


**TDMA**

Titanium Dioxide Manufacturers Association

(A sector group of  cefic )

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**TiO<sub>2</sub>**

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## Titanium Dioxide Product Safety Statement on Inhalation Toxicology

### Introduction

In February 2006 the International Agency for Research on Cancer (IARC) reclassified titanium dioxide (TiO<sub>2</sub>). The final Monograph was published in January 2011. This document explains the significance of this reclassification and the position of TDMA.

### Background/History

In 1989 IARC classified TiO<sub>2</sub> as Group 3: ('not classifiable for human carcinogenicity'). TiO<sub>2</sub> is usually used in toxicological studies as an inert comparator or control. However, three long term studies were specifically carried out on TiO<sub>2</sub>, at exposure concentrations far above those experienced in any workplace. After two years exposure at this „overload“ concentration, lung tumors were found in rats.

The TiO<sub>2</sub> industry commissioned a TiO<sub>2</sub> inhalation study in mice, rats and hamsters and two epidemiology studies in 15 TiO<sub>2</sub> plants in Europe and North America.

### Main findings of these studies

The epidemiology studies did not demonstrate an increased risk of lung cancer as a result of occupational exposure to TiO<sub>2</sub>.

The inhalation study clearly demonstrated that rats exhibited a different response to high TiO<sub>2</sub> dust concentrations compared with mice and hamsters.

The unique response developed by rats significantly adds to the evidence that the observed effects are not relevant to humans. It was the dust overload that fundamentally caused the problem in rats. There is no evidence that titanium dioxide *itself* has toxic properties that would lead to cancer, nor that it presents a carcinogenic risk to humans at exposures experienced in the workplace.

### Actions in 2006

In February 2006 IARC carried out a review which resulted in the classification for TiO<sub>2</sub> being changed from Group 3 to Group 2B, i.e. from: '*not classifiable for human carcinogenicity*' to: '*possible human carcinogen*'.

This reclassification was based *entirely* on the long term animal studies. The epidemiology studies led the panel to conclude there was '*insufficient evidence of carcinogenicity in humans*'. For the animal studies, the conclusion was: '*sufficient evidence of carcinogenicity in experimental animals*'.

## Explanation of IARC decision

The IARC rules state: there is "*Sufficient evidence of carcinogenicity: ...if... two or more independent studies in one species carried out at different times or in different laboratories or under different protocols*" show evidence of tumours. The IARC expert group judged the three studies on rats as qualifying.

Also, the new IARC rules require evidence of the 'mechanism' of the tumour formation to be taken into account. This means that, if the tumour formation process in the rat took place in a manner that was not applicable to humans, then this should not be part of the overall judgement.

The opinion of our experts is that the fact that the rat is uniquely sensitive should have kept TiO<sub>2</sub> in category 3. However the IARC Expert Panel did not agree.

## Conclusions on IARC

IARC assesses the potential hazard, not the risk. The epidemiology studies did not show an increase in lung cancer in the TiO<sub>2</sub> workforce as a result of exposure to TiO<sub>2</sub> dust.

We believe it is important that everyone should be fully informed on this issue, because there will inevitably be concern and possible misinterpretation of the term '*possible human carcinogen*'. Our M/SDS's have been updated accordingly.

Irrespective of the IARC ruling, TDMA members place paramount importance on the health and safety of their employees and the community at large, and strongly believe that it is always prudent to take all possible precautions against all potential work place exposures (noise, dust, chemicals etc.). We therefore support the continuous improvement of procedures and processes to minimize any potential exposure.