

SOLUTIA

Solutions for a better life.

MR 305682

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June 29, 2007

Via Overnight Courier (Fedex) (Signature Requested)

Document Processing Center (TS-790)
U.S. Environmental Protection Agency
Office of Toxic Substances
401 M Street S.W.
Washington DC 20460

Attention: TSCA 8(e) Coordinator

Re: THMBD HPV Testing

Dear Sir or Madam:

In accordance with Section 8(e) of the Toxic Substance Control Act, Solutia Inc. ("Solutia") hereby submits preliminary, unaudited data from a reproductive and developmental screening test conducted in accord with the OECD 421 guideline indicating effects on reproduction at the high dose level. The test material involved is Tetrabutylhexamethylenediamine (TBHMD), CAS no. 27090-63-7, which is being tested as part of the U.S. EPA's High Production Volume ("HPV") Chemicals Program. The test was conducted as proposed in our December 30, 2004 HPV submission. Solutia received this information on June 4, 2007.

In this study, groups of Sprague-Dawley rats of each sex received test material by gavage at 0, 2, 5 or 15 mg/kg-day for 14 days prior to mating. High-dose animals of each sex showed reduced weight gains and only 8 of 10 dams were sperm positive during the mating period and only three females gave birth to live young. These three litters, however, were of normal size and weight and without obvious malformations. The remaining high dose females did not show any evidence of implantations at necropsy. There were no treatment-related effects on mating or conception rates for animals of either sex treated with 5 or 2 mg/kg-day.

For the high-dose group, the mating index was 80% and the pregnancy index was 38%. These indices were 100% in the other two dose groups (5 mg/kg-day and 2 mg/kg-day) and the vehicle control group.



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Parental toxicity was clinically manifested for the high-dose females as reduction in weight gain during the pre-mating exposure period and reduced feed consumption during gestation and lactation. High-dose males' toxicity was clinically manifested as reduced feed consumption during the second week of the pre-mating period and a reduction in body weight over the entire experimental phase of the study.

No information is available yet that allows assignment of the apparent impaired reproduction to rats of a specific sex.

Tetrabutylhexamethylenediamine is manufactured in one reaction system at the Solutia Decatur Plant located at 1050 Chemstrand Ave., Decatur, AL 35601.

If the agency would like additional information please contact me via one of the following methods:

E-Mail – tlwill@solutia.com
Office Phone – 850-968-8682
Mobile Phone – 850-516-5027.

Sincerely,



Travis L. Willard
Product Stewardship Lead

Attachments:
Preliminary data and summary from Safepharm Labs

TBHMD:

**ORAL (GAVAGE) REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN THE
RAT (OECD 421)
SUMMARY**

Introduction. The study was designed to investigate the systemic toxicity and potential adverse effects on reproduction (including offspring development) of the test material and complies with the recommendations of the OECD Guidelines for Testing of Chemicals No. 421 "Reproduction/Developmental Toxicity Screening Test" (adopted 27 July 1995).

Methods. The test material was administered by gavage to three groups each of ten male and ten female Sprague-Dawley Crl:CD[®] (SD) IGS BR strain rats, at dose levels of 2, 5 and 15 mg/kg/day. A control group of ten males and ten females was dosed with vehicle alone (Corn oil).

Clinical signs, bodyweight gain and food consumptions were monitored during the study.

Pairing of animals within each dose group was undertaken on a one male: one female basis on Day 15 of the study, to produce litters. During the lactation phase, daily clinical observations were undertaken on all live offspring, together with litter size, offspring weights and assessment of developmental landmarks.

Females and their offspring were terminated on Day 5 *post partum*.

Results.

Mortality: There were no unscheduled deaths.

Clinical Observations. No clinical signs of toxicity were detected.

Bodyweight. Males treated with 15 mg/kg/day showed a reduction in bodyweight gain throughout the treatment period. Females from this treatment also showed a reduction in bodyweight gain throughout maturation, gestation and lactation. No such effects were detected in animals of either sex treated with 5 or 2 mg/kg/day.

Food consumptions. Males treated with 15 mg/kg/day showed a reduction in food consumption during Week 2 of treatment whilst females from this treatment group showed a reduction in food consumption during Week 2 of maturation and throughout gestation and lactation. No such effects were detected in animals of either sex treated with 5 or 2 mg/kg/day.

Reproductive Performance

Following the successful mating of all control, low and intermediate animals only eight high dose females mated and only three females gave birth to live young. The remaining high dose females did not show any evidence of implantations at necropsy.

There were no treatment-related effects on mating or conception rates for animals of either sex treated with 5 or 2 mg/kg/day. The distribution of pre-coital intervals for animals treated with 5 or 2 mg/kg/day was comparable to controls.

Gestation. Of the females that were pregnant, there were no differences in gestation lengths. The distribution for treated females was comparable to controls.

Litter Size and Viability. Of the litters born, litter size at birth and subsequently on Day 1 and 4 *post partum* were comparable to controls.

Offspring Growth and Development. Offspring weights were reduced from litters treated with 15 mg/kg/day on Days 1 and 4 *post partum*. Litter weights in these animals were also subsequently reduced on Days 1 and 4 *post partum*.

This summary has only outlined preliminary findings and the significance of these finding can not be confirmed until further evaluation of the data has been performed and preliminary histopathology data is available.

Prepared by:

J S Dunster BSc (Hons)
Study Director

Date: 01 June 2007

This summary has been subject to some checking procedures during preparation but it has not been inspected by the Safepharm Quality Assurance Unit. We reserve the right to make any necessary amendment during production of the final report.

Table 1 **Group Mean Bodyweights and Standard Deviations (SD) – Males**

Dose Level (mg/kg/day)	Number of Animals	Bodyweight (g) at Day							
			1	8	15	22	29	36	43
0 (Control)	10	mean	341	374	402	423	455	477	487
		sd	28	38	44	47	46	47	43
2	10	mean	344	378	403	428	454	480	496
		sd	21	25	27	29	30	32	36
5	10	mean	343	376	403	434	464	491	510
		sd	31	42	51	53	57	61	60
15	10	mean	341	362	369	380	402	417	428
		sd	17	20	29	32	33	37	37

Table 2 Group Mean Bodyweights and Standard Deviations (SD) – Females

Dose Level (mg/kg/day)	Number of Animals		Bodyweight (g) at Day								
			Maturation			Gestation				Lactation	
			0	7	15	0	7	14	20	1	4
0 (Control)	10	mean	229	241	258	261	303	339	424	326	346
		sd	15	16	21	20	26	30	34	36	28
2	10	mean	229	243	256	259	300	341	427	316	340
		sd	11	13	16	14	15	19	24	21	18
5	10	mean	230	237	250	256	289	325	410	310	321
		sd	12	15	13	16	14	20	23	26	32
15	10/3■	mean	234	240	239	260	265	278	362	267	276
		sd	15	16	18	13	13	32	28	23	3

■ = n=3 during gestation and lactation

Table 3 **Group Mean Bodyweight Gains and Standard Deviations (SD) – Males**

Dose Level (mg/kg/day)	Number of Animals		Bodyweight gain (g) during Week					
			1	2	3	4	5	6
0 (Control)	10	mean	33	28	21	32	22	10
		sd	12	7	9	4	7	9
2	10	mean	34	25	25	26	26	17
		sd	7	10	6	11	10	8
5	10	mean	33	26	32	30	27	19
		sd	14	11	8	10	6	8
15	10	mean	22	6	12	22	14	12
		sd	7	16	17	8	11	6

**Table 4 Group Mean Bodyweight Gains and Standard Deviations (SD) –
Females**

Dose Level (mg/kg/day)	Number of Animals		Bodyweight gain (g) during:					
			Maturation		Gestation			Lactation
			Week 1	Week 2	Days 0-7	Days 7-14	Days 14-20	Days 1-4
0 (Control)	10	mean	11	17	42	36	85	20
		sd	4	10	14	7	14	11
2	10	mean	15	12	41	41	86	25
		sd	9	9	6	4	8	9
5	10	mean	8	13	33	37	85	11
		sd	7	10	11	8	14	12
15	10/3■	mean	5	-1	5	14	84	9
		sd	6	6	2	33	29	21

■ = n=3 during gestation and lactation

Table 5 Group Mean Food Consumption – Males

Dose Level (mg/kg/day)	Number of Animals	Mean Food Consumption (g/rat/day) during Week					
		1	2	3#	4	5	6
0 (Control)	10	27	27		27	26	25
2	10	27 (0)	25 (-7)		26 (-4)	26 (0)	25 (0)
5	10	26 (-4)	24 (-11)		26 (-4)	27 (+4)	26 (+4)
15	10	25 (-7)	22 (-19)		#	24 (-8)	23 (-8)

= food consumption not recorded due to animals being in mating cages
() = % change compared to controls

Table 6 Group Mean Food Consumption – Females

Dose Level (mg/kg/day)	Number of Animals	Mean Food Consumption (g/rat/day) during:					
		Maturation		Gestation			Lactation
		Week 1	Week 2	Days 0-7	Days 7-14	Days 14-21	Days 1-4
0 (Control)	10	18	19	22	23	25	39
2	10	18	18	21	23	23	38
		(0)	(-5)	(-5)	(0)	(-8)	(-3)
5	10	17	17	19	21	22	34
		(-6)	(-11)	(-14)	(-9)	(-12)	(-13)
15	10/3■	17	16	13	13	19	25
		(-6)	(-16)	(-41)	(-43)	(-24)	(-36)

■ n = 3 during gestation and lactation

() = % change compared to controls

Table 7 Mating Performance and Fertility – Group Values

Dose Level (mg/kg/day)	Number of Males Paired	Number of Females			Pre-Coital Interval (Days)				Mating Index (%)	Pregnancy Index (%)
		Paired	Mated	Pregnant	1	2	3	4		
0 (Control)	10	10	10	10	5	1	2	2	100	100
2	10	10	10	10	4	1	2	3	100	100
5	10	10	10	10	4	1	3	2	100	100
15	10	10	8	3	1	1	3	3	80	38

Dose Level (mg/kg/day)	Gestation Lengths (Days)			Females with Live Offspring	Parturition Index (%)
	22	22½	23		
0 (Control)	3	2	5	10	100
2	5	2	3	10	100
5	7	1	2	10	100
15	0	0	3	3	100

Table 8 Litter and bodyweight Data – Group Mean litter values

Dose Group (mg/kg/day)		Number of Corpora Lutea	Number of Implantation Sites	Total number of Offspring Born	Number of Live Offspring		Litter Weight (g)		Offspring Weight (g)						Mean Offspring bodyweight change (g)	
					Day 1	Day 4	Day 1	Day 4	Day 1		Day 4		Days 1 - 4			
							Male	Female	Male	Female	Male	Females				
0 (Control)	Mean	18.3	15.5	15.0	14.9	14.8	103.0	147.7	7.1	6.9	10.4	10.0	3.3	3.1		
	SD	2.8	2.0	3.4	3.3	3.3	20.1	25.9	0.7	0.8	1.2	1.5	0.7	0.8		
	N	8	8	10	10	10	10	10	10	10	10	10	10	10		
2	Mean	17.6	16.3	15.9	15.7	15.6	105.7	149.3	6.9	6.5	9.8	9.2	2.9	2.7		
	SD	1.4	1.5	1.6	1.6	1.7	10.8	17.6	0.5	0.5	0.8	0.7	0.3	0.3		
	N	7	7	10	10	10	10	10	10	10	10	10	10	10		
5	Mean	18.0	16.5	14.8	14.6	14.5	97.1	141.6	6.9	6.6	10.0	9.7	3.2	3.2		
	SD	1.8	1.5	2.0	2.0	1.9	10.6	14.8	0.6	0.6	1.1	1.2	0.6	0.7		
	N	8	8	10	10	10	10	10	10	10	10	10	10	10		
15	Mean	17.0	14.0	14.3	14.0	14.0	85.9	113.1	6.4	5.9	8.5	7.8	2.0	1.4		
	SD	0.0	2.8	2.1	1.7	1.7	9.8	12.2	0.3	0.1	0.3	0.7	0.6	1.1		
	N	2	2	3	3	3	3	3	3	3	3	3	3	3		

N = number of litters

Table 9 Implantation losses and survival indices – Group Mean litter values

Dose Group (mg/kg/day)		Pre- Implantation Loss (%)	Post -Implantation Loss (%)	Live Birth Index	Viability Index
0 (Control)	Mean	14.6	8.5	99.4	99.4
	SD	8.0	12.6	1.9	1.9
	N	8	8	10	10
2	Mean	7.3	6.0	98.8	99.3
	SD	5.4	4.8	2.6	2.1
	N	7	7	10	10
5	Mean	8.0	8.4	98.8	99.4
	SD	7.1	10.7	4.0	1.9
	N	8	8	10	10
15	Mean	17.6	3.1	97.9	100.0
	SD	16.6	4.4	3.6	0.0
	N	2	2	3	3

N = number of litters

Table 10 Sex ratio – Group Mean litter values

Dose Group (mg/kg/day)	Number of litters	Sex Ratio (Post Partum) Day:											
		At birth				1				4			
		Male	Female	% Male		Male	Female	% Male		Male	Female	% Male	
0 (Control)	Mean	7.4	7.6	49.6		7.4	7.5	49.8		7.3	7.5	49.7	
	SD	2.8	3.0	15.0		2.8	2.8	14.8		2.6	2.8	14.5	
2	Mean	9.3	6.6	58.7		9.1	6.6	58.1		9.0	6.6	57.7	
	SD	1.9	2.1	12.6		2.0	2.1	13.0		2.2	2.1	13.4	
5	Mean	6.4	8.4	42.7		6.4	8.2	43.1		6.4	8.1	43.4	
	SD	2.0	1.7	10.7		2.0	1.3	10.1		2.0	1.2	10.1	
15	Mean	6.3	8.0	44.0		6.3	7.7	45.0		6.3	7.7	45.0	
	SD	1.2	1.0	2.5		1.2	0.6	2.9		1.2	0.6	2.9	