden, tranen en longfunctieveranderingen t.g.v. reflectoire bronchoconstrictie

AGW → LBW: bronchiale hyperreactiviteit met luchtwegobstructie en longschade (ernstige bronchospasmen en verlamming van de ademhalingsspieren), long- en glottisoedeem

Boven LBW: glottisoedeem, sterfte door ademstilstand

Toxiciteit bij eenmalige, inhalatoire blootstelling

- Inhalatie van zwaveldioxide veroorzaakt een type-I-inhalatoire intoxicatie. Zwaveldioxide werkt irriterend op de ogen en luchtwegen via de vorming van bisulfiet. Bij een betrekkelijk geringe blootstelling bestaan de verschijnselen vooral uit tranende ogen, neusirritatie, keelpijn, hoesten, een brandend gevoel achter het borstbeen en pijn bij doorzuchten.
- Zwaveldioxide veroorzaakt longfunctie-veranderingen als gevolg van reflectoire bronchoconstrictie.
- Het effect van zwaveldioxide op bronchoconstrictie is groter bij lichamelijke inspanning en voor astmatici
- Bij blootstelling aan zeer hoge concentraties kan glottisoedeem optreden met mogelijk asfyxie tot gevolg.
- De effecten treden snel (binnen enkele minuten) op. Bij langere blootstellingsduur (enkele tot meerdere uren) lijkt de duur van de blootstelling minder invloed te hebben op de bronchiale effecten of nemen deze effecten zelfs af.

Effecten bij blootstelling aan vloeistof

Huidcontact: bevriezingsletsel
Oogcontact: conjunctivitis, branderigheid, roodheid, bevriezingsletsel

Carcinogeniteit

IARC classificatie: 3
CRP: niet afgeleid

Beknopte medische informatie

Ontsmetting damp

inademing: frisse lucht, rust, halfzittende houding en direct spoedeisende medische hulp inzetten.
huid: verontreinigde kleding uittrekken en huid afspoelen met water.
ogen: minimaal 15 min. spoelen met water (evt. contactlenzen verwijderen), dan naar oogarts brengen, blijven spoelen tijdens vervoer.

Ontsmetting vloeistof n.v.t. (gas). ,

huid: *in geval van bevriezingsletsel*: spoelen met veel water, niet-verkleefde kleding verwijderen (adembescherming dragen), onmiddellijk arts raadplegen.
ogen: zie hierboven.
inslikken: n.v.t. (gas > –10°C). In geval van inslikken gekoelde vloeistof: mond spoelen (uitspugen!) en direct spoedeisende hulp inzetten

Specifieke behandeling en materialen*: geen.*

Neem contact op met het NVIC (Tel:+31 (0)30 274 8888) voor aanvullende informatie met betrekking tot medisch handelen

National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

Stofdocument deel B

CAS-nr: 7446-09-5 **Sulfur dioxide** **SO_2** **UN-nr: 1079**

Basis for the Dutch Intervention Values

VRW: Same study but different point of departure as for AEGL, 2 h value added

AGW: Same study but different point of departure and different approach as for AEGL, 2 h value added, time scaling from 2-8 h

LBW: Same point of departure as for AEGL values, but using different uncertainty factors, time scaling from 10 minutes to 8 hour, 2 h value added

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Dutch Intervention Values (mg/m^3)

	10 min	30 min	1 h	2 h	4 h	8 h	End point
VRW	2.0	2.0	2.0	2.0	2.0	2.0	LOAEL for moderate bronchoconstriction in exercising asthmatics
AGW	20	20	20	19	15	7.6	10 min - 1 hr VRW × 10, 2 h – 8 h 1/10 x LBW
LBW	440	310	240	190	150	76	Calculated $BMCL_{05}$ for rats

Derivation of the Dutch Intervention Values

VRW: A weight of evidence approach based on exercising human asthmatic data was also used to derive the VRW values. The data suggest that 0.75 ppm (2.0 mg/m^3) induces a moderate respiratory response for exposure durations of 10-minutes to 3 hours, as indicated by an increase in airway resistance (SRaw) of 150%, a decrease in FEF of 22%, and a decrease in FEV_1 of 8% in exercising asthmatics exposed for 10-40 minutes, and an increase in SRaw of 322%, 233%, 26% and 5%, 10 minutes, 20, minutes, 1 hour and 2 hours into exposure, respectively. No uncertainty factors were applied, because the point of departure is a study in humans, using a sensitive population (exercising asthmatics). The role of exposure duration to the magnitude of bronchoconstriction after SO_2 exposure in asthmatics appears to decrease with extended exposure. This can be derived from the findings that during exposure to 0.75 ppm (2.0 mg/m^3), the SRaw increases were 322%, 233%, 26% and 5%, 10 minutes, 20, minutes, 1 hour and 2 hours into exposure, respectively. After 3 hours into exposure even a decrease of 12% was observed. Therefore, the VRW values can be held constant over time.

AGW: No adequate data are available that meet the definition of AGW effects. LBW values are not suitable for derivation of AGW values since deaths in experimental animals start to occur at concentrations that are orders of magnitude higher than for respiratory effects. Nevertheless, AGW values are so important that they are derived from the VRW values by a weight-of-evidence approach. AGW values are thus based on data obtained with exercising asthmatics (see VRW for description). In this population, an exposure concentration of 0.75 ppm (2.0 mg/m^3) induces a moderate respiratory response (*i.e.*, bronchoconstriction). Higher concentrations will result in more severe bronchoconstriction whether or not accompanied by additional effects that lead to a further increase in breathing difficulties. It is assumed that a tenfold higher exposure concentration might lead to respiratory difficulties in asthmatics which may impair their ability to escape from an incident location. With this assumption AGW values are derived by multiplying the VRW values by a factor of 10, but with the restriction that they should not be higher than 1/10 of the LBW to avoid damage to the respiratory epithelium that occurs at higher (lethal) concentrations.

LBW: LBW values are based on a calculated $BMCL_{05}$ of 573 ppm (1500 mg/m^3) in rats exposed to SO_2 for 4-hours. The default total uncertainty factor of 10 (3x3) was considered sufficient to account for inter- and intraspecies differences. Because data were not sufficient to ascertain whether a maximal response to SO_2 for a lethal end point is obtained within 10 min, time scaling was applied for the derivation of the LBW values. Time scaling was performed using $C^n * t = k$, with the default values of n = 1 and n = 3 for extrapolation to longer and shorter exposure durations, respectively.

Additional toxicological information (including relevant results of a general literature search, if any)

Sulfur dioxide is a water-soluble irritant of the upper respiratory tract and eyes, which may induce increased airway resistance via reflex bronchoconstriction. The exact mechanism for this bronchoconstriction is unknown. However, the rapid onset and reversibility of SO_2-induced bronchoconstriction observed in asthmatics is likely due to decreased airway caliber caused by contraction of airway smooth muscle. Sulfur oxide may act either directly on smooth muscle or may cause a release of chemical mediators from this tissue. Asthma and physical exercise increase the bronchoconstrictive effect. With regard to respiratory tract, the effects occur rapid (within several minutes). The influence of exposure duration diminishes over time, showing even a decrease in effect level after several hours.
Conjunctivitis, corneal burns, and corneal opacity may occur from direct contact with high concentrations of sulfur dioxide. Death from respiratory arrest may occur from acute over-exposure, while survivors may develop bronchitis, bronchopneumonia, and fibrosing obliterative bronchiolitis. Bronchoconstriction accompanied by increased pulmonary resistance may be asymptomatic or may occur with high-pitched rales.
Co-exposure to respirable particles may increase the severity of adverse effects caused by sulfur dioxide. Although the main effects of SO2 are on the respiratory tract, much of an inhaled dose may be transferred into systemic circulation. Most inhaled SO2 is detoxified in the liver by the sulfite-oxidase pathway, which forms S-sulfonates that can be found in the plasma and sulfates that are excreted in the urine. The S-sulfonates are long-lived and supply the circulation with bisulfite that may reach many tissues.

The VRW and AGW values are based on effect levels in asthmatics and are expected to have no effect on healthy individuals. This is confirmed by two studies in which healthy volunteers were exposed to 0.5, 1.0 and 2.0 ppm (1.33, 2.66 and 5.32 mg/m^3) for 4 hours, with periods of light to moderate exercise. No effects were found on exhaled nitric oxide (FeNO) and airway inflammation biomarkers measured in exhaled breath condensate and nasal lavage fluid (Raulf-Heimsoth et al., 2010), eye blink frequency, nasal airflow, and lung function measured by spirometry (van Thriel et al., 2010).

Sulfur dioxide was generally not a developmental or reproductive toxicant in animal studies.

H314: Causes severe skin burns and eye damage; H331: Toxic if inhaled.

Carcinogenicity and derivation of the CRP value

IARC classification: 3 (not classifiable as to carcinogenicity to humans)

No carcinogenic risk potency (CRP) was derived.

Genotoxic studies regarding exposure to SO_2 are equivocal and the carcinogenicity study, although suggesting a possible increase in pulmonary tumors, is of poor quality and thus of limited use. No information suggesting an increased cancer incidence from SO_2 exposure in humans was located.

Odour and derivation of the LOA value

Odor: foul, pungent, irritating odor

ODT: 2.3 mg/m^3 [Nagata, 2003]
LOA = 11.8 * ODT * 1.33 = 36 mg/m^3

(The concentration Level leading to distinct Odor Awareness (I=3) is calculated using the formula: I = 2.33 * log (C/OT_{50}) + 0.5. A correction factor of 1.33 is applied to this value)

The LOA lies between the AGW and the LBW.

Other standards and guidelines (1h values in mg/m^3, unless otherwise indicated)

VRW level **2.0**	*AEGL-1* 0.53	*ERPG-1* 0.30		*IDLH:* 270 mg/m^3 (10 min)
AGW level **20**	*AEGL-2* 2.0	*ERPG-2* 3.0		
LBW level **240**	*AEGL-3* 80	*ERPG-3* 25		