

TSCA NON-CONFIDENTIAL BUSINESS INFORMATION

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Attention: TSCA 8(e) Coordinator

Subject: Notice in Accordance with TSCA Section 8(e) – Results of OECD 422 Combined Repeated-Dose Toxicity Study with the Reproduction/ Developmental Toxicity Screening Test in Wistar rats with Methylaminoethanol (CAS No. 109-83-1)

Dear TSCA 8(e) Coordinator:

The American Chemistry Council's (ACC) Amines Panel¹ is submitting on behalf of its Panel member companies further results of a combined repeated-dose toxicity study with the reproduction/developmental toxicity screening test in Wistar rats [CrI:WI(HAN)] with Methylaminoethanol (CAS No. 109-83-1). The aim of this study was to obtain information on the possible effects of Methylaminoethanol on the integrity and performance of the male and female reproductive systems including gonadal function, mating behavior, conception, gestation and parturition. The data provided is being submitted in accordance with the U.S. Environmental Protection Agency's interpretation of Section 8(e) of the Toxic Substances Control Act (TSCA).

The study was carried out in accordance with the requirements of the following guidelines:

- OECD Guidelines for Testing of Chemicals; No. 422, Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (22 March 1996)
- EPA, Health Effects Test Guidelines; OPPTS 870.3650: Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (July 2000)

The dose levels were 0; 50, 150 and 450 mg/kg body weight/day (gavage). All animals were observed daily for any clinical signs during the administration period of 6 (males) and 9 weeks (females).

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¹ Panel members include: Arkema, BASF Corporation, Celanese, CEPESA QUIMICA, The Dow Chemical Company, DuPont, MGC, MRC, Momentive Performance Materials and Taminco.

After a 14-day pre-mating period, the male and female parental animals were mated overnight in a 1:1 ratio until evidence of copulation (vaginal smear). The day on which sperm was detected was designated as gestation day (GD) 0 and the following day as GD 1. The parental females were allowed to deliver and rear their pups until postnatal day (PND) 4. On PND 4, all pups were sacrificed and examined.

Toward the end of the administration period (males: study week 6; females study week 9) a functional observation battery (FOB) was performed and motor activity was recorded for parental animals. In addition, blood and urine samples were taken and examined for 5 male and 5 female parental animals from all test groups.

All surviving parental animals were sacrificed and examined after the end of the administration period. The organs were fixed and histologically processed. A histopathological examination by light microscopy was performed for the animals of all test groups.

The following is a summary of the most relevant results:

Test group 3 (450 mg/kg body weight/day):

Males (x out of 10 animals or, if not noted, test group means):

Target: gonads

- Testes: tubular degeneration (10)
- Epididymides: oligospermia (9)

Target: kidney

- Kidneys: tubular degeneration (10)
- Decreased urea clearance (group mean vs. control)
- Blood in urine (group mean vs. control)

Target: liver

- Liver: central fatty change (5)
- Liver: peripheral fatty change (2)
- Increased albumin level (group mean vs. control)

Target: blood

- Spleen: extramedullary hematopoiesis (8)
- Haemolytic anemia (group mean vs. control)

Target: stomach

- Forestomach: erosiodulceration (3)
- Glandular stomach: erosion/ulceration (3)

Dams (x out of 10 animals or, if not noted, test group means):

Target: gonads

- Ovaries: vacuolization of sex cord stroma (10)

Target: kidney

- Kidneys: tubular degeneration (9)
- Decreased urea clearance (group mean vs. control)
- Blood in urine (group mean vs. control)

Target: liver

- Liver: central hypertrophy (9)
- Increased albumin level (group mean vs. control)

Target: blood

- Spleen: extramedullar hematopoieses (8)
- Haemolytic anemia (group mean vs. control)

Target: stomach

- Forestomach: erosion/ulceration (1)

Test group 2 (150 mg/kg body weight/day):

Males (x out of 10 animals or, if not noted, test group means):

Target: kidney

- Kidneys: tubular degeneration (10)
- Decreased urea clearance (group mean vs. control)
- Blood in urine (group mean vs. control)

Target: liver

- Liver: peripheral fatty change (8)

Target: blood

- Haemolytic anemia (group mean vs. control)

Dams (x out of 10 animals or, if not noted, test group means):

Target: gonads

- Ovaries: vacuolization of sex cord stroma (4)

Target: kidney

- Kidneys: tubular degeneration (9)
- Blood in urine (group mean vs. control)

Target: blood

- Spleen: extramedullar hematopoieses (3)
- Haemolytic anemia (group mean vs. control)

Test group 1 (50 mg/kg body weight/day):

Males (x out of 10 animals or, if not noted, test group means):

- Kidneys: tubular degeneration (6)

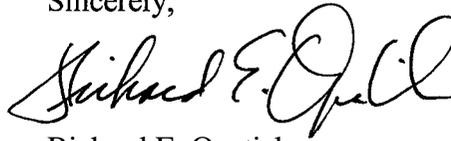
The kidneys of males of all treatment groups as well as in females of test groups 2 (150 mg/kg bw/d) and 3 (450 mg/kg bw/d) revealed a minimal to severe tubular degeneration (see next table) which was regarded as treatment-related. The severity increased dose-dependently:

Test group (mg/kg body weight/day)	Male animals				Female animals			
	0	1 (50)	2 (150)	3 (450)	0	1 (50)	2 (150)	3 (450)
Number of animals	10	10	10	10	10	10	10	10
Degeneration, tubular		6	10	10			9	9
minimal		3	1	1			9	7
slight		3	4	1				2
moderate			5	6				
severe				2				

This submission is a follow-up to the Panel's June 17, 2009 and February 13, 2009 (8EHQ-09-17418) TSCA 8 (e) notifications summarizing the reproductive effects noted and the observations related to parental toxicity. The Panel has not determined whether a substantial **risk** of injury to health or the environment is presented by these findings. However, the Panel recognizes that EPA could consider this information to constitute a substantial **risk**. Therefore, in an abundance of caution, the Panel is submitting this information to EPA under 8(e).

If you have any questions, please contact me, the Amines Panel Director at 703-741-5623 or richard_opatick@americanchemistry.com.

Sincerely,

A handwritten signature in black ink, appearing to read "Richard E. Opatick". The signature is fluid and cursive, with the first name being the most prominent.

Richard E. Opatick
Director, Amines Panel
American Chemistry Council