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September 10, 2003

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Attn: TSCA Section 8(e)
U.S. Environmental Protection Agency
1201 Constitution Avenue, NW
Washington, DC 20460-0001

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RE: Diethanolamine—Subchronic Inhalation Study With Rats

Attention: TSCA 8(e) Coordinator



Dear Sir or Madam:

The American Chemistry Council hereby submits this letter regarding diethanolamine (CAS No. 111-42-2) on behalf of its Alkanolamines Panel. The letter is intended to inform EPA of certain findings from a subchronic study in which rats were administered diethanolamine by inhalation exposure. The Agency may regard this information as reportable under the provisions of TSCA Section 8(e). While the information is being submitted in accordance with the Agency's interpretation of relevant TSCA 8(e) guidance, the Panel has not made a determination as to whether a significant risk of injury to health or the environment is actually presented by the findings.

The member companies of the Alkanolamines Panel consist of: BASF Corporation, The Dow Chemical Company, Equistar Chemicals LP, Huntsman Corporation, and Ineos LLC.

The information reported here comes from the final report of a 90-day inhalation study sponsored by CEFIC (European Chemical Industry Council). The report is titled: *Diethanolamine – Subchronic inhalation toxicity study in Wistar rats, liquid aerosol/vapor exposure. Study focus on irritation of upper respiratory tract.* The final report is appended to this letter.

The final report states the following in section 1, page 14:

"Substance related pathological findings were confined to the larynx, in which squamous metaplasia and inflammatory cell infiltration at the base of the epiglottis was observed at the high concentration (8 mg/m³). This change is considered to be an adverse effect due to the concurrence of epithelial change and inflammatory response. However it is considered to be borderline because it showed full reversibility during the 3-month recovery period.

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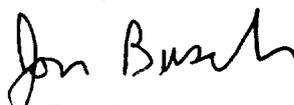
MR 269457

The intermediate concentration (3 mg/m³) led to a reversible focal squamous metaplasia at the base of the epiglottis without inflammation in a minority of male animals (3 of 10) examined at the end of the exposure period. This change is considered to represent an adaptive response, rather than a frank adverse effect.

No substance related histopathology was present at the low concentration (1.5 mg/m³)."

If you have any questions about this submission, please contact me at (703) 741-5633 or at jon_busch@americanchemistry.com.

Sincerely,



Jon Busch
Manager, Alkanolamines Panel
Director, CHEMSTAR Panels

Attachment

STUDY TITLE

Report

Diethanolamine - Subchronic inhalation toxicity study in Wistar rats
liquid aerosol / vapor exposure
Study focus on irritation of upper respiratory tract

DATA REQUIREMENT

inhalation exposure following
OECD - Guideline method 413
EEC Guidelines 87/302/EEC
U.S. EPA OPPTS Guidelines 870.3465
examinations according to the aim of the study

AUTHORS

Dr. A.O. Gamer (Study Director)
Dr. E. Leibold
Dr. W. Kaufmann
Dr. B. van Ravenzwaay

STUDY COMPLETED ON

April 02, 2002

PERFORMING LABORATORY

Experimental Toxicology and Ecology
BASF Aktiengesellschaft
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LABORATORY PROJECT IDENTIFICATION

5110299/99125

SPONSOR

CEFIC Amines Sector Group
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VOLUME I OF III
(REPORT SECTION AND SUMMARY TABLES)

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1. SUMMARY

Scope of examinations

The present study was performed in order to elucidate the dose response curve of laryngeal findings at low concentrations of Diethanolamine as a follow up of a 90-day inhalation study (Proj. No.: 50I0075/93011) sponsored by BG-Chemie, Heidelberg, Germany.

Male and female Wistar rats were head-nose exposed to dynamic atmospheres of Diethanolamine liquid aerosol / vapor mixtures for 6 hours per working day for about 3 month (65 exposures). The target concentrations were 1.5, 3 and 8 mg/m³. Animals exposed to clean air were used as controls.

The following test groups and treatment regimens were used:

Test group	Exposure [mg/m ³]	Male animals	Female animals	Recovery period
0	conditioned air	10	10	no
1	1.5	10	10	no
2	3	10	10	no
3	8	10	10	no
0.1	conditioned air	-	10	3 months
2.1	3	-	10	3 months
3.1	8	-	10	3 months

The concentrations of the inhalation atmospheres were analyzed by spectrophotometry of Biuret treated absorption samples in all test groups including control.

Daily means were calculated based on 2 measured samples per concentration and exposure and one measured sample per week in the control group. From the daily mean values of each concentration, mean concentrations and standard deviations for the entire study were derived.

The constancy of concentrations in each inhalation system (except the control system) was continuously monitored by scattered light photometers.

Particle size distributions were determined by cascade impactor measurements.

The general state of health was controlled twice on workdays and once on weekends or holidays. On exposure days clinical observation was performed before, during and after exposure. During the chamber adaptation (preflow) period and on post exposure days clinical findings were recorded once each working day. Body weight of the animals was determined weekly, as a rule.

A complete necropsy including weighing of selected organs and gross pathological evaluation was performed.

Histopathology of the nasal cavity (4 levels), larynx (3 levels), trachea, lung, mediastinal lymph node, liver and gross lesions was performed.

Results

The following study means of concentrations and particle size distributions were determined analytically:

Test group	Treatment Target concentration (mg/m ³)	Measured concentration Mean \pm SD (mg/kg)	Particle size distribution Mean MMAD (μ m) / GSD
0	0 (conditioned air)	0	n.a.
1	1.5	1.57 \pm 0.33	0.6 / 3.3
2	3	3.43 \pm 0.80	0.6 / 2.8
3	8	8.18 \pm 1.45	0.7 / 2.5

MMAD = mass median aerodynamic diameter n.a. = not applicable
 GSD = geometric standard deviation

According to the available data on vapor pressure, a considerable part of the low concentration was expected to consist of vapor. This could not be verified during the cascade impactor particle size measurements, as even in the low exposure level the test substance concentration was present in total as deposit on the impactor stages.

No substance related clinical findings were observed. The body weight development of treated and control animals was comparable.

Substance related pathological findings were confined to the larynx, in which squamous metaplasia and inflammatory cell infiltration at the base of the epiglottis was observed at the high concentration (8 mg/m³). This change is considered to be an adverse effect due to the concurrence of epithelial change and inflammatory response. However it is considered to be borderline because it showed full reversibility during the 3-month recovery period.

The intermediate concentration (3 mg/m³) led to a reversible focal squamous metaplasia at the base of the epiglottis without inflammation in a minority of male animals (3 of 10) examined at the end of the exposure period. This change is considered to represent an adaptive response, rather than a frank adverse effect.

No substance related histopathology was present at the low concentration (1.5 mg/m³)

Conclusion

In the present study, 90-day inhalation exposure of rats to Diethanolamine aerosols resulted in a Low Observed Adverse Effect Concentration (LOAEC) for upper respiratory tract irritation in form of squamous metaplasia of the laryngeal epithelium at the base of the epiglottis accompanied by some inflammatory cell infiltration at the concentration of 8 mg/m³. These findings are considered to represent a borderline adverse effect and were fully reversible within the 3-month recovery period. No changes were observed in the nasal cavity or the lower respiratory tract at this concentration.

The No Observed Adverse Effect Concentration (NOAEC) was found to be 3 mg/m³.