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COMMENTS:

DOES NOT CONTAIN CBI

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Vice President

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3M

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August 31, 2010

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Document Processing Center
EPA East – Room 6428 Attn: FYI
Office of Pollution Prevention and Toxics, US EPA
1200 Pennsylvania Avenue NW
Washington DC 20460-0001

8EHQ-10-18095

RE: TSCA 8(e) Substantial Risk Notice on: CASRN 112-57-2; N- (2-aminoethyl)-N'-{2- (2-aminoethyl)amino}ethyl}-1,2-ethanediamine; tetraethylenepentamine (TEPA)

To Whom It May Concern:

3M recently generated data in an acute systemic injection test on tetraethylenepentamine (TEPA) that did not meet the requirements of the ISO-10993-11 guidelines for the Systemic Injection Test. The results of this study demonstrate a significant difference from previously published toxicity values using the same exposure route. All TEPA animal groups that received intravenous (IV) injections of the test article solutions contained mice that died or exhibited convulsions followed by death immediately after dosing. The TEPA test article solution high and low concentrations correlate with delivered doses of 23.5 mg/kg and 14 mg/kg, respectively. All animals that died during the study underwent a necropsy with no abnormal findings.

The TEPA material used in this study was manufactured by The Dow Chemical Company, 2030 Willard H. Dow Center, Midland, Michigan, 48674. The batch number of the TEPA material used in this study is, XC0101HZ74. The final report for this study is enclosed. Data in the final report, relevant to a material not subject to TSCA 8(e) Substantial Risk Notice, has been redacted.

Please contact Jeanette McCauley at 651-733-9384 or jamccauley2@mmm.com if you have any questions or if we can provide additional information.

Sincerely,

Jean B. Sweeney (JAMC)

Jean B. Sweeney
Staff Vice President, Environmental Health and Safety Operations

Enclosure

DCN:88100000420

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TEST RESULT CERTIFICATE

Sponsor	3M[redacted]	**Technical Initiation**	7/6/2010
Address	[redacted]	**Technical Completion**	7/9/2010
Contact	[redacted]	**Final Report Date**	7/22/2010
P.O. Number	[redacted]	**Project Number**	10-3008-NI

Test Article	TEPA, High Concentration, Solution 1 TEPA, High Concentration, Solution 2 (Autoclaved) TEPA, Low Concentration, Solution 3 TEPA, Low Concentration, Solution 4 (Autoclaved) [redacted]
Lot/Batch #	Not Supplied By Sponsor
Study	Direct Systemic Injection Test – ISO
Comments	The Sponsor provided 8 solutions for direct IV & IP injection. The 8 test article solutions were stored at 4 ± 2 °C. The pH of the 8 test article solutions was measured prior to dosing, and if necessary was adjusted using HCL to within a pH range of 6-8.

REFERENCES: The study was conducted based upon the following references: ISO 10993–11, 2006, Biological Evaluation of Medical Devices – Part 11: Tests for Systemic Toxicity. ISO 10993–12, 2007, Biological Evaluation of Medical Devices – Part 12: Sample Preparation and Reference Materials.

ISO/IEC 17025, 2005, General Requirements for the Competence of Testing and Calibration Laboratories.

GENERAL PROCEDURE: The Systemic Injection Study is designed to screen test articles for potential toxic effects as a result of a single-dose systemic injection in mice. Per Sponsor's request, the pH of all solutions was measured prior to dosing. The pH of solutions #1 - #4 ranged from 10.8 – 11; the solutions were adjusted prior to dosing with HCL to a pH between 6 – 8. [redacted] The 8 test article solutions were injected intravenously (IV) and intraperitoneally (IP) at 50 mL per kg in groups of five mice. Similarly, groups of mice were injected IV and IP with control article USP 0.9% Sodium Chloride for Injection (NaCl). Mice that died prior to the end of the observation period underwent a gross necropsy.

RESULTS: All groups that received IV injections of the 8 solutions contained mice that died or exhibited convulsions followed by death immediately after dosing: Solution 1, 2 mice died; Solution 2, 2 mice; Solution 3, 1 mouse; Solution 4, 1 mouse; [redacted] All animals that received IP injections of solutions #1 - #4 did not exhibit biological reactions greater than the controls. [redacted]. All animals that died during the study underwent a necropsy with no abnormal findings.

CONCLUSION: All the groups treated with the 8 test article solutions dosed IV exhibited biological reactions greater than controls. The groups treated with test article solutions #1 - #4 dosed IP survived. [redacted]

AUTHORIZED PERSONNEL:

Claudine Kos, Ph.D.
Study Director

Jamie Lynne Metzinger, B.A., B.S.
Quality Assurance

TABLE 1
Animal Weights and Clinical Observations

Group	Animal #	Sex	Dose (mL)	Body Weight (g) Day 0 07/06/10	Day 1 07/07/10	Day 2 07/08/10	Day 3 07/09/10	Weight Change	Signs of Toxicity*	Necropsy Obs
TEPA, High Concentration, Solution 1 Test IV	1	Female	0.9	17.5	18.9	20.1	20.9	3.4	3A	N/A
	2	Female	1.0	20.0	20.8	22.7	24.0	4.0	3A	N/A
	3	Female	1.0	19.6	19.9	21.2	22.5	2.9	3A	N/A
	4	Female	0.9	17.4	N/A	N/A	N/A	N/A	3A, 13A	None
	5	Female	1.0	20.2	N/A	N/A	N/A	N/A	3A, 13A	None
TEPA, High Concentration, Solution 1 Test IP	6	Female	0.1	22.8	23.6	24.4	25.2	2.4	None	N/A
	7	Female	0.9	17.4	18.2	18.8	19.7	2.3	None	N/A
	8	Female	1.0	20.3	21.7	22.4	23.6	3.3	None	N/A
	9	Female	1.1	22.0	22.9	23.3	24.1	2.1	None	N/A
	10	Female	1.1	22.8	24.2	25.0	26.0	3.2	None	N/A
TEPA, High Concentration, Solution 2 (Autoclaved) Test IV	11	Female	1.0	19.0	20.2	20.6	21.4	2.4	3A	N/A
	12	Female	1.1	21.4	21.9	22.7	23.1	1.7	3A	N/A
	13	Female	0.9	18.9	19.9	20.3	21.6	2.7	3A	N/A
	14	Female	1.0	19.4	N/A	N/A	N/A	N/A	3A, 13A	None
	15	Female	0.9	17.7	N/A	N/A	N/A	N/A	3A, 13A	None
TEPA, High Concentration, Solution 2 (Autoclaved) Test IP	16	Female	1.0	20.5	21.4	22.2	23.4	2.9	None	N/A
	17	Female	0.9	18.3	19.1	19.8	21.2	2.9	None	N/A
	18	Female	1.0	19.0	19.7	20.3	21.3	2.3	None	N/A
	19	Female	0.9	17.7	19.0	19.9	21.1	3.4	None	N/A
	20	Female	0.9	17.6	18.8	19.8	20.9	3.3	None	N/A
TEPA, Low Concentration, Solution 3 Test IV	21	Female	0.9	17.5	18.8	19.8	20.4	2.9	3A, 2C	N/A
	22	Female	1.0	20.0	21.2	22.5	23.6	3.6	3A, 2C	N/A
	23	Female	1.2	23.0	23.6	24.2	25.6	2.6	3A, 2C	N/A
	24	Female	1.1	21.9	22.3	23.1	23.8	1.9	3A, 2C	N/A
	25	Female	1.1	21.7	N/A	N/A	N/A	N/A	3A, 13A	None
TEPA, Low Concentration, Solution 3 Test IP	26	Female	1.0	19.6	20.7	21.7	23.0	3.4	None	N/A
	27	Female	1.0	19.7	21.0	22.0	22.7	3.0	None	N/A
	28	Female	1.0	20.1	20.8	21.6	22.9	2.8	None	N/A
	29	Female	0.9	18.3	18.8	19.3	20.6	2.3	None	N/A
	30	Female	1.1	21.0	22.1	23.4	24.0	3.0	None	N/A
TEPA, Low Concentration, Solution 4 (Autoclaved) Test IV	31	Female	1.1	22.0	22.6	23.4	24.3	2.3	3A, 2C	N/A
	32	Female	1.1	21.6	22.8	23.9	24.3	2.7	3A, 2C	N/A
	33	Female	1.1	22.6	23.1	24.5	25.8	3.2	3A, 2C	N/A
	34	Female	1.0	19.0	20.1	21.1	22.2	3.2	3A, 2C	N/A
	35	Female	1.0	20.5	N/A	N/A	N/A	N/A	3A, 13A	None
TEPA, Low Concentration, Solution 4 (Autoclaved) Test IP	36	Female	1.0	20.6	21.3	21.7	22.2	1.6	None	N/A
	37	Female	1.1	21.6	21.8	22.9	23.8	2.2	None	N/A
	38	Female	0.9	18.4	19.1	19.4	20.8	2.4	None	N/A
	39	Female	1.1	22.2	23.1	24.0	24.5	2.3	None	N/A
	40	Female	0.9	17.6	18.6	19.0	19.8	2.2	None	N/A

* Summary of clinical observations, Immediately, 4, 24, 48, and 72 h after injection.

3A Clonic convulsions
2C Animals unresponsive for approximately 1 min then appeared drowsy until gently prodded.
13A Observed Death

TABLE 1
Animal Weights and Clinical Observations (Cont.)

Group	Animal #	Sex	Dose (mL)	Body Weight (g) Day 0 07/06/10	Day 1 07/07/10	Day 2 07/08/10	Day 3 07/09/10	Weight Change	Signs of Toxicity*	Necropsy Obs
[redacted]										

* Summary of clinical observations, Immediately, 4, 24, 48, and 72 h after injection.

[redacted]

TABLE 1
Animal Weights and Clinical Observations (Cont.)

Group	Animal #	Sex	Dose (mL)	Body Weight (g) Day 0 07/06/10	Day 1 07/07/10	Day 2 07/08/10	Day 3 07/09/10	Weight Change	Signs of Toxicity*
NaCl Control 50 mL/kg Test IV	81	Female	1.0	20.6	21.0	21.7	22.2	1.6	None
	82	Female	0.9	18.5	19.1	19.7	20.2	1.7	None
	83	Female	1.1	22.5	23.8	24.8	25.5	3.0	None
	84	Female	0.9	17.8	18.7	19.7	20.2	2.4	None
	85	Female	0.9	18.3	18.9	19.8	20.5	2.2	None
NaCl Control 50 mL/kg Test IP	86	Female	1.1	21.2	21.9	22.3	23.7	2.5	None
	87	Female	1.0	20.3	21.4	22.0	22.4	2.1	None
	88	Female	1.0	19.2	20.3	21.3	22.7	3.5	None
	89	Female	0.9	17.0	18.1	18.5	19.6	2.6	None
	90	Female	1.1	22.1	23.0	23.9	24.3	2.2	None

* Summary of clinical observations, Immediately, 4, 24, 48, and 72 h after injection.

TABLE 2

Solution	pH	Adjusted pH
TEPA, High Concentration, Solution 1	10.9	7.4
TEPA, High Concentration, Solution 2 (Autoclaved)	10.9	7.4
TEPA, Low Concentration, Solution 3	11.0	6.7
TEPA, Low Concentration, Solution 4 (Autoclaved)	10.8	7.2
[redacted]		

* Dosed as received

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