

## Position Statement of the Cefic Amines Sector Group Regarding the Available Cancer Evidence for Triethanolamine

September 17, 2004

The carcinogenic potential of triethanolamine (TEA) has been investigated over many years. TEA was not carcinogenic in various long term experiments in rats and mice, as well as in short-term cancer experiments using a transgenic mouse model. TEA has not shown mutagenic activity in a comprehensive series of tests, a conclusion also confirmed by the US National Toxicity Program (NTP) and the International Agency for Research on Cancer (IARC).

In 1999, NTP [1] published the results of a cancer study in rats and mice. TEA did not cause tumours in rats, but the findings in mice were spoiled due to a bacterial infection [2]. Consequently, NTP repeated the study, and published the findings this year [3]. Dermal exposure of mice to TEA caused liver tumours in the females. However, these findings are not relevant to humans, for the following reasons:

- The strain of mouse used is unusually sensitive to liver tumours. EU classification guidelines specifically discount tumour findings where they occur "only in particular organs of certain species known to be susceptible to a high spontaneous tumour formation" [4].
- Although the incidence of tumours in treated animals was higher than that in the untreated animals, it did not increase with increasing dose of TEA, which is what would be expected otherwise.
- Research work has identified that dose levels of TEA that cause tumours also cause deficiency of the nutrient choline. Chronic choline deficiency has been shown to cause liver tumours in rodents via a relatively well characterised mechanism with an observable threshold level. Humans, however, are relatively resistant to the development of choline deficiency.
- TEA does not lead to nitrosamine formation under the experimental condition of the NTP mouse study. It is noteworthy that TEA cosmetic grade is of very high purity and contains negligible levels of nitrosamine.

Further mechanistic work is ongoing. The findings for TEA are similar to those of a related chemical, diethanolamine (DEA), which also causes choline deficiency and liver tumours in the same strain of mouse. In this case, the EU recently decided not to classify DEA as a carcinogen. We, the ethanolamines producers of the Cefic Amines Sector Group expect major results of the research work within the next 6 months and will keep you updated.

## Amines Sector Group

The available scientific data (weight of evidence from animal cancer bioassays, lack of genotoxicity, well-defined mode of tumourigenic action, and resistance of humans) support the conclusion that the human cancer risk for TEA is negligible. Taking these aspects into consideration, the use of TEA is considered safe.

For further information on TEA, please contact Graeme Wallace at CEFIC, Brussels (E-mail: [gwa@cefic.be](mailto:gwa@cefic.be) and telephone: +32 2 676 7410).

- 1 NTP is a federally-funded research agency of the U.S. Department of Health and Human Services.
- 2 NTP Technical Report on the Toxicology and Carcinogenesis Studies of Triethanolamine (CAS No. 102-71-6) in F344/N Rats and B6C3F<sub>1</sub> Mice (Dermal Studies), NTP TR 449, NIH Publication No. 00-3365 (Nov. 1999) (Final Technical Report)
- 3 NTP Technical Report on the Toxicology and Carcinogenesis Studies of Triethanolamine (CAS No. 102-71-6) in B6C3F<sub>1</sub> Mice (Dermal Study), NTP TR 518, NIH Publication No. 03-4452 (Aug. 2004) (Final Technical report).
- 4 Commission Directive 2001/59/EC, Annex VI (4.2.1.2.)