

8EHQ-1294-13285



CHEMICAL MANUFACTURERS ASSOCIATION

DEC 15 94 DEC 15 1994

(A)

Langley A. Spurlock, Ph.D., CAE  
Vice President, CHEMSTAR



8EHQ-94-13285  
INIT 12/15/94

December 15, 1994

**ORIGINAL**

**Contains No CBI**

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U.S. Environmental Protection Agency  
401 M Street SW  
Washington, DC 20460

Attention: 8(e) Coordinator



88950000075

Dear Sir or Madam:

The Chemical Manufacturers Association (CMA) submits the following information on behalf of its Alkanolamines Panel. The Environmental Protection Agency may regard this information as reportable under provisions of TSCA Section 8(e).

The National Toxicology Program (NTP) recently issued a draft technical report regarding its two-year dermal studies on triethanolamine (CAS No. 102-71-6). The studies were conducted with F344/N rats and B6C3F<sub>1</sub> mice. The abstract of the draft NTP report is attached.

According to the draft NTP report, there was "some evidence of carcinogenic activity" of triethanolamine in female B6C3F<sub>1</sub> mice based on increased incidences of hepatocellular neoplasms (see p.11 of Abstract, Conclusions). The female mice were administered triethanolamine (purity > 98%) in acetone topically 5 days a week for 103 weeks at doses of either 0, 100, 300, or 1,000 mg/kg. The Alkanolamines Panel has not made any determination that this study suggests unreasonable or substantial health risk.

Because the finding noted above was stated in a draft NTP report that was intended for peer review, the EPA should obtain the final version of the NTP report when available to verify that the NTP conclusion remains the same.

mm  
12/30/94

The four member companies of the CMA Alkanolamines Panel on whose behalf this submission is being made include:

The Dow Chemical Company  
2020 Dow Center  
Midland, MI 48674-2020  
Panel Contact: Dr. Neil Hawkins  
Telephone No. (517) 636-8237

Huntsman Corporation  
3040 Post Oak Boulevard/Room 1846  
Houston, TX 77056  
Panel Contact: Mr. Raymond Papciak  
Telephone No. (713) 235-6094

Occidental Chemical Corporation  
Technical Center, V-81  
53rd Street & Buffalo Avenue  
Niagara Falls, NY 14303  
Panel Contact: Mr. Charles Tramel  
Telephone No. (716) 278-7206

Union Carbide Corporation  
39 Old Ridgebury Road  
Room P4623  
Danbury, CT 06817-0001  
Panel Contact: Ms. Patricia Cody  
Telephone No. (203) 794-3451

If you have any questions regarding this letter, please contact Jonathon T. Busch at CMA. Mr. Busch is the Alkanolamines Panel Manager, and he can be reached by fax at 202/887-5427 and by telephone at 202/887-1189.

Sincerely,



Langley A. Spurlock Ph.D., CAE  
Vice President, CHEMSTAR

cc: Dow Chemical Corporation/Neil Hawkins  
Huntsman Corporation/Ray Papciak  
Occidental Chemical Corporation/Charles Tramel  
Union Carbide Corporation/Patricia Cody  
Alkanolamines TRTG

**NTP TECHNICAL REPORT**  
**ON THE** **Contains No GDI**  
**TOXICOLOGY AND CARCINOGENESIS**  
**STUDIES OF**  
**TRIETHANOLAMINE**  
**(CAS NO. 102-71-6)**  
**IN F344/N RATS AND B6C3F<sub>1</sub> MICE**  
**(DERMAL STUDIES)**

**Scheduled Peer Review Date: November 29, 1994**

**NOTICE**

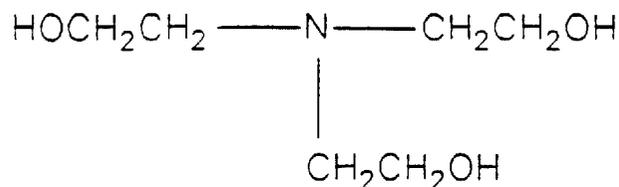
This is a DRAFT Technical Report prepared for public review and comment. Until this DRAFT has been reviewed and approved by the NTP Board of Scientific Counselors' Technical Reports Review Subcommittee in public session, the interpretations described herein do not represent the official scientific position of the National Toxicology Program. Following peer review, readers should contact NTP for the final version of this Technical Report.

**NTP TR 449**

**NIH Publication No. 94-3365**

**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES**  
**Public Health Service**  
**National Institutes of Health**

## ABSTRACT



### TRIETHANOLAMINE

CAS No. 102-71-6

Chemical Formula:  $\text{C}_6\text{H}_{15}\text{NO}_3$       Molecular Weight: 149.19

**Synonyms:** Nitriolo-2,2',2''-triethanol; 2,2',2''-nitrioltriethanol; 2,2',2''-nitrioltriethanol; TEA; triethanolamin-NG; triethanolamin; triethylolamine; tri(hydroxyethyl)amine; 2,2',2''-trihydroxytriethylamine; trihydroxytriethylamine; tris(hydroxyethyl)amine; tris(2-hydroxyethyl)amine; triethylolamine; triolamine

**Trade Names:** Daltogen; Sterolamide; Thiofaco T-35

Triethanolamine is widely used as an ingredient in emulsifiers, thickeners, wetting agents, detergents, and alkalizing agents in cosmetic products; as a chemical intermediate for anionic and nonionic surfactants and surface active agents in household cleaning agents, textiles, herbicides, pharmaceutical ointments, and other products; as a vulcanization accelerator in the manufacture of rubber; and in many other industrial applications. Triethanolamine was studied because of the widespread human exposure, the potential for exposure of industrial workers, and the potential for conversion to the carcinogen N-nitrosodiethanolamine. Male and female F344/N rats and B6C3F<sub>1</sub> mice received triethanolamine (purity 98% or greater) by dermal application for 13 weeks or 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium*, cultured Chinese hamster ovary cells, *Drosophila melanogaster*, and peripheral blood erythrocytes of mice.

### **13-WEEK DERMAL STUDY IN RATS**

Groups of 10 male and 10 female rats were topically administered 0, 125, 250, 500, or 1,000 mg triethanolamine per kilogram body weight in acetone or 2,000 mg/kg neat triethanolamine, 5 days per week, for 13 weeks. All rats survived to the end of the study. Final mean body weights and weight gains of males and females administered 2,000 mg/kg and the body weight gain of females administered 1,000 mg/kg were significantly less than those of the controls. Clinical observations included irritation, scaliness, and crustiness of the skin at the site of application for males and females. Males also had discoloration, and two males administered 2,000 mg/kg had ulceration at the site of application. Changes in clinical pathology parameters were minor and were consistent with inflammation at the site of application.

Absolute and relative right kidney weights were generally greater in males and females administered 500, 1,000, or 2,000 mg/kg than in the controls. There were no biologically significant differences in sperm morphology or vaginal cytology parameters between dosed and control rats. Microscopic lesions attributed to triethanolamine administration included acanthosis and inflammation at the site of application, renal nephropathy in females, and hypertrophy of the pituitary gland pars intermedia in males and females. These lesions occurred with dose-related increases in incidence and severity in males administered 250 mg/kg or higher and females administered 500 mg/kg or higher.

### **13-WEEK DERMAL STUDY IN MICE**

Groups of 10 male and 10 female mice were topically administered 0, 250, 500, 1,000, or 2,000 mg triethanolamine per kilogram body weight in acetone or 4,000 mg/kg neat triethanolamine, 5 days per week, for 13 weeks. All mice survived to the end of the study. The final mean body weight and weight gain of males in the 250 mg/kg group were lower than those of the controls. Clinical findings were

of animals in which these findings were observed increased with increasing dose level. At the 15-month interim evaluation, the absolute left and right kidney weights and relative right kidney weight of females administered 250 mg/kg were significantly greater than those of the controls.

### ***Pathology Findings***

The incidence of acanthosis at the site of application in males administered 125 mg/kg and the incidences of acanthosis, inflammation, and ulceration in dosed females were greater than in the controls at the 15-month interim evaluation and at the end of the 2-year study. Males in the 125 mg/kg group also had greater incidences of inflammation and ulceration than the controls, and females receiving 125 or 250 mg/kg had greater incidences of epidermal erosion than the controls at 2 years. There were no skin neoplasms at or away from the site of application that were considered related to treatment with triethanolamine.

At the end of the study, renal tubule adenomas were observed in dosed males and in one control female and one female in the 63 mg/kg group. One male in the 125 mg/kg group and one female in the 250 mg/kg group had renal tubule hyperplasia. Extended (step-section) evaluation of the kidneys of all male rats revealed renal tubule adenomas in one control male, one male in the 32 mg/kg group, two males in the 63 mg/kg group, and three males in the 125 mg/kg group (including one male from the 15-month interim evaluation). An oncocytoma was also identified in one male in the 32 mg/kg group. Hyperplasia was identified in eight additional control males and in 19 additional dosed males. The total incidences (combined standard and extended evaluations) of renal tubule adenoma in dosed male rats were slightly greater than the control incidence (control, 1/50; 32 mg/kg, 2/50; 63 mg/kg, 6/49; 125 mg/kg, 4/50). The total incidence of hyperplasia in dosed and control males was similar (9/50, 8/50, 7/49, 6/50). The severity of hyperplasia in males in the 32 and 125 mg/kg groups was greater than that in the controls.

## **2-YEAR DERMAL STUDY IN MICE**

observed only in mice in the 4,000 mg/kg groups and included scaliness, irritation, and discoloration at the site of triethanolamine application for males and females and skin erosion at this site in one male.

The absolute right kidney and liver weights of males and females administered 4,000 mg/kg were greater than those of the controls; relative right kidney weights of males administered 1,000 mg/kg or higher and females in all dosed groups were also greater than those of the controls. There were no differences in sperm morphology or vaginal cytology parameters between dosed and control mice.

Microscopic examination of the skin of dosed mice indicated acanthosis and inflammation at the site of application. Acanthosis occurred in all dosed groups and in one control female; the severity increased with increasing dose in males and females. Inflammation was observed males and females in the 4,000 mg/kg groups and in one female in the 2,000 mg/kg group.

## **2-YEAR DERMAL STUDY IN RATS**

Based on the presence of acanthosis and inflammation at the site of application at the higher doses in the 13-week study, triethanolamine dose levels selected for the 2-year dermal study in rats were 32, 63, and 125 mg/kg for males and 63, 125, and 250 mg/kg for females. Groups of 60 male and 60 female rats were topically administered triethanolamine in acetone 5 days per week for 103 weeks. Ten male and ten female rats from each group were evaluated at 15 months for organ weights and histopathology.

### ***Survival, Body Weights, Clinical Findings, and Organ Weights***

The survival rate of females in the 250 mg/kg group was slightly lower than that of the controls. The mean body weight of females administered 250 mg/kg ranged from 9% to 12% less than that of the controls between weeks 73 and 93. Male and female rats receiving triethanolamine had irritated skin at the site of application; in dosed females, the site of application also had a crusty appearance. The number

At the 15-month interim evaluation, hepatocellular carcinomas were observed in dosed and control males and hepatocellular adenomas in dosed and control males and females; however, the incidences were not dose related. Nonneoplastic lesions observed at 15 months included foci of cellular alteration in a few dosed males and females; eosinophilic foci were also observed in two control females.

At the end of the 2-year study, the incidences of single and multiple hepatocellular adenomas in males in the 2,000 mg/kg group were significantly greater than the incidences in the controls. Three males in the 2,000 mg/kg group had hepatoblastomas. The combined incidence of hepatocellular neoplasms (hepatoblastoma, adenoma, and carcinoma) in males administered 2,000 mg/kg was also significantly greater than that in the controls. In females in the 1,000 mg/kg group, the incidences of single and multiple hepatocellular adenomas and the incidence of hepatocellular adenomas and carcinomas (combined) were significantly greater than the incidences in the controls. The incidence of hepatocellular carcinoma in females administered 300 mg/kg was significantly greater than that in the controls. The incidences of eosinophilic foci in males in the 2,000 mg/kg group and females in the 300 mg/kg group were significantly greater than the incidences in the controls. Lesions consistent with a *Helicobacter hepaticus* infection (oval cell hyperplasia and karyomegaly) were noted in the livers of some dosed and control male mice, and special stains revealed the presence of the organism in a few liver samples. The presence of this infection, which is recognized to increase the incidences of liver neoplasms in infected mice, was considered to be a confounding factor in the interpretation of the relationship between triethanolamine exposure and liver neoplasms in male mice.

## GENETIC TOXICOLOGY

Triethanolamine was not mutagenic in any of the *in vitro* or *in vivo* short term tests performed by the NTP. It did not induce mutations in *Salmonella typhimurium*, and no induction of sister chromatid exchanges or chromosomal aberrations in cultured Chinese hamster ovary cells exposed to triethanolamine

Based on dose-related inflammation at the site of application in the 13-week study, triethanolamine dose levels selected for the 2-year dermal study in mice were 200, 630, and 2,000 mg/kg for males and 100, 300, and 1,000 mg/kg for females. Groups of 60 male and 60 female mice were topically administered triethanolamine in acetone 5 days per week for 103 weeks. Ten male and ten female mice from each group were evaluated at 15 months for organ weights and histopathology.

### ***Survival, Body Weights, Clinical Findings, and Organ Weights***

Survival rates of all dosed groups of males and females were similar to those of the controls. The mean body weight of males administered 2,000 mg/kg ranged from 8% to 10% less than that of the controls from week 69 through the end of the study. Clinical findings included irritation and discoloration of the skin at the site of application for most males in the 2,000 mg/kg group and a few females in the 1,000 mg/kg group; males administered 200 or 630 mg/kg also had skin irritation. In the 2,000 mg/kg group, one male had thin skin and one male had crusty skin at the site of application. At the 15-month interim evaluation, the absolute and relative right kidney weights of male mice that received 630 or 2,000 mg/kg and the absolute and relative left kidney weights of males that received 2,000 mg/kg were significantly greater than those of the controls.

### ***Pathology Findings***

Acanthosis and inflammation of the skin were observed at the site of application in male and female mice at the 15-month interim evaluation and at the end of the 2-year study. In males, the incidences of both lesions were significantly greater than those in the controls at both time points; however, the severity of acanthosis and inflammation did not increase with dose. At the end of the study, the incidence of inflammation in females in the 1,000 mg/kg group was significantly greater than that in the controls. One control male and two males in each of the 630 and 2,000 mg/kg groups had ulcers at the site of application.

was noted. These *in vitro* tests were conducted with and without S9 metabolic activation.

Triethanolamine did not induce sex-linked recessive lethal mutations in germ cells of adult male *Drosophila melanogaster* exposed by feeding or injection. No increase in the frequency of micronucleated erythrocytes was observed in peripheral blood samples of male and female mice that received dermal applications of triethanolamine for 13 weeks.

## CONCLUSIONS

Under the conditions of these dermal studies, there was *equivocal evidence of carcinogenic activity\** of triethanolamine in male F344/N rats based on a marginal increase in renal tubule cell adenomas. There was *no evidence of carcinogenic activity* in female F344/N rats receiving 63, 125, or 250 mg triethanolamine per kilogram body weight. There was *equivocal evidence of carcinogenic activity* in male B6C3F<sub>1</sub> mice based on a marginal increase in hepatocellular adenomas and hepatoblastomas. The presence of an infection of male mice with *Helicobacter hepaticus* complicated interpretation of the relationship of triethanolamine with liver neoplasms in these animals. There was *some evidence of carcinogenic activity* of triethanolamine in female B6C3F<sub>1</sub> mice based on increased incidences of hepatocellular neoplasms.

Dosed rats and mice had varying degrees of inflammation and acanthosis, and exposed rats had ulceration, at the site of application.

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\* Explanation of Levels of Evidence of Carcinogenic Activity is on page 14.

## Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of Triethanolamine

	Male F344/N Rats	Female F344/N Rats	Male B6C3F <sub>1</sub> Mice	Female B6C3F <sub>1</sub> Mice
Doses	32, 63, or 125 mg/kg	63, 125, or 250 mg/kg	200, 630, or 2,000 mg/kg	100, 300, or 1,000 mg/kg
Body weights	Dosed groups similar to controls	250 mg/kg group slightly less than controls	2,000 mg/kg group slightly less than controls	Dosed groups similar to controls
2-Year survival rates	21/50, 11/50, 18/49, 19/50	25/50, 29/50, 25/50, 18/50	46/50, 40/50, 39/50, 41/50	39/50, 40/50, 38/50, 37/50
Nonneoplastic effects	<u>Skin</u> (site of application): acanthosis (1/50, 1/50, 1/49, 9/50); inflammation (0/50, 2/50, 0/49, 8/50); ulcer (0/50, 0/50, 0/49, 5/50) <u>Kidney</u> (standard and extended evaluations): severity of hyperplasia (1.7, 2.6, 1.5, 2.5)	<u>Skin</u> (site of application): acanthosis (2/50, 10/50, 30/50, 32/50); epidermal erosion (1/50, 6/50, 16/50, 14/50); inflammation (2/50, 10/50, 30/50, 32/50); ulcer (2/50, 7/50, 22/50, 27/50)	<u>Skin</u> (site of application): acanthosis (2/50, 1/50, 6/50, 11/50); hair follicle, sebaceous gland atrophy (0/50, 0/50, 1/50, 15/50); inflammation (2/50, 0/50, 7/50, 11/50) <u>Liver</u> : eosinophilic foci (10/50, 17/50, 11/50, 23/50)	<u>Skin</u> (site of application): acanthosis (0/50, 2/50, 1/50, 3/50); inflammation (0/50, 2/50, 2/50, 5/50) <u>Liver</u> : eosinophilic foci (9/50, 10/50, 18/50, 16/50)
Neoplastic effects	None	None	None	<u>Liver</u> : hepatocellular adenoma (22/50, 22/50, 24/50, 40/50); hepatocellular carcinoma (1/50, 4/50, 7/50, 5/50); hepatocellular adenoma or carcinoma (23/50, 26/50, 28/50, 41/50)
Uncertain findings	<u>Kidney, renal tubule</u> (standard evaluation): adenoma (0/50, 1/50, 4/49, 2/50); (standard and extended evaluation): adenoma (1/50, 2/50, 6/49, 4/50)	None	<u>Liver</u> : hepatocellular adenoma (27/50, 27/50, 29/50, 37/50); hepatoblastoma (0/50, 0/50, 0/50, 3/50); hepatocellular adenoma, hepatocellular carcinoma, or hepatoblastoma (31/50, 34/50, 33/50, 42/50)	None
Level of evidence of carcinogenic activity	Equivocal evidence	No evidence	Equivocal evidence	Some evidence

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**Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of Triethanolamine (continued)**

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**Genetic toxicology**

<i>Salmonella typhimurium</i> gene mutations:	Negative in strains TA98, TA100, TA1535, and TA1537 with and without S9
Sister chromatid exchanges	
Cultured Chinese hamster ovary cells <i>in vitro</i> :	Negative with and without S9
Chromosomal aberrations	
Cultured Chinese hamster ovary cells <i>in vitro</i> :	Negative with and without S9
Sex-linked recessive lethal mutations	
<i>Drosophila melanogaster</i> :	Negative when administered in feed or by injection
Micronucleated erythrocytes	
Mouse peripheral blood <i>in vivo</i> :	Negative

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

Langley A. Spurlock, Ph.D., CAE  
Vice President, CHEMSTAR  
Chemical Manufacturers Association  
2501 M Street, N.W.  
Washington, D.C. 20037

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

FEB 09 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)  
Attn: TSCA Section 8(e) Coordinator  
Office of Pollution Prevention and Toxics  
U.S. Environmental Protection Agency  
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan  
Risk Analysis Branch

Enclosure



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13285 A

**EPA INFORMATION REQUESTS**

Document ID: 8EHQ-1294-13285

**EPA requests:**

1.  No additional information at this time.
2.  Additional information or clarification on
  
3.  A full copy of the final report (including the actual experimental protocol, applicable results of gross or histopathologic examinations, data, results of any statistical analyses, etc.) from each study mentioned in your submission.
4.  A description of all voluntary actions taken by your company in response to the findings indicated in your submission.
5.  A complete copy of the current and/or revised Material Safety Data Sheets and labels for the following chemical(s) listed in your submission:  

6.

Please direct questions regarding these requests to Mr. Terry O'Bryan (202-260-3483) or Mr. John Myers (202-260-3543) of the OPPT Risk Analysis Branch.

1-1

### Triage of 8(e) Submissions

Date sent to triage: MAR 08 1995

NON-CAP

CAP

Submission number: 13285 A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO

AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX

SBTOX

SEN

w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

~~STOX~~

CTOX

EPI

RTOX

~~GTOX~~

STOX/ONCO

~~CTOX/ONCO~~

IMMUNO

CYTO

NEUR

Other (FATE, EXPO, MET, etc.): \_\_\_\_\_

Notes:

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Contractor reviewer: LPS (by PAM) Date: 1/25/95



CECATS DATA: BEHO 1994-13285 SEQ. A

TYPE: INT. SUPP FLWP  
 SUBMITTER NAME: Chemical Manufacturers Association

INFORMATION REQUESTED: FLWP DATE: \_\_\_\_\_  
 0501 NO INFO REQUESTED  
 0502 INFO REQUESTED (TECH)  
 0503 INFO REQUESTED (VOL. ACTIONS)  
 0504 INFO REQUESTED (REPORTING RATIONALE)  
 DISPOSITION:  
 0505 REFER TO CHEMICAL SCREENING  
 0578 CAP NOTICE

OPTIONAL ACTIONS:  
 0601 AND ATTN: RI PR (T) D  
 0602 STUDIES PLANNED (T) M W A V  
 0603 NOTIFICATION (I) W W W R R O T T I E M  
 0604 LABORATORY (T) M A N I S  
 0605 PROFESSIONAL (I) M I N G (T) M A N I S  
 0606 APP USE DISCONTINUED  
 0607 PRODUCTION DISCONTINUED  
 0608 CONFIDENTIAL

SUB. DATE: 12/15/94 12/15/94 CSRAD DATE: 12/30/94

CHEMICAL NAME: \_\_\_\_\_  
 CASE: 102-71-6

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPICLIN	01 02 04	0241 IMBALINO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 IMBALINO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEMIST'S PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 BOVAQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCUREL/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 BMBR ENCI OF ENV CONTAM	01 02 04	0247 DNA DAMAGE/PAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQUEST DELAY	01 02 04	0248 PRODUSE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PRODCOMP/CHEM ID	01 02 04	0251 MSDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	0226 CONFIDENTIAL	01 02 04		
0212 ACUTE TOX. (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0229 METAB/PHARMACOD (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0249 METAB/PHARMACOD (HUMAN)	01 02 04		

TRADE DATA: NON-CELL INVENTORY ONGOING REVIEW: YES (DROPPED/REPER) SPECIES: MOS TOXICOLOGICAL CONCERN: LOW USE: \_\_\_\_\_ PRODUCTION: \_\_\_\_\_

CAS SR: NO NO (CONTINUE) NO (CONTINUE) NO (CONTINUE) NO (CONTINUE)

IN TERMIN: NO NO NO NO

**Stox**  
 Non - COP Rats (F-344/N) and mice (B6C3F1) were typically administered 0, 125, 250, 500 or 1000 mg/kg, 0, 250, 500 or 1000 or 2000 mg/kg and neat 2000, and 4000 mg/kg respectively. The principal effect observed was an increase in the incidence of bladder cancer in both species. Renal neoplasms were also observed and hyperplasia of the prostatic acini was observed in males administered 250 mg/kg or higher. Treatment included acamkinin or in flomandim in both species. Renal neoplasms were also observed in incidence and severity in males administered 250 mg/kg or higher.

CECATS/STRIDGE TRACKING DBASE ENTRY FORM

CECATS DATA: SEHO: 1294-13285 SEQ. A

Submission # 1294-13285

TYPE: INT SUPP FLWP  
 SUBMITTER NAME: Chemical Manufacturers Association

INFORMATION REQUESTED: FLWP DATE:  
 0501 NO INFO REQUESTED  
 0502 INFO REQUESTED (TECH)  
 0503 INFO REQUESTED (VOL ACTIONS)  
 0504 INFO REQUESTED (REPORTING RATIONALE)  
 DISPOSITION:  
 0505 REFER TO CHEMICAL SCREENING  
 0578 CAP NOTICE

SUB. DATE: 12/15/94 ON DATE: 12/15/94 CIRAD DATE: 12/30/94

CHEMICAL NAME:

CASE # 102-71-6

NONJUDICIAL ACTIONS:

0401 ACTION REFINED  
 0402 STUDY'S PLANNING  
 0403 INTERCATION IN WORK  
 0404 LABELS (TAMPS)  
 0405 PROCESSING, INC. (TAMPS)  
 0406 APP USE DISCONTINUED  
 0407 PRODUCTION DISCONTINUED  
 0408 CONFIDENTIAL

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPICLN	01 02 04	0241 BAKING (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 BAKING (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEMISTS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 BOVAQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCURENCE/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 BIER ENCI OF ENV CONTAM	01 02 04	0247 DNA DAMAGE/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQUEST DELAY	01 02 04	0248 PRODUSE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PRODCOMP/CHEM ID	01 02 04	0251 MSDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	0299 OTHER	01 02 04
0211 ACUTE TOX. (ANIMAL)	01 02 04	0226 CONFIDENTIAL	01 02 04		
0212 CHR. TOX. (HUMAN)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0229 METAB/PHARMACD (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0230 METAB/PHARMACD (HUMAN)	01 02 04		

GT0X

TRIGGER DATA: NON-CELL INVENTORY YES (YES) ONGOING REVIEW YES (DROPPED/REFER) NO (CONTINUE) NO (CONTINUE)  
 CAS SR NO (CONTINUE) NO (CONTINUE)  
 SPECIES: MUS LOW TOXICOL/OCUL/RESPIR  
RAT MED  
 USE: PRODUCTION:  
 animal fibers, hickories, walking agents, detergents, intermediate etc...  
 IN PLANNING REPT-R HIGH

UNCLASSIFIED Non-Cap

5)

8EHQ-1294-13285: Rank - low.

Chemical: triethanolamine (CAS# 102-71-6).

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), NIH Publication No. 94-3365: Negative for gene mutations in the Salmonella typhimurium/mammalian microsomal (Ames) assay in strains TA98, TA100, TA1535, TA1537 and TA1538 both without and with metabolic activation.

Negative for gene mutations in the Drosophila melanogaster sex-linked recessive lethal (SRL) assay administered in feed or by injection.

Negative for chromosome mutations (aberrations) in Chinese hamster ovary (CHO) cells in vitro both without and with activation.

Negative for chromosome mutations (micronuclei) in mouse peripheral blood in vivo.

Does not Induce DNA effects in the form of sister chromatid exchanges (SCEs) in CHO cells in vitro without but not with activation.

**NOTE**

Although the mutagenicity tests were negative, this 8e was submitted because of signs of carcinogenicity. This toxicity was not addressed by this reviewer.

CECATS DATA: Submission # BEHQ-1294-13285 SEQ. A

TYPE: INT SUPP FLWP

SUBMITTER NAME: Chemical Manufacturers Association

SUB. DATE: 12/15/94 ORG DATE: 12/15/94 CSRAD DATE: 12/30/94

CHEMICAL NAME: CASE

102-71-6

INFORMATION REQUESTED: FLWP DATE: \_\_\_\_\_

- 0301 NO INFO REQUESTED
- 0302 INFO REQUESTED (TECH)
- 0303 INFO REQUESTED (VOL ACTIONS)
- 0304 INFO REQUESTED (REPORTING RATIONALE)
- DISPOSITION:
- 0305 REFER TO CHEMICAL SCREENING
- 0306 CAP NOTICE

VOLUNTARY ACTIONS:

- 0401 (M) ACTION REFINITID
- 0402 STUDIES PLANNED/IN PROGRESS
- 0403 INTERACTION IN WORKING RELATIONSHIPS
- 0404 LABEL/ASDS (TANKS) S
- 0405 PROCESS/LANDFILL INC. (TANKS) S
- 0406 A/P/AUSE DISCONTINUED
- 0407 PRODUCTION DISCONTINUED
- 0408 CONFIDENTIAL

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPICLIN	01 02 04	0241 BARBINO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 BARBINO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEM/PHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 BCOAQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCUREL/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04	0247 DNA DAM/REPAR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REPORT DELAY	01 02 04	0248 PRODUSE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PRODCON/SCHEM ID	01 02 04	0251 NASDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	0226 CONFIDENTIAL	01 02 04		
0212 ACUTE TOX. (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0229 METAB/PHARMACD (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0230 METAB/PHARMACD (HUMAN)	01 02 04		

TRIALS DATA: NON-CELL INVENTORY Ongoing Review: YES (DROP/REFER) Species: MOS Toxicological Concern: Onco Production: USE: animal fibers, thickners, washing agents, detergents, intermediate etc...

CAS SR: NO IN PHASE: REF:R

Species: RAT Toxicological Concern: LOW MED HIGH

UNRECORDED Non-Cop

-CPSS- 1002951130

0 0 0 0 0 0 0 0 0 0 0  
> <ID NUMBER>  
8(e)-13285A

> <TOX CONCERN>  
L/M

> <COMMENT>  
A TWO YEAR ONCOGENICITY STUDY IN RATS IS LOW CONCERN. 4 GROUPS (60/SEX) OF RATS WERE TOPICALLY ADMINISTERED 32 (FEMALES ONLY), 63, 125, AND 250 (MALES ONLY) MG/KG FOR 5 DAYS/WEEK FOR 103 WEEKS. NO DOSE-RELATED ADVERSE EFFECTS WERE NOTED ON THE INCIDENCE OF ANIMALS WITH TISSUE MASSES. A TWO YEAR ONCOGENICITY STUDY IN MICE IS MEDIUM CONCERN. 3 GROUPS OF 60 FEMALE MICE WERE TOPICALLY ADMINISTERED 100, 300, OR 1000 MG/KG FOR 5 DAYS/WEEK FOR 103 WEEKS. 3 GROUPS OF MALE MICE WERE TOPICALLY ADMINISTERED 20, 630, AND 2000 MG/KG FOR 5 DAYS/WEEK FOR 103 WEEKS. 1 GROUP SERVED AS CONTROLS. AN INCREASE IN THE INCIDENCE OF HEPATOCELLULAR CARCINOMAS WAS NOTED IN FEMALES MICE AND AN INCREASE IN THE INCIDENCE OF HEPATOCELLULAR NEOPLASMS (HEPATOBLASTOMA, ADENOMA, AND CARCINOMA) WAS NOTED IN MALE MICE.

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