

# Pulmonary toxicity is the most sensitive endpoint for deriving MAK values for aluminium compounds

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## Introduction

The German MAK Commission proposes maximum workplace concentrations (MAK values) for industrial chemicals in order to provide comprehensive information for workplace safety professionals and researchers and to give scientific policy advice. Recently, the MAK Commission re-evaluated the MAK value of aluminium and aluminium compounds at the workplace.

## Objectives

**Long-known:** Aluminosis & neurodegenerative diseases occur in workers of the aluminium industry (e.g. welding)

**MAK value (2007), aluminium-containing dust (poorly soluble):** 1.5 mg/m<sup>3</sup> (R), 4 mg/m<sup>3</sup> (I)

**New data:**

- aluminium-exposed workers: preclinical neurotoxic effects
- inhalation toxicity studies in rats: pulmonary effects

## Re-evaluation of the MAK value

## Methods

A comprehensive literature search was conducted on the toxicity of aluminium compounds. Reviews by other regulatory agencies and original studies, particularly on neurotoxicity, inhalation toxicity, genotoxicity and carcinogenicity, were evaluated.

## Results

### Longitudinal studies with aluminium welders

- preclinical neurotoxic effects: LOAEC 4.5-6.8 mg/m<sup>3</sup>, NOAEC 0.47-0.67 mg/m<sup>3</sup>
- pulmonary effects: LOAEC 0.47-0.67 mg/m<sup>3</sup>

However: confounding by co-exposure (ozone) and high proportion of smokers and ex-smokers in the study collective

Thus: NOAEC for lung effects of aluminium could not be derived

### Studies in animals

#### Differentiation according to solubility and irritation

Compound	Aluminium oxyhydroxide	Aluminium chlorohydrate	Aluminium chloride
Solubility	poorly soluble	soluble	soluble
Eye irritation <sup>#</sup>	not irritating	slightly irritating	very irritating
<b>Inhalation studies in rats</b>			
Effects in lung	<ul style="list-style-type: none"> <li>• pulmonary inflammation,</li> <li>• elimination half-time ↑,</li> <li>• enlarged and foamy macrophages</li> </ul>	<ul style="list-style-type: none"> <li>• pulmonary inflammation</li> </ul>	<ul style="list-style-type: none"> <li>• pulmonary inflammation</li> </ul>
<b>NOAEC [mg Al/m<sup>3</sup>]</b>	<b>1.18-1.32</b>	<b>0.027</b>	<b>0.007</b>

## MAK value derivation

- **poorly soluble aluminium compounds** e.g. aluminium oxide, aluminium hydroxide: **0.05 mg Al/m<sup>3</sup> (R)**
- **soluble, slightly or not irritating aluminium compounds** e.g. aluminium chlorohydrate: **0.005 mg Al/m<sup>3</sup> (I)**
- **soluble, irritating aluminium compounds** e.g. aluminium chloride, aluminium sulfate: **0.0002 mg Al/m<sup>3</sup> (I)**

## Carcinogen Category 4 for poorly soluble aluminium compounds

- lung overload effects clearly seen → lung carcinogenicity at higher concentrations cannot be ruled out
- if the MAK value is complied with → no or at most a very slight contribution to the cancer risk is to be expected

<sup>#</sup> according to CLP (ECHA), I: inhalable fraction, NOAEC: no observed adverse effect concentration, LOAEC: Lowest observed adverse effect concentration, R: respirable fraction

