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Dear Dr Jameson

SULPHURIC ACID MIST

This letter and attachment is the response by the European Sulphuric Acid Association (ESA) to your call for "Public Comments" issued in the Federal Register of 11 July 1997 regarding Sulphuric Acid Mist and your intention to list it as carcinogenic.

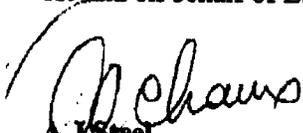
ESA (of which I am Chairman) is a sector group of CEPIC - The European Chemical Industry Council - whose membership is comprised, through National Delegations of Europe, of manufacturers of Sulphuric Acids, Oleums and Sulphur Trioxide.

Through our Technical Committee we have reviewed the scientific data relevant to the debate on the carcinogenicity of "Sulphuric acid contained in strong inorganic mists" and are most concerned that the intention of NTP to classify sulphuric acid mist singularly as carcinogenic is fundamentally flawed.

The attachment to this letter concisely presents the scientific case for curtailing your proposed intention. In particular we argue that at best there is a case to investigate the singular effects of sulphuric acid mist, a study which ESA has commissioned, and that your deliberations should not be brought to a conclusion until the results of this study are available.

The resources of ESA are at your disposal in aiding you in your work.

Yours faithfully
for and on behalf of ESA


A. J. Steel
Chairman - ESA

(p.o. M. Michaux, Sector Group Manager)



INORGANIC ACID MISTS
ESA RESPONSE TO THE PROPOSED INCLUSION OF
SULPHURIC ACID MISTS INTO THE NTP

The European Sulphuric Acid Association (ESA) has noted the intended review of sulphuric acid mists by the NTP (Fed Reg 11 July 1977), and the call for public comment.

The ESA presumes that the decision to review sulphuric acid mists is consequential to the view of IARC that "occupational exposure to strong inorganic mists containing sulphuric acid is carcinogenic to man", and the subsequent classification by the ACGIH of "sulphuric acid contained in strong inorganic mists" as a suspected human carcinogen. The ESA believes that the basis for both these classifications should be clearly understood, and that new data should be considered. In a review specifically of sulphuric acid mists, (as opposed to strong inorganic mists containing sulphuric acid), it will be important to consider both the experimental animal data on sulphuric acid, and the extent of confounding factors in the epidemiological studies.

Following the IARC review US and European sulphuric acid producers commissioned a review of the same data by epidemiologists at the University of Alabama, Birmingham, which was recently published in CRC Critical Reviews in Toxicology (Sathiakumar et al, 1997). The conclusions are broadly similar to those of IARC, but the authors did not feel the data sufficiently certain to classify in the way done by IARC. The authors considered that while cancer of the larynx may be caused by exposure to strong inorganic mists containing sulphuric acid, it was also possible that some other correlated agent may be involved. This conclusion is drawn due to the various deficiencies in the epidemiology studies, particularly the lack of exposure data, the various co-exposures to other agents, and the general inadequacy of control for other relevant factors particularly alcohol and tobacco consumption. Investigation of sulphuric acid itself was not the prime aim of most of the studies considered.

Since the IARC review, two further papers are relevant for consideration (Suaraz-Almazor et al 1992, and Coggon et al, 1996). The former of these papers is a reassessment of published data (Soskolne et al 1984), defining the exposures in different ways. Using the more usual "cumulative exposure index" resulted in a negative dose-response for laryngeal cancer and exposure to acid mist. This must call into question the conclusions of the original work, which itself was a key paper in the deliberations of IARC.

The paper by Coggon et al describes a cohort study, in which workers exposed to acid (mainly sulphuric) mists had no increased mortality from laryngeal or lung cancer compared to controls. In a follow up case-control study, risk of "upper aerodigestive cancer" was modestly, but not statistically significantly increased (OR 2.0). This increase was essentially due to inclusion of cancer of the lip - a finding never before associated with acid mist

exposure, and having other known risk factors. While the authors concluded that the study data was consistent with other studies, it was also concluded that any risk from exposure to sulphuric acid mist below 1 mg/m^3 was small. The ESA consider that this study does not support the conclusion that exposure to strong acid mists is associated with increased cancer of the larynx.

In a review of sulphuric acid mist, full weight should be given to the existing animal and other experimental data. Sulphuric acid is negative in the Ames test. However chromosomal damage observed in vitro on exposure to sulphuric acid was a result of the lowering of pH, which occurs at pH6.5 and lower, and is independent of the acid used. ESA is aware that there have been lifetime carcinogenicity studies performed in the USA, but the ESA does not have the reports. These studies reportedly showed no carcinogenic effect. Overall the experimental data does not indicate an alert for carcinogenic activity with inhalation of sulphuric acid.

Considering the experimental data alongside the uncertainty of the epidemiological data, it is the conclusion of ESA that sulphuric acid itself has not been shown to be carcinogenic.

In order to further understand the toxic effects of sulphuric acid mist on the respiratory tract, ESA has decided to commission subacute "state of the art" inhalation studies in rats at occupationally relevant concentrations. The programme comprises extensive examination of the lung, larynx and nasal passages to determine any pathological response to exposure and specialist techniques to determine levels of cell proliferation in these tissues. These studies are currently in progress, but results are unlikely to be available until mid 1998. We intend to publish the results and can make the data available to the NTP when final reports are issued. ESA considers that until this study is complete and the results known, there is insufficient data to support NTP inclusion in its listing.

References:

- Surarez-Almazor et al 1992, Scand J Work Environ Health, 1992: 18, 233-241
- Coggon et al, 1996. Occup Environ Med, 1996: 53, 445-449
- Soskolne et al 1984. Am J Epidemiol, 1984: 120, 358-369
- Sathiakumar et al 1997. Crit Rev Toxicol, 1997: 27, 233-251