

toxicology on hydrazine sulfate yielded positive results in the *Salmonella* assay and negative results in the *Drosophila* test for sex-linked recessive lethal gene mutations.

Carcinogenic Classification

IARC: Group 2B, possibly carcinogenic to humans.

MAK: Group A2, carcinogenic in animal experimentation.

NIOSH: Carcinogen, with no further classification.

NTP: Group 2, reasonably anticipated to be a carcinogen.

TLV: A3, animal carcinogen.

Other Nations

Australia: 0.1 ppm, Category II, established animal carcinogen, skin, sensitizer (1993); Federal Republic of Germany: no MAK, Group A2, unmistakably carcinogenic in animal experimentation only, skin, sensitizer (1995); Sweden: 0.1 ppm, short-term limit 0.3 ppm, 15 minutes, skin, carcinogenic, sensitizer (1993); United Kingdom: Risk Phrase "R45" (may cause cancer); under consideration for assignment of a MEL (maximum exposure limit) (1995).

References

1. National Institute for Occupational Safety and Health: Occupational Safety and Health Guideline for Hydrazine Potential Human Carcinogen. In: Occupational Safety and Health Guidelines for Chemical Hazards. DHHS (NIOSH) Pub. No. 88-118; NTIS Pub. No. PB-89-203-129. National Technical Information Service, Springfield, VA (1988).
2. International Agency for Research on Cancer: IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man, Vol. 4, Some Aromatic Amines, Hydrazine and Related Substances, N-Nitroso Compounds and Miscellaneous Alkylating Agents, pp. 127-136. IARC, Lyon, France (1974).
3. Reinhardt, C.F.; Brittelli, M.R.: Heterocyclic and Miscellaneous Nitrogen Compounds. In: Patty's Industrial Hygiene and Toxicology, 3rd Rev. ed., Vol. 2A, Toxicology, pp. 2791-2805. G.D. Clayton and F.E. Clayton, Eds. John Wiley & Sons, New York (1981).
4. McDougal, N.N.; George, M.E.; Clewell, III, H.J.; et al.: Dermal Absorption of Hydrazine Vapors in Rats. *Toxicologist* 6:243 (1986).
5. Witkin, L.B.: Acute Toxicity of Hydrazine and Some of Its Methylated Derivatives. *Arch. Ind. Health* 13:34-36 (1956).
6. Rothberg, S.; Cope, O.B.: Toxicity Studies on Hydrazine, Methylhydrazine Symmetrical Dimethylhydrazine, Unsymmetrical Dimethylhydrazine, and Dimethylnitrosamine. Technical Report CWLR-2027. Chemical Warfare Laboratories, U.S. Army Chemical Center, MD (1956).
7. Montgomery, V.; Reeves, L.: Lectures in Aerospace Medicine (AD-651 391). Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, OH (1960).
8. U.S. Army Chemical Center: Unpublished Preliminary Data on the Acute Toxicity of Hydrazine and Hydrazine Hydrate. Medical Division, U.S. Army Chemical Center, MD (1949).
9. Thienes, C.H.; Roth, H.P.; Swenson, E.; et al.: Acute and Chronic Toxicity of Hydrazine. University of Southern California School of Medicine, Department of Pharmacology and Toxicology, Los Angeles (June 1948).
10. Preece, N.E.; Ghatineh, S.; Timbrell, J.A.: Course of ATP Depletion in Hydrazine Hepatotoxicity. *Arch. Toxicol.* 64:49 (1990).
11. Chemical Manufacturers' Association: Hydrazine 64% Aqueous Solution: Acute Inhalation Toxicity in Rats 1-Hour Exposure. Report No. CMA 8/930523. CMA, Washington, DC (1993).
12. Haun, C.C.; Kinkead, E.R.: Chronic Inhalation Toxicity of Hydrazine. In: Proceedings of the 4th Annual Conference on Environmental Toxicology, pp. 351-363. Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, OH (1973).
13. Comstock, C.C.; Lawson, L.H.; Greene, E.A.; Oberst, F.W.: Inhalation Toxicity of Hydrazine Vapour. *Arch. Ind. Hyg. Occup. Med.* 10:476-490 (1954).
14. Biancifiori, C.: Pulmonary and Hepatic Tumors Caused by Hydrazine Sulfate at Reduced Doses in BALB/c/Cb/Se Mice. *Lav. Inst. Anat. Istol. Pathol. Perugia* 30:89-99 (1970).
15. Severi, L.; Biancifiori, C.: Hepatic Carcinogens in CBA/Cb/Se Mice and Cb/Se Rats by Isonicotinic and Hydrazide and Hydrazine Sulfate. *J. Natl. Cancer Inst.* 41:331-349 (1968).
16. Biancifiori, C.: Hepatomas in CBA/Cb/Se Mice and Liver Lesions in Golden Hamsters Induced by Hydrazine Sulfate. *J. Natl. Cancer Inst.* 44:943-949 (1970).
17. Juhasz, J.; Balo, J.; Szende, B.: Tumor-Inducing Effect of Hydrazine in Mice. *Nature* 210:1377 (1966).
18. Juhasz, J.; Balo, J.; Szende, B.: Carcinogenic Properties of Hydrazine. *Magy. Onkologia* 11:31-36 (1967).
19. Bhide, S.V.; D'Souza, R.A.; Sawia, M.S.; Ranadive, A.J.: Lung Tumor Incidence in Mice Treated with Hydrazine Sulfate. *Int. J. Cancer* 18:530-535 (1976).
20. Biancifiori, C.: Existence of a Hormonal Factor in the Pulmonary Carcinogenicity of Hydrazine. *Lav. Inst. Anat. Istol. Patol. Univ. Studi Perugia* 29:29-41 (in Italian) (1969).
21. Milia, U.; Biancifiori, C.; Santilli, F.E.G.: Late Findings in Pulmonary Carcinogenesis by Hydrazine Sulfate in Newborn BALB/c/Cb/Se Substrain Mice. *Lav. Inst. Anat. Istol. Patol. Univ. Studi Perugia* 25:165-171 (1965).
22. Roe, F.J.C.; Grant, G.A.; Millican, D.M.: Carcinogenicity of Hydrazine and 1,1-Dimethylhydrazine for Mouse Lung. *Nature* 216:375-376 (1967).
23. Kelly, M.G.; O'Gara, R.W.; Yancey, S.; et al.: Comparative Carcinogenicity of N-Isopropyl-alpha-(2-methyl-hydrazino)-p-toluamide, HCl (Procarbazine Hydrochloride), Its Degradation Products, Other Hydrazines, and Isonicotinic Acid Hydrazine. *J. Natl. Cancer Inst.* 42:337-344 (1969).
24. Maru, G.B.; Bhide, S.V.: Effects of Antioxidants and Antitoxins on the Formation of Lung Tumours in Mice by Isoniazid and Hydrazine Sulfate. *Cancer Lett.* 17:75-80 (1982).
25. Toth, B.: Hydrazine, Methylhydrazine, and Methylhydrazine Sulfate Carcinogenesis in Swiss Mice. Failure of Ammonium Hydroxide to Interfere in the Development of Tumours. *Int. J. Cancer* 9:109-118 (1972).
26. Menon, M.M.; Bhide, S.V.: Perinatal Carcinogenicity of Isoniazid (INH) in Swiss Mice. *J. Cancer Res. Clin. Oncol.* 105:258-261 (1983).
27. Yamamoto, R.S.; Weisburger, J.H.: Failure of Arginine Glutamate to Inhibit Lung Tumor Formation by Isoniazid and Hydrazine in Mice. *Life Sci.* 9(II):285-289 (1970).
28. Toth, B.: Lung Tumour Induction and Inhibition of Breast Adenocarcinomas by Hydrazine Sulfate in Mice. *J. Natl. Cancer Inst.* 42:469-475 (1969).
29. Steinhoff, D.; Mohr, U.: The Question of Carcinogenic Effects of Hydrazine. *Exp. Pathol.* 33:133-143 (1988).
30. Biancifiori, C.; Giornelli-Santilli, F.E.; Milia, V.; Severi, L.: Pulmonary Tumors in Rats Induced by Oral Hydrazine Sulfate. *Nature* 212:414-415 (1966).
31. Toth, B.: Tumorigenesis Studies with 1,2-Dimethyl-hydrazine Dihydrochloride, Hydrazine Sulfate, and Isonicotinic Acid in Golden Hamsters. *Cancer Res.* 32:804-807 (1972).
32. MacEwen, J.D.; McConnell, E.E.; Back, K.C.: The Effects of 6-Month Chronic Low Level Inhalation Exposures to Hydrazine on Animals. In: Proceedings of the 5th Annual Conference on Environmental Toxicology, pp. 225-235. Aerospace Medical Research Laboratory,

- Wright-Patterson Air Force Base, OH (1974).
33. MacEwen, J.D.; Vernot, E.H.; Haun, C.C.: Chronic Effects of Inhalation Exposure to Hydrazine. In: Proceedings of the 10th Annual Conference on Environmental Toxicology, pp. 261-282. Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, OH (1979).
 34. Vernot, E.H.; MacEwen, J.D.; Bruner, R.H.; et al.: Long-Term Inhalation Toxicity of Hydrazine. *Fund. Appl. Toxicol.* 5:1050-1064 (1985).
 35. Lee, S.H.; Aleyassine, H.: Hydrazine Toxicity in Pregnant Rats. *Arch. Environ. Health* 21:615-619 (1970).
 36. Keller, W.C.; Olson, C.T.; Back, K.C.: Evaluation of the Embryotoxicity of Hydrazine in Rats. AFAMRL-TR-82-29 (AD/A119706). Air Force Aerospace Medicine Research Laboratory, Wright-Patterson Air Force Base, OH (1982).
 37. Lyng, R.D.; Keller, W.C.; Back, K.C.: Effects of Hydrazine on Pregnant ICR Mice. AFAMRL-TR-80-19 (AD/A084023). Air Force Aerospace Medicine Research Laboratory, Wright-Patterson Air Force Base, OH (1980).
 38. Savchenkov, M.F.; Samoilova, T.J.: Effect of Hydrazine Nitrate on Reproductive Function of Albino Rats. In: Problems of Limitation of Environmental Pollutants. Ufa, pp. 82-84 (in Russian) (1984).
 39. Duamin, V.V.; Denisov, V.L.; Andropova, S.N.; Maletin, V.P.: Influence of Hydrazine on Reproductive Function of Animals when Administered in Organisms by Different Routes. *Gig. Sanit.* 9:25-28 (in Russian) (1984).
 40. Freese, E.B.; Gerson, J.; Taber, H.; et al.: Inactivating DNA Alterations Induced by Peroxides and Peroxide-Producing Agents. *Mutat. Res.* 4:517-531 (1967).
 41. Bresler, S.E.; Kalinin, V.L.; Perumov, D.A.: Inactivation and Mutagenesis on Isolated DNA. II. Kinetics of Mutagenesis and Efficiency of Different Mutagens. *Mutat. Res.* 5:1-14 (1968).
 42. Jain, H.K.; Shukla, P.T.: Locus Specificity of Mutagens in *Drosophila*. *Mutat. Res.* 14:440-442 (1972).
 43. Reddy, G.M.; Reddy, T.P.: Induction of Mutations by Hydrazine in Rice. *Indian J. Genet. Plant Breed.* 32:388-391 (1972).
 44. Hsie, A.W.; O'Neill, J.P.; Machanoff, R.; et al.: Screening for Mutagenic Response of Four Coded Chemical by the CHO/HGPRT System. In: Evaluation of Short-Term Tests for Carcinogens. Report of the International Collaborative Programme. F.J. de Serres and J. Ashby, Eds. *Prog. Mutat. Res.* 1:602-607 (1981).
 45. Rogers, A.M.; Back, K.C.: Comparative Mutagenicity of Hydrazine and Three Methylated Derivatives in L5178Y Mouse Lymphomas Cells. *Mutat. Res.* 89:321-328 (1981).
 46. Kumari, H.L.; Dudi, D.V.; Iype, P.T.: Hydrazine-induced Mutation in Rat Liver Epithelial Cells. *Proc. Am. Assoc. Cancer Res.* 33:192 (1992).
 47. Purchase, I.F.H.; Longstaff, E.; Ashby, J.: An Evaluation of Six Short-Term Tests for Detecting Organic Chemical Carcinogens. *Br. J. Cancer* 37:873-935 (1978).
 48. Bridges, B.A.; MacGregor, D.; Zeiger, E.: Summary Report on the Performance of Bacterial Mutation Assays. In: Evaluation of Short-Term Tests for Carcinogens. Report of the International Collaborative Programme. F.J. de Serres and J. Ashby, Eds. *Prog. Mutat. Res.* 1:45-67 (1981).
 49. Rosenkranz, H.S.; Poirier, L.A.: Evaluation of the Mutagenicity and DNA-Modifying Activity of Carcinogens and Non-Carcinogens in Microbial Systems. *J. Natl. Cancer Inst.* 62:873-892 (1979).
 50. Mehta, R.D.; Von Boistel, R.C.: Mutagenic Activity of 42 Uncoded Compounds in the Haploid Yeast Reversion Assay, Strain XV 185-¹⁴C. In: Evaluation of Short-Term Tests for Carcinogens. Report of the International Collaborative Programme. F.J. de Serres and J. Ashby, Eds. *Prog. Mutat. Res.* 1:414-423 (1981).
 51. Rohrborn, G.; Propping, P.; Buselmaier, W.: Mutagenic Activity of Isoniazid and Hydrazine in Mammalian Test Systems. *Mutat. Res.* 16:189-194 (1972).
 52. Shukla, P.T.: Analysis of Mutagen Specificity in *Drosophila melanogaster*. *Mutat. Res.* 16:363-371 (1972).
 53. Gupta, R.S.; Grover, N.S.: Hydrazine-Induced Breaks in Chromosomes of *Cicia faba*. *Mutat. Res.* 10:519-520 (1970).
 54. Heindorff, K.; Rieger, R.; Veleminsky, J.; Gichner, T.: A Comparative Study of the Clastogenicity of Maleic Hydrazine and Some of its Putative Degradation Products. *Mutat. Res.* 140:123-126 (1984).
 55. Natarajan, A.T.; Van Kesteren-Van Leeuwen, A.C.: Mutagenic Activity of 20 Coded Compounds in Chromosome Aberrations/Sister Chromatid Exchanges Assay Using Chinese Hamster Ovary (CHO) Cells. In: Evaluation of Short-Term Tests for Carcinogens. Report of the International Collaborative Programme. F.J. de Serres and J. Ashby, Eds. *Prog. Mutat. Res.* 1:551-559 (1981).
 56. MacRae, W.D.; Stich, H.F.: Induction of Sister Chromatid Exchanges in Chinese Hamster Ovary Cells by Thiol and Hydrazine Compounds. *Mutat. Res.* 68:351-365 (1979).
 57. Baker, R.S.U.; Mitchell, G.A.; Meher-Homji, K.M.; Podobna, E.: Sensitivity of Two Chinese Hamster Cell Lines to SCE Induction by a Variety of Chemical Mutagens. *Mutat. Res.* 118:103-116 (1983).
 58. Speit, G.; Wick, C.; Wolf, M.: Induction of Sister Chromatid Exchanges by Hydroxylamine, Hydrazine, and Isoniazid and Their Inhibition by Cysteine. *Hum. Genet.* 54:155-158 (1980).
 59. Salomone, M.F.; Heddle, J.A.; Katz, M.: Mutagenic Activity of 41 Compounds in the *in vivo* Micronucleus Assay. In: Evaluation of Short-Term Tests for Carcinogens. Report of the International Collaborative Programme. F.J. de Serres and J. Ashby, Eds. *Prog. Mutat. Res.* 1:686-697 (1981).
 60. Kirkhart, B.: Micronucleus Test on 21 Compounds. In: Evaluation of Short-Term Tests for Carcinogens. Report of the International Collaborative Programme. F.J. de Serres and J. Ashby, Eds. *Prog. Mutat. Res.* 1:698-704 (1981).
 61. Tsuchimoto, T.; Matter, B.E.: Activity of Coded Compounds in the Micronucleus Test. In: Evaluation of Short-Term Tests for Carcinogens. Report of the International Collaborative Programme. F.J. de Serres and J. Ashby, Eds. *Prog. Mutat. Res.* 1:705-711 (1981).
 62. Wargovich, M.J.; Goldberg, M.T.; Newmark, H.L.; Bruce, W.R.: Nuclear Aberrations as a Short-Term Test for Genotoxicity to the Colon: Evaluation of 19 Agents in Mice. *J. Natl. Cancer Inst.* 71:133-137 (1983).
 63. Epstein, S.S.; Arnold, E.; Andrea, J.; et al.: Detection of Chemical Mutagens by the Dominant Lethal Assay in the Mouse. *Toxicol. Appl. Pharmacol.* 23:288-325 (1972).
 64. Evans, D.M.: Two Cases of Hydrazine Hydrate Dermatitis Without Systemic Intoxication. *Br. J. Ind. Med.* 16:126-127 (1959).
 65. Frost, J.; Hjorth, N.: Contact Dermatitis from Hydrazine Hydrochloride in Soldering Flux. Cross-Sensitization to Apresoline and Isoniazid. *Acta Derm. Venereol.* 39:82-86 (1959).
 66. Wheeler, C.E.; Penn, S.R.; Cawley, E.P.; Hill, C.: Dermatitis from Hydrazine Hydrobromide Solder Flux. *Arch. Dermatol.* 91:235-239 (1965).
 67. Zina, G.; Bonu, G.: Occupational Dermatitis from Hydrazine and Derivatives. *Minerva Dermatol.* 37:197-200 (in Italian) (1962).
 68. Schultheiss, E.: Hypersensitivity to Hydrazine. *Berufsdermatosen* 7:131-136 (in German) (1959).
 69. Hovding, G.: Occupational Dermatitis from Hydrazine Hydrate Used in Boiler Protection. *Acta Derm. Venereol.* 47:293-297 (1967).
 70. Von Keilg, W.; Speer, U.: Occupational Allergic Contact Dermatitis from Hydrazine. *Derm. Beruf Umwelt.* 31:25-27 (in German) (1983).
 71. Von Brandt, B.: On Allergic Skin Damage by Hydrazine Sulfate. *Dermatol. Wochenschr.* 141:376-381 (in German) (1960).
 72. Sonneck, H.J.; Umlauf, H.: Occupationally Sustained Skin Damage by Hydrazine. *Zeitschrift Haut Geschlechtskr.* 3:179-184 (in German) (1961).

73. Van Ketal, W.G.: Contact Dermatitis from a Hydrazine Derivative in a Stain Remover. Cross-Sensitization to Apresoline and Isoniazid. *Acta Derm. Venereol.* 44:49-53 (1964).
74. Drews, A.; Eversmann, K.; Fritze, E.: On Oral Poisoning by Hydrazine. *Med. Welt* 23:1295-1297 (in German) (1960).
75. Reid, F.J.: Hydrazine Poisoning. *Br. Med. J.* 5472:1246 (1965).
76. Harati, Y.; Niakan, E.: Hydrazine Toxicity, Pyridoxine Therapy, and Peripheral Neuropathy. *Ann. Intern. Med.* 104:728-729 (1986).
77. Kirklin, J.K.; Watson, M.; Bondoc, C.C.; Burke, J.F.: Treatment of Hydrazine-Induced Coma with Pyridoxine. *N. Engl. J. Med.* 294:938-939 (1976).
78. Frierson, W.M.: Use of Peridoxine HCl in Acute Hydrazine and UDMH Intoxication. *Ind. Med. Surg.* 34:650-651 (1965).
79. Sotaniemi, E.; Hirvonen, J.; Isomaki, H.; et al.: Hydrazine Toxicity in the Human. Report of a Fatal Case. *Ann. Clin. Res.* 3:30-33 (1971).
80. Wald, N.; Boreham, J.; Doll, R.; Bonsai, J.: Occupational Exposure to Hydrazine and Subsequent Risk of Cancer. *Br. J. Ind. Med.* 41:31-34 (1984).
81. Goodman, G.; Wilson, R.: Quantitative Prediction of Human Cancer Risk from Rodent Carcinogenic Potencies — A Closer Look at the Epidemiological Evidence for Some Chemicals Not Definitively Carcinogenic in Humans. *Regul. Toxicol. Pharmacol.* 14:118-146 (1991).
82. Roe, F.J.C.: Letter to the Editor. Hydrazine. *Ann. Occup. Hyg.* 21:323-326 (1978).
83. Hamill, P.V.V.: Number of Heart Attack Cases Among Workers of the Lake Charles Hydrazine Plant, 1953-78. Submitted to the U.S. Environmental Protection Agency by the Olin Corporation, Stamford, CT, under Toxic Substances Control Act, Section 8(e).
84. Kinkead, E.R.; Haun, C.C.; Vernot, E.H.; et al.: A Chronic Inhalation Toxicity Study of Monomethylhydrazine. AFAMRL-TR-85-025. Air Force Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, OH (1985).
85. U.S. Department of Labor, Occupational Safety and Health Administration: 29 CFR Part 1910.1000, Air Contaminants; Final Rule. Fed. Reg. 54(12):2332-2983 (January 19, 1989).
86. U.S. Court of Appeals for the Eleventh Circuit: AFL-CIO v. OSHA, CA 11, No. 89-7185 (July 7, 1992).
87. U.S. Department of Labor, Occupational Safety and Health Administration: 29 CFR Part 1910.1000 — Air Contaminants, Table Z-1; Amended by Fed. Reg. 58:35308, 35340 (June 30, 1993); corrected by Fed. Reg. 58:40191 (July 27, 1993).
88. National Institute for Occupational Safety and Health: Hydrazine. In: Documentation for Immediately Dangerous to Life or Health Concentrations (IDLHs), pp. 250-251. H.R. Ludwig, S.G. Cairelli, and J.J. Whalen, Eds. NTIS Pub. No. PB94-195047. National Technical Information Service, Springfield, VA (1994).
89. National Institute for Occupational Safety and Health: Criteria for a Recommended Standard — Occupational Exposure to Hydrazines. DHEW (NIOSH) Pub. No. 78-172; NTIS Pub. No. PB-81-225-690. National Technical Information Service, Springfield, VA (1978).