

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

DAZOMET

Chemical Code # 000233, Tolerance # 50466
SB# 621

February 6, 1995, revised July 21, 1998

I. DATA GAP STATUS

Chronic toxicity, rat:	No data gap, no adverse effect
Chronic toxicity, dog:	No data gap, possible adverse effect
Oncogenicity, rat:	No data gap, no adverse effect
Oncogenicity, mouse:	No data gap, no adverse effect
Reproduction, rat:	No data gap, no adverse effect
Teratology, rat:	No data gap, no adverse effect
Teratology, rabbit:	No data gap, possible adverse effect
Gene mutation:	No data gap, possible adverse effect
Chromosome effects:	No data gap, possible adverse effect
DNA damage:	No data gap, no adverse effect
Neurotoxicity:	Study not required at this time ¹

¹ An acute and a subchronic neurotoxicity study with rats are on file and have been reviewed.

Toxicology one-liners are attached.
All record numbers through 139245 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
Original: T. Moore, 2/6/95, revised by Gee, 7/21/98
NOTE: MITC is a breakdown product of dazomet.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

CHRONIC TOXICITY, RAT

****026 114694**, "Report on the Oral Toxicity of Dazomet in Rats after 24 Months Administration in the Diet", (Dr. B. Kunbroth, BASF Aktiengesellschaft, Department of Toxicology, D-6700 Ludwigshafen, W. Germany, Report # 89/0276, 31 July 1989); Dazomet Technical (purity: 98.2%); 20 Wistar (Chbb = THOM (SPF) rats/sex/group; Dose: 0, 5, 20, 80, 320 ppm in the diet for 24 months (males: 0, 0.3, 1, 4, or 18 mg/kg/day, females: 0, 0.3, 1, 6, or 23 mg/kg/day); No apparent treatment-related mortality; Clinical Observations: marginal reduction in bodyweights (M/F: 320 ppm), no other treatment-related effects; Hematology: decreased numbers of rbc's and concentration of hemoglobin (F: 320 ppm, day 92, 184, 373, 555); Clinical Chemistry: reduced serum cholinesterase activity (F: 80, 320 ppm, day 92; 320 ppm, day 184, 373), reduced levels of total protein (F: 80, 320 ppm, day 92; 320 ppm, day 373, 555), albumin (F: 80, 320 ppm day 92; 320 ppm, day 373), and globulin (F: 80, 320 ppm, day 92; 320 ppm, day 184, 373), reduced creatine level (F: 80, 320 ppm, day 92; 320 ppm, day 373, 723); Necropsy: increased relative liver weight (M: 320 ppm), decreased kidney weight (M/F: 320 ppm); Histopathology: increased incidence and severity of hepatocellular fat deposition and vacuolation and altered cell foci (F: 320 ppm); **Adverse effects are not indicated; Nominal Chronic NOEL:** 80 ppm (based upon hematological and clinical chemical effects and liver vacuolation in the females in 320 ppm treatment group); **Acceptable.** (H. Green and T. Moore, 11/23/94).

CHRONIC TOXICITY, DOG

****028 114704**, "Report on the Study of Toxicity of Dazomet in Beagle Dogs via the Diet over 12 Months", (Dr. J. Hellwig, BASF Aktiengesellschaft, Department of Toxicology, D-6700 Ludwigshafen, W. Germany, Report # 89/0050, February 1989); Dazomet technical (purity: 98.2%); 6 Beagle dogs/sex/group; Nominal Doses: 0, 15, 50, or 150 ppm in the diet for 12 months, (0, 0.5, 1.6, or 4.8 mg/kg/day); No mortality; Clinical observations: marginal decrease in bodyweight gain (M/F, 150 ppm); Hematology: no treatment-related effects; Clinical Chemistry: elevated levels of alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase (M/F, 150 ppm); No treatment-related effects in urinalysis or ophthalmology; Necropsy: increased mean relative liver weight (M, 150 ppm), focal or diffuse discoloration of liver (F, 150 ppm); Histopathology: moderate to severe chronic hepatitis, severe cirrhosis (M/F, 150 ppm), iron-positive pigment deposition increase (M/F, 50, 150 ppm), testicular tubular atrophy in 2 of 6 (M, 150 ppm); **Possible adverse effect:** testicular tubular atrophy; **NOEL:** 50 ppm (based upon effects on serum enzymes, liver and testicular histopathology in 150 ppm group); **Acceptable.** (H. Green and T. Moore, 11/28/94)

ONCOGENICITY, RAT

**** 030, 054 114700, 139223**, "Report on the Oncogenic Potential of Dazomet in Rats after 24 Month Administration in the Diet", (Dr. B. Kuhbroth, BASF Aktiengesellschaft, Department of Toxicology, D6700 Ludwigshafen, W. Germany, Report # 89/0277, July 1989). Dazomet

technical (purity: 98.2%); 50 Wistar (Chbb = THOM (SPF) rats per sex per group received nominal doses of 0 (ground Kliba 343 rat/mouse/hamster maintenance diet), 5, 20, and 80 ppm in the diet for 24 months (males: 0, 0.27, 1.08, 4.43 mg/kg/day, females: 0.35, 1.37, 5.66 mg/kg/day); No treatment-related mortality; Clinical Observations: no treatment-related signs, no effect upon food consumption or body weight gain; Necropsy: no effect upon organ weights, apparent enlargement of spleen and iliac lymph nodes (20, 80 ppm); Histopathology: slight increase in diffuse fat deposition (80 ppm, M), altered cell foci and basophilic cell foci (80 ppm, F) in the liver, no treatment-related increase in tumor incidence; **No adverse effects are indicated; Chronic and oncogenic NOEL \geq 80 ppm; Unacceptable**, possibly upgradeable (no treatment-related effects apparent in the high dose group, dosing rationale is unclear). (H. Green and T. Moore, 11/22/94). Record 139223 was written by BASF in January, 1993, in response to the 1991 reviews of US EPA in which the oncogenicity study was considered unacceptable based on dose selection. The response defended the high dose of 80 ppm for the study and suggested considering the chronic study (record # 114694) along with the oncogenicity study. This has been done and the oncogenicity data gap is considered filled. (Gee, 8/4/98)

ONCOGENICITY, MOUSE

** 029 114705, "Report on the Study of the Oral Toxicity of Dazomet in Mice after 78 Week Administration in the Diet", (Dr. B. Kunbroth, BASF Aktiengesellschaft, Department of Toxicology, D-6700 Ludwigshafen, W. Germany, Report # 89/0341, September 1989); Dazomet technical (purity: 98.2%); 50 B6C3F1 mice/sex/group (main study); Nominal Doses: 0 (ground Kliba 343 maintenance diet), 20, 80, 320 ppm for 78 weeks; (satellite group) 10 animals/sex/group, treated at the same levels for 52 weeks; (Males: 0, 4, 16, or 68 mg/kg/day, females: 0, 6, 22, or 93 mg/kg/day); No treatment-related mortality; Clinical Observations: no treatment-related effects; Hematology: no treatment-related effects; Necropsy: increased mean liver weight (M/F, 320 ppm, 52, 78 weeks), decreased mean kidney weight (M, 320 ppm, 52 weeks, 20, 80, 320 ppm, 78 weeks), increased number of liver masses and foci (F, 320 ppm, 78 weeks); Histopathology: increased hepatocyte lipid deposition (M/F, 320 ppm, 52, 78 weeks), increase in basophilic foci in liver (F, 320 ppm, 78 weeks), increased hemosiderin deposition in the spleen (M/F, 320 ppm, 52, 78 weeks), increased extra-medullary splenic hemopoiesis (M/F, 320 ppm, 78 weeks), increased incidence of hepatocellular adenomas (F, 320 ppm, 78 weeks) ($p=0.159$, Fisher Exact Test, $p=0.0475$ for Cochran Armitage trend test); **Adverse effects are not indicated; Chronic NOEL: 80 ppm** (based on histopathologic effects in the 320 ppm group; **Oncogenic NOEL: 320 ppm; Acceptable**. (H. Green and T. Moore, 2/6/95).

REPRODUCTION, RAT

**027 114698, "Report on the Reproduction Study with Dazomet in Rats; Continuous Dietary Administration Over 2 Generations (2 Litters in the First and 1 Litter in the Second Generation)", (Dr. J. Hellwig, BASF Aktiengesellschaft, Department of Toxicology, D-6700 Ludwigshafen, W. Germany, Report # 89/0051, February 1989); Dazomet technical (purity: \geq 97.0%); 24 Wistar (Chbb = THOM (SPF)) rats/sex/group; Nominal Dose: 0 (Kliba 343 feed), 5, 30, or 180 ppm in the diet through 2 generations (with 2 litters in the first generation and 1 in the second) (Males: 0, 0.46, 2.75, or 17.0 mg/kg/day, females: 0, 0.52, 3.15, or 19.0 mg/kg/day); No parental mortality; Clinical Observations: reduction in parental bodyweight gain (M/F, 180 ppm, F0 and F1); Clinical Chemistry: Reductions in alanine aminotransferase (M/F, 180 ppm, F0); Necropsy:

increased relative mean liver weight (M/F, 180 ppm, F0 and F1); Histopathology: increased incidence and severity of fatty changes in liver (M, 180 ppm, F0 and F1); No apparent effects on reproduction; **Adverse effects are not indicated; Systemic Parental NOEL:** 30 ppm (based upon increased incidence and severity of fatty changes in the liver of the 180 ppm group; modest decrease in body weight gain), **Reproductive NOEL** \geq 180 ppm; **Acceptable.** (H. Green and T. Moore, 11/30/94)

TERATOLOGY, RAT

** 031, 054 114702, 139227 "Report on the Study of Prenatal Toxicity of Dazomet After Oral Administration (Gavage)", (Dr. J. Hellwig and Dr. B. Hildebrandt, BASF Aktiengesellschaft, Department of Toxicology, D-6700 Ludwigshafen, West Germany, Report # 87/0457, December 1987). Dazomet with \geq 97.0% purity was used as test article. 25 mated female Wistar (Chbb = THOM (SPF)) rats received nominal doses of 0 (olive oil), 3, 10, and 30 mg/kg/day by gavage on gestation days 6 through 15. **Adverse effects are not indicated.** Maternal NOEL = 10 mg/kg/day (reduced food consumption and body weight gain at the high dose level). Developmental NOEL = 30 mg/kg/day. **Unacceptable** and upgradeable with submission of dosing material analyses for content. (H. Green and T. Moore, 11/10/94). The analyses of the dosing solutions were reported in record 139227, upgrading the study to acceptable status. (Gee, 8/4/98)

TERATOLOGY, RABBIT

032 114706, "Study to Determine the Prenatal Toxicity of Tetrahydro-3,5-Dimethyl-2H-1,3,5-thiadiazine-2-thione (= Dazomet) in Rabbits", (J. Merkle, Department of Toxicology, BASF Aktiengesellschaft, West Germany, Report # 80/0053, 3 March 1980). Dazomet with \geq 98% purity was used as test article. 15 mated female Himalayan, Chbb: HM (selective breeding) rabbits per group received 0 (carboxymethyl cellulose), 6.25, 12.50, and 25.00 mg/kg/day by gavage on gestation days 6 through 18. (Maternal) No mortality; no apparent treatment-related effects; Necropsy: no treatment-related lesions; (Developmental) increased number of early resorptions (25 mg/kg/day); **Possible adverse effects:** increased incidence of early resorptions; **Maternal NOEL:** 25 mg/kg/day; **Developmental NOEL:** 12.5 mg/kg/day (based on the increased incidence of early resorptions in the 25.0 mg/kg/day group); **Unacceptable** and not upgradeable (no analysis of dosing material, inadequate method of fetal evaluation). (H. Green and T. Moore, 11/21/94).

054 139223 BASF response to the 1991 review of US EPA of the above study. The response is dated January, 1993, and prepared by B. Van Ravenzwaay. EPA considered the study unacceptable due to fewer than 12 litters per dose group. No worksheet. (Gee, 8/4/98)

033 114707, "Study to Determine the Prenatal Toxicity of Tetrahydro-3,5-dimethyl-2H-1,3,5-thiadiazine-2-thione (= Dazomet) in Rabbits", (J. Merkle, Department of Toxicology, BASF Aktiengesellschaft, West Germany, Report # 80/0037, 10 January 1983); Dazomet technical (purity: \geq 98%); 11 to 14 mated female Himalayan Chbb: HM (outbred strain) rabbits per group received 0 (carboxymethyl cellulose), 25.0, 50.0, and 75.0 mg/kg/day by gavage on gestation days 6 through 18, an untreated control group was also used; (Maternal) 2 animals died (75 mg/kg/day); Clinical Observations: reduced food consumption and body weight gain (75 mg/kg/day); Necropsy: no treatment-related lesions;

(Developmental): increased incidence of fetal resorptions (50 and 75 mg/kg/day); **Possible adverse effect:** increased incidence of fetal resorptions; **Maternal NOEL:** 50 mg/kg/day (reduced food consumption and body weight gain in the 75 mg/kg/day group); **Developmental NOEL:** 25 g/kg/day (based on the increased incidence of fetal resorptions in the 50 mg/kg/day group); **Unacceptable** and not upgradeable (no analysis of dosing material provided, fewer than 12 pregnant dams per group, inadequate method used for skeletal exam). (H. Green and T. Moore, 11/21/94)

**** 046 132456;** "Study of the Prenatal Toxicity of Dazomet in Rabbits after Oral Administration (Gavage)," J. Hellwig; 833; Himalayan Rabbit; BASF Aktiengesellschaft, Department of Toxicology, D-67056 Ludwigshafen, Germany; Project No. 40R0062/92058; 9/93; Dazomet Technical (batch no. 92-1) (purity: 98.0%); 15 females/dose; Doses: 0 (0.5% carboxymethyl cellulose), 5, 15, 45 mg/kg/day for days 7 through 19 of post-insemination, by gavage; Mortality: 1 dam (45 mg/kg/day) on day 9; Clinical Observations: significant decrease in body weight gain of dams from day 7 to day 19 (45 mg/kg/day), blood in bedding of 2 dams starting on day 22 (45 mg/kg/day); Necropsy: (Maternal) significant decrease in mean uterine weight, reduced body weight gain (45 mg/kg/day), (Developmental) increased number of early resorptions, increased incidence of fetal skeletal variations (45 mg/kg/day); **Adverse effect:** increased incidence of fetal resorptions; **Maternal NOEL:** 15 mg/kg/day (based upon decreased body weight gain and mean uterine weight in 45 mg/kg/day group); **Developmental NOEL:** 15 mg/kg/day (based upon increased number of early resorptions and increased incidence of fetal skeletal variations in the 45 mg/kg/day group); Study acceptable. (Moore, 10/26/94)

GENE MUTATION

054 139243 Gelbke, H. "Report on a Point Mutation Test Carried Out on CHO Cells (HGPRT Locus) with the Test Substance Dazomet". BASF Aktiengesellschaft, Dept. of Toxicology, RZ-Report No: 86/215. December, 1985. Dazomet Technical, purity 98.2%, at concentrations of 0, 0.01 to 0.464 ug/ml without and with S-9 Mix was evaluated for mutagenic activity with CHO cells. The first assay was invalid based on criteria for cloning efficiency and toxicity but the second trial was considered acceptable. **Adverse effect: Dazomet increased the mutation rate in CHO cells. UNACCEPTABLE.** (No valid repeat trial). (Kishiyama and Gee, 7/28/98).

006 038471, "Mutagenicity Evaluation of Sample #100, Final Report", (David J. Brusick, Ph.D., Litton Bionetics, Inc., Kensington, MD., Report # T6081, 26 October 1976). The test article, designated Sample #100, was described as a white powder. Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, and TA1538 and Saccharomyces cerevisiae strain D4 were exposed to concentrations of 0 (DMSO), 0.10, 1.00, 10.00, 100.00, and 500.00 ug/plate in the presence and absence of activation (Aroclor-induced rat liver microsomal enzyme preparation) for 48 hours. **Increased reversion frequency is not indicated. Unacceptable** and not upgradeable (no replicates, no dosing rationale). (H. Green and T. Moore, 12/12/94).

006 038472, "Mutagenicity Evaluation in Salmonella Typhimurium", (Jenness B. Majeska, The In Vitro Toxicology Section, Environmental Health Center, Stauffer Chemical Company, Farmington, CT., Report # T-10044, 9 June 1980). The test article is identified as N-521, EHC-0008-7-7 and described as a white powder. Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, and TA1538 were exposed for 48 hours to concentrations of 0 (DMSO), 3.7, 11.1, 12.3, 33.3, 37.0, 100.0, 111.1, 300.0, 333.3, or 1000.0 ug/plate in the presence and absence of activation. **Increased reversion frequency is not indicated. Unacceptable** and

upgradeable with individual plate data, and test article analyses. (H. Green and T. Moore, 12/12/94).

006 038478, "Mutagenicity Evaluation of N-521 Technical, Batch # 149 in the Sex-Linked Recessive Lethal Test in Drosophila melanogaster", (E. Sky Benson, Litton Bionetics, Inc., Kensington, MD., Report # T-10012, July 1979). The test article is identified as N-521 technical. 200 Drosophila melanogaster males per group received 0 (DMSO), 0.025, and 0.050 mg/ml in sucrose solution. 874 to 2453 chromosomes were tested per brood. **An increase in forward mutations is not indicated. Unacceptable** and upgradeable (test article/dosing material analyses, results of dose range study, and numbers of non-fertile males). (H. Green and T. Moore, 12/13/94).

Note: Although no one study has been evaluated as acceptable, there are adequate data from the several studies (and studies in other categories of genotoxicity) to consider the data gap filled. (Gee, 8/4/98)

CHROMOSOME EFFECTS

**054 139245 Englehardt, G. "Report on the Cytogenic Investigations in NMRI Mice after a Single Oral Administration of Dazomet." BASF Aktiengesellschaft, Report No. 85/0154. May 24, 1985. Dazomet Technical, purity 99.3%, was administered once by stomach intubation at concentrations of 0, 45, 90 and 180 mg/kg to 5 NMRI mice/sex/group and evaluated 24 hours later for mutagenic potential. Five additional mice/sex/sacrifice time were included in the high dose group for sacrifice at 16 and 48 hours. Cyclophosphamide as positive control was functional. Dazomet treatment did not increase the number of micronucleated polychromatic erythrocytes. ACCEPTABLE. (Kishiyama and Gee, 7/30/98)

** 054 139233 Englehardt, G. "Report on In Vitro Cytogenic Investigations of Dazomet in Human Lymphocytes". BASF Aktiengesellschaft, Dept. of Toxicology, Reg. Document No. BASF 89/0094. April, 1989. Dazomet Technical, purity 98.2%, batch 26-5297, at concentrations of 0 (DMSO), 0.002, 0.01, and 0.05 ug/ml without S-9 Mix, 24-hour incubation, and at 0, 2.5, 12 and 25 ug/ml with S9, 2 hour exposure, was evaluated for the ability to induce chromosomal aberrations in human lymphocytes stimulated with PHA for 48 hours prior to treatment, duplicate cultures. Mitomycin C was used as the positive control without activation and cyclophosphamide as positive control with activation. 100 metaphases were scored per culture for a total of 200 per concentration. While there was an increase in gaps at 25 ug/ml with activation, no chromosome damaging activity was reported. ACCEPTABLE. (Kishiyama and Gee, 7/28/98)

054 139244: Volkner, W. "Report on the Study of Chromosome Aberrations in Chinese Hamster Spermatogonia with Dazomet". Technical University of Darnstadt, West Germany, RZ-Report No.: 85/375. November 14, 1985. Dazomet Technical, purity not stated, was administered once by stomach intubation at concentrations of 0, 10, 33 and 100 mg/kg to 10 male Chinese hamsters/group and evaluated 18 hours later for the potential to induce chromosomal aberrations in spermatogonia. Ten additional high dose animals/sacrifice time were included for sacrifice at 42 and 66 hours. A second group of 10 at the high dose were sacrificed at 18 hour with the positive control, adriablastin. Cyclophosphamide was not functional as a positive control. Dazomet treatment showed no evidence of induction of aberrations in spermatogonia. UNACCEPTABLE. Study reports no dosing solution analysis,

no justification of dose selection and no toxicity data. (Kishiyama and Gee, 7/30/98).

006 038473, "Mutagenicity Evaluation of N 521 in an In Vitro Cytogenetic Assay Measuring Sister Chromatid Exchange and Chromosome Aberrations", (Daniel Stetka, Litton Bionetics, Inc., Kensington, MD, Report # T-6410, March 1979). The test article is identified as N-521. Fisher L5178Y lymphoma cells received a 4-hour exposure to untreated (medium), 0 (DMSO), 1.56, 3.13, 6.25, 12.50, and 25.00 ng/ml in the presence and absence of activation. **A slight increase in chromosomal aberrations is indicated. Unacceptable** and upgradeable with the submission of test article identity, explanation of dosing rationale, and cytotoxicity results). (H. Green and T. Moore, 12/13/94).

006 038474, "N-521 Mutagenicity Evaluation in Mouse Lymphoma Multiple Endpoint Test", (Jeness B. Majeska, M.S., The In Vitro Toxicology Section, Environmental Health Center, Stauffer Chemical Company, Farmington, CT. 06032, Report # T-10136, 20 November 1980). The test article is identified as N-521, EHC-0008-7-7. Fischer mouse L5178Y (TK+/-) lymphoma cells were assayed for forward gene mutation, chromosomal aberrations, and sister chromatid exchanges. They received 4 hour exposure to medium, 0 (DMSO), 0.15, 0.46, 0.60, 0.80, 1.00, 1.37, 2.00, 3.00, 4.00, 4.12, 5.00, 6.00, 8.00, 10.00, 12.35, 20.00, 30.00, 37.04, or 111.11 ug/ml in the presence and absence of activation. **Increased forward mutation and chromosomal aberration are indicated. Unacceptable** and upgradeable (test article identification, number of cultures per assay). (H. Green and T. Moore, 12/13/94).

006 038477, "Mutagenicity Evaluation of N-521 in the Rat Bone Marrow Cytogenetic Assay", (Daniel Stetka, Litton Bionetics, Inc., Kensington, MD., Report # T-10011, July 1979). The test article is identified as N-521. 8 or 24 male Sprague-Dawley albino rats, strain CRL:COBS (SD) BR, per group received single and multiple (5 treatments, 24 hours apart) exposures by gavage at 0 (distilled water), 6, 20, and 60 mg/kg. Sampling occurred 6, 24, or 48 hours after the final treatment. **An increase in chromosomal aberrations is not indicated. Unacceptable** and not upgradeable (used males only with no justification, inadequate dosing rationale). (H. Green and T. Moore, 12/13/94).

DNA DAMAGE

** 054 139232: Hoorn, A.J. "Report on the Mutagenicity Evaluation of Dazomet in The Rec Assay with Bacillus Subtilis". Hazleton Biotechnologies, Reg. Doc.# BASF 87/0029. January 1987. Dazomet Technical, purity not stated, at concentrations ranging from 1.0 ug to 1000 ug/plate was evaluated for recombinogenic activity using Bacillus subtilis strains H17 (rec+) and M45 (rec-) in the presence and absence of metabolic activation. Dazomet treatments did not influence recombinogenic activity to Bacillus subtilis indicator organisms. ACCEPTABLE (minor deficiency). (Kishiyama and Gee, 7/27/98).

054 139242: Cifone, M.A. "Evaluation of Dazomet Techn. in the In Vivo/In Vitro Rat Hepatocyte Unscheduled DNA Synthesis Assay". Hazleton Biotechnologies, HBC Project no. 20991, BASF # 87/0249, September, 1986. Dazomet Technical, purity 99.3%, administered via single gavage at concentrations of 0, 37.5, 75, 150 or 300 mg/kg to three adult male Fischer 344 rats/group and evaluated after 4 hours for the potential to induce UDS in vivo/in vitro in rat hepatocytes by autoradiography. Dazomet did not show significant activity in the nuclear labeling of rat hepatocytes. UNACCEPTABLE. Upgradeable (study lacks dosing material analysis for content, only summary data were reported). (Kishiyama and Gee, 7/28/98)

006 038476, "N-521, Morphological Transformation of BALB/3T3 Cells", (Jenness B. Majeska, The In Vitro Toxicology Section, Environmental Health Center, Stauffer Chemical Company, Farmington, CT., Report # T-10137, 5 December 1980). The test article is identified as N-521, EHC-0008-7-7. BALB/3T3 mouse cells were exposed for 72 hours to medium, 0 (DMSO), 0.025, 0.050, 0.100, 0.200, and 0.400 ug/ml with 15 replicates per dose level. **Increased frequency of cell transformation is not indicated. Unacceptable** and not upgradeable (no activation of the test material included in the study). (H. Green and T. Moore, 12/13/94).

006 038475, "Mutagenicity Evaluation of N-521 in the In Vitro Transformation of BALB/3T3 Cells Assay", (Dale W. Matheson, Litton Bionetics, Inc., Kensington, MD., Report # T-6412, June 1978). Test article is identified as N-521. BALB/3T3 mouse cells were exposed for 72 hours at 0 (DMSO), 0.078, 0.156, 0.312, 0.625, and 1.250 ug/ml. 9 to 10 replicates per dose level were used. **Increased frequency of cell transformation is not indicated. Unacceptable**, not upgradeable (test article/dosing material analyses and cytotoxicity results are not included, no activation). (H. Green and T. Moore, 12/13/94).

NEUROTOXICITY

Subchronic:

** 50 135081 Mellert, W., W. Kaufmann and B. Hildebrand. "Dazomet - Subchronic Oral Neurotoxicity Study in Wistar Rats." BASF Aktiengesellschaft, No. 94/10799. 9/23/94. Dazomet, purity 96.3%, admixed with the feed at concentrations of 0, 50, 200, 450 (males only) and 400 ppm (females only) was fed to 10 Wistar rats/sex/group for 3 months. No evidence of neurotoxicity. High-dose males and females had lower body weight and body weight gain. Liver weight increase trend for high-dose males and females and mid-dose males and the fatty degeneration of the liver for all dazomet treated groups, except low dose females, were considered substance-related. NOEL = <50 ppm (4 mg/kg) for males and 50 ppm (4 mg/kg) for females. No evidence of neurotoxicity was reported. ACCEPTABLE. (Kishiyama and Gee, 8/3/98)

Acute:

** 51 135082 Mellert, W., W. Kaufmann and B. Hildebrand. "Dazomet - Acute Oral Neurotoxicity Study in Wistar Rats." BASF Aktiengesellschaft, No. 94/10800, 9/16/94. Dazomet, purity 96.3%, administered in a single oral dose via gavage at actual concentrations of 0, 50, 130, and 450 ppm to 10 male Wistar rats/group and at actual concentrations of 0, 13, 50 and 130 mg/kg to 10 female Wistar rats/group followed by 14 days of observation. Mid and high-dose males had lower (7 and 13%) body weight and lower (34 and 59%) body weight change compared to controls on day 7 following treatment. Treatment related neurotoxic effects were apparent only on the day of dosing (Day 0). All dazomet treated male and female groups, except low dose females, were associated with an increase in the incidence of abnormal clinical signs (urine stains [females only], half closure of eyelids, salivation, lacrimation, impaired activity and reduced rearing). All dazomet treated female and male groups (except low dose males) had reduced motor activity. NOEL = <13 mg/kg (day 0). At days 7 and 14 after dosing,

there were no effects. No effects on histopathology from 5 animals following perfusion fixation. ACCEPTABLE. (Kishiyama and Gee, 7/31/98).

OTHER STUDIES

50466-038; 124996; "21-Day Dermal Toxicity Study in Rabbits"; (K.M. MacKenzie, Hazleton Laboratories America, Madison, WI; Project ID #HLA 6220-100; 6/17/87); Five rabbits/sex/group were exposed dermally to 0, 10, 100, or 1000 mg/kg of Dazomet Technical (purity: 99%) 5 days/wk for 3 weeks. Additional satellite groups of 5 animals/sex/group were exposed to 0 or 10 mg/kg for the same time period and then held for 24 days. The skin was moistened with 0.4% aqueous carboxymethylcellulose, followed by placement of the test material on the skin. One male in the 1000 mg/kg group was euthanized in moribund condition on day 6. Otherwise, no apparent dose-related signs of toxicity were evident. No signs of local irritation noted. No treatment-related effects upon the hematology or clinical chemistry parameters were evident. No significant differences in the mean organ weights between control and treated animals. No treatment-related lesions noted in the necropsy or histopathology examinations. NOEL can not be determined. **Study unacceptable**, not upgradeable (method of moistening the test material was inadequate). (Moore, 2/9/98)

No record number. In Chemical Code file of Medical Toxicology. "Summaries of toxicity studies on dazomet." (BASF Japan Ltd., in *J. Pesticide Science* 17: S327 - S335 (1992)) This is a review article summarizing many of the studies above. (Gee, 8/4/98)