1,1-DIMETHYLHYDRAZINE

Data were last reviewed in IARC (1974) and the compound was classified in *IARC Monographs* Supplement 7 (1987).

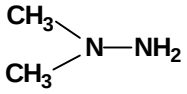
1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 57-14-7
Chem. Abstr. Name: 1,1-Dimethylhydrazine
IUPAC Systematic Name: 1,1-Dimethylhydrazine
Synonyms: Dimazine; dimazin; UDMH

1.1.2 *Structural and molecular formulae and relative molecular mass*



$C_2H_8N_2$ Relative molecular mass: 60.10

1.1.3 *Chemical and physical properties of the pure substance*

(*a*) *Description*: Flammable, hygroscopic liquid. Fumes in air and gradually turns yellow. Characteristic ammonia-like fishy odour of aliphatic hydrazines (Budavari, 1996)
(*b*) *Boiling-point*: 63.9°C (Lide, 1995)
(*c*) *Melting-point*: –58°C (Lide, 1995)
(*d*) *Solubility*: Miscible with water with evolution of heat. Also miscible with ethanol, diethyl ether, dimethylformamide and hydrocarbons (Budavari, 1996)
(*e*) *Vapour pressure*: 17 kPa at 25°C; relative vapour density (air = 1), 2.07 (Verschueren, 1996)
(*f*) *Flash point*: –15°C, closed cup (Lewis, 1993)
(*g*) *Explosive limits*: upper limits, 95%; lower, 2% by volume in air (American Conference of Governmental Industrial Hygienists, 1991)
(*h*) *Conversion factor*: $mg/m^3 = 2.46 \times ppm$

1.2 Production and use

1,1-Dimethylhydrazine is used as a component of jet and rocket fuels, for chemical synthesis, as a stabilizer for organic peroxide fuel additives, as an absorbent for acid gases, in photography and as a plant growth control agent (Lewis, 1993).

1.3 Occurrence

1.3.1 *Occupational exposure*

No data were available to the Working Group.

1.3.2 *Environmental occurrence*

Production and use of 1,1-dimethylhydrazine may result in its release to the environment (United States National Library of Medicine, 1997).

1.4 Regulations and guidelines

The American Conference of Governmental Industrial Hygienists (ACGIH) (1997) has recommended 0.025 mg/m^3 as the threshold limit value for occupational exposures to 1,1-dimethylhydrazine in workplace air. Similar values have been used as standards or guidelines in many countries (International Labour Office, 1991).

No international guideline for 1,1-dimethylhydrazine in drinking-water has been established (WHO, 1993).

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

1,1-Dimethylhydrazine was tested for carcinogenicity in mice after oral administration, producing tumours at various sites including a high incidence of vascular tumours. The observation of a few liver tumours after high oral doses of 1,1-dimethylhydrazine occurring in rats after a long latent period was inadequate for evaluation of the carcinogenic effect in this species (IARC, 1974).

3.1 Subcutaneous injection

Hamster: Groups of 15 male and 15 female European hamsters (*Cricetus cricetus*) [age unspecified] were given weekly subcutaneous injections of 1/10 of the LD_{50} (LD_{50}: 373 mg/kg bw for males and 325 mg/kg bw for females) of 1,1-dimethylhydrazine in saline for life. A group of eight males and eight females served as controls. Hamsters were observed until spontaneous death. Six males and six females treated with 1,1-dimethylhydrazine developed peripheral nerve sheath tumours (neurofibrosarcoma,

melanotic and unpigmented schwannoma). No tumour of this type was observed in the untreated controls (Ernst *et al*., 1987).

Groups of 12 male and 12 female Syrian golden hamsters (*Mesocricetus auratus*) were given subcutaneous injections of 8, 17 or 35 (1/10 of the LD_{50}) mg/kg bw 1,1-dimethylhydrazine weekly for life. A group of seven males and seven females given saline served as controls. Nonsignificant increases in the incidence of malignant lymphomas in females given the intermediate dose (4/12 versus 1/7) and that of benign phaeochromocytoma in males given the lowest dose (4/12 versus 1/7) were observed (Jeong & Kamino, 1993).

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

No data were available to the Working Group.

4.1.2 *Experimental systems*

Godoy *et al*. (1984) have studied the metabolic fate of 1,1-dimethylhydrazine in the context of its role as a reductive metabolite of the carcinogen *N*-nitrosodimethylamine. In rat liver slices, [^{14}C]dimethylhydrazine is activated to metabolites which bind to nucleic acids. In rat liver microsomes and 9000 × *g* supernatants (microsomes plus cytosol), it is converted to formaldehyde. In microsomes, this process has the characteristics of a cytochrome P450-mediated reaction, requiring NADPH and oxygen, but in the 9000 × *g* supernatant, this cofactor dependence was not seen, suggesting that the reaction was non-enzymatic. Metabolism in these systems also resulted in covalent binding of radioactivity that showed comparable enzymatic and non-enzymatic components. These data show that 1,1-dimethylhydrazine might not be a detoxication product of *N*-nitrosodimethylamine but contributes to its covalent binding to nucleic acids and proteins.

4.2 Toxic effects

4.2.1 *Humans*

No data were available to the Working Group.

4.2.2 *Experimental systems*

In female Sprague-Dawley rats, daily intraperitoneal injections of 10, 30, 50 or 70 mg/kg bw 1,1-dimethylhydrazine resulted in the death of 0, 5, 6 and 9 out of 10 animals per group (Cornish & Hartung, 1969). Surviving animals showed diuresis, increased serum transaminase levels and histopathological signs of mild kidney damage.

Daily intraperitoneal injection of BALB/c and C57BL/6 mice with 5, 10, 25, 50 or 75 mg/kg bw 1,1-dimethylhydrazine for seven days resulted in a significant increase in one-way mixed lymphocyte response (MLR) (Tarr *et al*., 1988). When only the responder

mice (C57BL/6) were treated, the response was also increased. The authors suggested that B cells and/or macrophages may represent a target cell subpopulation for the immunoenhancing effect of 1,1-dimethylhydrazine. Since prostaglandin E_2 production by adherent splenocytes (enriched for macrophages) *in vitro* was significantly reduced at 10 μg/mL of 1,1-dimethylhydrazine, the authors suggested that inhibition of prostaglandin E_2 synthesis, a suppressor of the MLR, might explain the immunoenhancement by 1,1-dimethylhydrazine.

The 48-h concanavalin A-induced lymphoblastogenic responses in splenocytes isolated from BALB/c mice treated with *Corynebacterium parvum* and 1,1-dimethylhydrazine mice were significantly increased in comparison with *C. parvum* treatment alone (Frazier *et al*., 1992), indicating that 1,1-dimethylhydrazine can overcome certain types of immunosuppression.

In murine splenocytes in culture, however, 10–50 μg/mL 1,1-dimethylhydrazine inhibited concanavalin A-stimulated DNA synthesis (Bauer *et al*., 1990). Similar suppression was observed in interleukin 2-dependent CTLL-20 cells when DNA synthesis was stimulated with interleukin 2.

4.3 Reproductive and developmental effects

4.3.1 *Humans*

No data were available to the Working Group.

4.3.2 *Experimental systems*

Keller *et al*. (1984) investigated the embryotoxicity and teratogenicity of 1,1-dimethylhydrazine in pregnant Fischer 344 rats. In the high-dose group treated intraperitoneally with 60 mg/kg bw 1,1-dimethylhydrazine per day on days 6–15 of gestation, maternal weight gains and mean fetal weights were significantly reduced. The numbers of implants and of viable fetuses per litter were also less than in controls, although not reduced significantly, and the number of malformations (unfused ossification centres of vertebrae, anophthalmia or severe microphthalmia, hydronephrosis, agenesis of kidney, hydrocephalic fetus, unossified sternebrae) was moderately increased. At a daily dose of 30 mg/kg bw, these effects were not observed.

4.4 Genetic and related effects

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems* (see Table 1 for references)

In mammalian cells treated *in vitro*, 1,1-dimethylhydrazine induced gene mutations in Chinese hamster lung V79 cells and in mouse lymphoma L5178Y cells, chromosomal aberrations in Chinese hamster ovary cells and unscheduled DNA synthesis in mouse hepatocytes but not in rat hepatocytes. In a single study, it induced somatic mutations in *Drosophila melanogaster*. There is conflicting evidence as to its mutagenicity to bacteria.

Table 1. Genetic and related effects of 1,1-dimethylhydrazine

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
PRB, Prophage induction, SOS repair test, DNA strand breaks, cross-links or related damage	NT	–	17000	Ho & Ho (1981)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	2000	Brusick & Matheson (1976)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	+	250	Bruce & Heddle (1979)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	1500	Von Wright & Tikkanen (1980)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	4800	De Flora (1981)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	4015	Parodi *et al.* (1981)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	NG	De Flora *et al.* (1984)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	–	NG	Matsushita *et al.* (1993)
SA2, *Salmonella typhimurium* TA102, reverse mutation	+	–	NG	Matsushita *et al.* (1993)
SA3, *Salmonella typhimurium* TA1530, reverse mutation	(+)	NT	5000	Tosk *et al.* (1979)
SA3, *Salmonella typhimurium* TA1530, reverse mutation	–	–	15000	Bartsch *et al.* (1980)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	2000	Brusick & Matheson (1976)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	250	Bruce & Heddle (1979)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	4800	De Flora (1981)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	4015	Parodi *et al.* (1981)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	500	Rogan *et al.* (1982)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	NG	De Flora *et al.* (1984)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	2000	Brusick & Matheson (1976)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	250	Bruce & Heddle (1979)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	4800	De Flora (1981)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	4015	Parodi *et al.* (1981)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	500	Rogan *et al.* (1982)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	NG	De Flora *et al.* (1984)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	2000	Brusick & Matheson (1976)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	4800	De Flora (1981)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	4015	Parodi *et al.* (1981)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	NG	De Flora *et al*. (1984)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	4800	Brusick & Matheson (1976)
SA9, *Salmonella typhimurium* TA98, reverse mutation	(+)	(+)	NG	De Flora (1981)
SA9, *Salmonella typhimurium* TA98, reverse mutation	(+)	(+)	1262	Parodi *et al.* (1981)
SA9, *Salmonella typhimurium* TA98, reverse mutation	(+)	(+)	NG	De Flora *et al*. (1984)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	+	250	Bruce & Heddle (1979)
SAS, *Salmonella typhimurium* TAG46, reverse mutation	–	–	15000	Bartsch *et al*. (1980)
ECW, *Escherichia coli* WP2 *uvr*A, reverse mutation	–	–	2000	Brusick & Matheson (1976)
ECW, *Escherichia coli* WP2 *uvr*A, reverse mutation	–	NT	120	Von Wright & Tikkanen (1980)
SCG, *Saccharomyces cerevisiae*, gene conversion	–	–	2000	Brusick & Matheson (1976)
ANF, *Aspergillus nidulans*, forward mutation	+	NT	100	Bignami *et al*. (1981)
DMM, *Drosophila melanogaster*, somatic mutation (*white/white+)*	+		150 feed	Vogel & Nivard (1993)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutations	–		1200 inj	Zijlstra & Vogel (1988)
DIA, DNA strand breaks, rat hepatocytes *in vitro*	+	NT	2	Sina *et al*. (1983)
URP, Unscheduled DNA synthesis, ACI/N rat primary hepatocytes *in vitro*	–	NT	60	Mori *et al.* (1988)
UIA, Unscheduled DNA synthesis, C3HeN mouse primary hepatocytes *in vitro*	+	NT	60	Mori *et al.* (1988)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus *in vitro*	+	+	80	Brusick & Matheson (1976)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus *in vitro*	+	NT	6	Rogers & Back (1981)
G51, Gene mutation, mouse lymphoma L5178Y cells, ouabain resistance and cytosine arabinoside resistance *in vitro*	–	NT	300	Rogers & Back (1981)
G9H Gene mutation, Chinese hamster lung V79 cells, *hprt* locus (metabolic activation with rat liver perfusate) *in vitro*	–	+	300	Beije *et al.* (1984)
CIC, Chromosomal aberrations, Chinese hamster ovary CHO cells *in vitro*	+	(+)	20	JETOC (1997)
HMM, Host-mediated assay, *Salmonella typhimurium* TA1950 in NMRI mouse host	–		140 po × 1	Von Wright & Tikkanen (1980)
DVA, DNA fragmentation, Swiss albino mouse lung *in vivo*	+		42 ip × 5	Parodi *et al.* (1981)
DVA, DNA fragmentation, Swiss albino mouse liver *in vivo*	+		42 ip × 5	Parodi *et al.* (1981)
UVR, Unscheduled DNA synthesis, Fischer 344 rat kidney cells *in vivo*	–		50 ip × 1	Tyson & Mirsalis (1985)
MVM, Micronucleus test, CD1 mouse splenocytes *in vivo*	+		13.8 ip × 1	Benning *et al.* (1994)
MVM, Micronucleus test, CD1/CR mouse bone-marrow cells *in vivo*	–		83 ip × 1	Cliet *et al.* (1993)
MVM, Micronucleus test, CD1/CR mouse spermatids *in vivo*	+		83 ip × 1	Cliet *et al.* (1993)
MVM, Micronucleus test, CD1/CR mouse hepatocytes *in vivo*	+		14 ip × 2	Cliet *et al.* (1989)
MVM, Micronucleus test, (C57BL/6 × C3H/He) F_1 mouse bone-marrow *in vivo*	–		500 ip × 5	Bruce & Heddle (1979)
MVM, Micronucleus test, mouse bone marrow (BALB/c AnNCrj) *in vivo*	–		20 ip × 1	Suzuki *et al.* (1994)
DLM, Dominant lethal test, ICR/Ha Swiss mice *in vivo*	–		63 ip × 1	Epstein *et al.* (1972)
DLM, Dominant lethal test, mice *in vivo*	–		12.5 ip × 5	Brusick & Matheson (1976)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
BVD, Binding (covalent) to DNA, formation of *N*7-methylguanine in Sprague-Dawley rat liver DNA *in vivo*	+		19 po × 1	Sagelsdorff *et al.* (1988)
SPM, Sperm abnormality test, (C57BL/6 × C3H/He) F_1 mouse *in vivo*	–		500 ip × 5	Bruce & Heddle (1979)
SPM, Sperm morphology, (C57BL/6 × C3H/He) F_1 mice *in vivo*	–		100 ip × 5	Wyrobek & Bruce (1975)
Colonic nuclear aberration assay in C57BL/6J mice, *in vivo*	–		100 po × 1	Wargovich *et al.* (1983)

[a] +, positive; (+), weak positive; –, negative; NT, not tested
[b] LED, lowest effective dose; HID, highest ineffective dose; in-vitro tests, μg/mL; in-vivo tests, mg/kg bw/day; NG, not given; inj, injection; ip, intraperitoneal; po, oral

In a single study, 1,1-dimethylhydrazine formed *N*7-methylguanine with DNA in the liver of rats treated *in vivo*. Given to mice *in vivo*, it did not induce sperm abnormalities, nuclear aberrations in the colon or micronucleus formation in the bone marrow, but, in single studies, it did induce micronucleus formation in spermatids, splenocytes and hepatocytes. In one study, 1,1-dimethylhydrazine induced DNA fragmentation in lung and in liver of mice *in vivo.* It failed to induce unscheduled DNA synthesis in kidney cells of rats in a single study conducted *in vivo*. It produced negative results in a host-mediated assay using mice.

5. Evaluation

No epidemiological data on the carcinogenicity of 1,1-dimethylhydrazine were available.

There is *sufficient evidence* in experimental animals for the carcinogenicity of 1,1-dimethylhydrazine.

Overall evaluation

1,1-Dimethylhydrazine is *possibly carcinogenic to humans (Group 2B)*.

6. References

American Conference of Governmental Industrial Hygienists (1991) *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 6th Ed., Vol. 1, Cincinnatti, OH, pp. 491–494

American Conference of Governmental Industrial Hygienists (1997) *1997 TLVs®* and *BEIs®*, Cincinnatti, OH, p. 23

Bartsch, H., Malaveille, C., Camus, A.-M., Martel-Planche, G., Brun, G., Hautefeuille, A., Sabadie, N., Barbin, A., Kuroki, T., Drevon, C., Piccoli, C. & Montesano, R. (1980) Validation and comparative studies on 180 chemicals with *S. typhimurium* strains and V79 Chinese hamster cells in the presence of various metabolizing systems. *Mutat. Res.*, **76**, 1–50

Bauer, R.M., Tarr, M.J. & Olsen, R.G. (1990) Effect of 1,1-dimethylhydrazine on lympho-proliferation and interleukin 2 immunoregulatory function. *Arch. environ. Contam. Toxicol.*, **19**, 148–153

Beije, B., Onfelt, A. & Olsson, U. (1984) Influence of dietary selenium on the mutagenic activity of perfusate and bile from rat liver, perfused with 1,1-dimethylhydrazine. *Mutat. Res.*, **130**, 121–126

Benning, V., Brault, D., Duvinage, C., Thybaud, V. & Melcion, C. (1994) Validation of the in vivo CD1 mouse splenocyte micronucleus test. *Mutagenesis*, **9**, 199–204

Bignami, M., Conti, G., Crebelli, R. & Carere, A. (1981) Growth-mediated metabolic activation of promutagens in *Aspergillus nidulans*. *Mutat. Res.*, **80**, 265–272

Bruce, W.R. & Heddle, J.A. (1979) The mutagenic activity of 61 agents as determined by the micronucleus, *Salmonella*, and sperm abnormality assays. *Can. J. Genet. Cytol.*, **21**, 319–334

Brusick, D. & Matheson, D. (1976) Mutagenic evaluation of 1,1-dimethylhydrazine, methylhydrazine and *N*-phenyl-α-naphthylamine. In: *Proceedings of the 7th Annual Conference on Environmental Toxicology*, Kensington, MD, Litton Bionetics

Budavari, S., ed. (1996) *The Merck Index*, 12th Ed., Whitehouse Station, NJ, Merck & Co., p. 549

Cliet, I., Fournier, E., Melcion, C. & Cordier, A. (1989) In vivo micronucleus test using mouse hepatocytes. *Mutat. Res.*, **216**, 321–326

Cliet, I., Melcion, C. & Cordier, A. (1993) Lack of predictivity of bone marrow micronucleus test versus testis micronucleus test: comparison with four carcinogens. *Mutat. Res.*, **292**, 105–111

Cornish, H.H. & Hartung, R. (1969) The subacute toxicity of 1,1-dimethylhydrazine. *Toxicol. appl. Pharmacol.*, **15**, 62–68

De Flora, S. (1981) Study of 106 organic and inorganic compounds in the *Salmonella*/microsome test. *Carcinogenesis*, **2**, 283–298

De Flora, S., Zanacchi, P., Camoirano, A., Bennicelli, C. & Badolati, G.S. (1984) Genotoxic activity and potency of 135 compounds in the Ames reversion test and in a bacterial DNA-repair test. *Mutat. Res.*, **133**, 161–198

Epstein, S.S., Arnold, E., Andrea, J., Bass, W. & Bishop, Y. (1972) Detection of chemical mutagens by the dominant lethal assay in the mouse. *Toxicol. appl. Pharmacol.*, **23**, 288–325

Ernst, H., Rittinghausen, U., Wahnschaffe, U. & Mohr, U. (1987) Induction of malignant peripheral nerve sheath tumors in European hamsters with 1,1-dimethylhydrazine (UDMH). *Cancer Lett.*, **35**, 303–311

Frazier, D.E., Jr, Bauer, R.M., Tarr, M.J. & Olsen, R.G. (1992) Effect of 1,1-dimethylhydrazine (UDMH) on *Corynebacterium parvum*-associated immunosuppression in mice. *Int. J. Immunopharmacol.*, **14**, 27–34

Godoy, H.M., Díaz Gomez, M.I. & Castro, J.A. (1984) Metabolism and activation of 1,1-dimethylhydrazine and methylhydrazine, two products of *N*-nitrosodimethylamine reductive biotransformation. In: O'Neill, I.K., von Borstel, R.C., Miller, C.T., Long, J. & Bartsch, H., eds, N-*Nitroso Compounds: Occurrence, Biological Effects and Relevance to Human Cancer* (IARC Scientific Publications No. 57), Lyon, IARC, pp. 479–484

Ho, Y.L. & Ho, S.K. (1981) Screening of carcinogens with the prophage λcl*ts*857 induction test. *Cancer Res.*, **41**, 532–536

IARC (1974) *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*, Lyon, pp. 137–143

IARC (1987) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Supplement 7, *Overall Evaluations of Carcinogenicity: An Updating of* IARC Monographs *Volumes 1 to 42*, Lyon, p. 62

International Labour Office (1991) *Occupational Exposure Limits for Airborne Toxic Substances*, 3rd. Ed. (Occupational Safety and Health Series No. 37), Geneva, pp. 170–171

Jeong, J. & Kamino, K. (1993) Lack of tumorigenic activity of 1,1-dimethylhydrazine in Syrian golden hamsters treated by subcutaneous injection. *Exp. Toxicol. Pathol.*, **45**, 61–63

JETOC (1997) *Mutagenicity Test Data of Existing Chemical Substances*, Tokyo, Japan Chemical Industry Ecology-Toxicology and Information Center, pp. 282–283

Keller, W.C., Olson, C.T., Back, K.C. & Gaworski, C.L. (1984) Teratogenic assessment of three methylated hydrazine derivatives in the rat. *J. Toxicol. environ. Health*, **13**, 125–131

Lewis, R.J., Jr (1993) *Hawley's Condensed Chemical Dictionary*, 12th Ed., New York, Van Nostrand Reinhold, p. 417

Lide, D.R., ed. (1995) *CRC Handbook of Chemistry and Physics*, 76th Ed., Boca Raton, FL, CRC Press, p. 3-196

Matsushita, H., Jr, Endo, O., Matsushita, H., Yamamoto, M. & Mochizuki, M. (1993) Mutagenicity of alkylhydrazine oxalates in *Salmonella typhimurium* TA100 and TA102 demonstrated by modifying the growth conditions of the bacteria. *Mutat. Res.*, **301**, 213–222

Mori, H., Sugie, S., Yoshimi, N., Iwata, H., Nishikawa, A., Matsukubo, K., Shimizu, H. & Hirono, I. (1988) Genotoxicity of a variety of hydrazine derivatives in the hepatocyte primary culture/DNA repair test using rat and mouse hepatocytes. *Jpn. J. Cancer Res.*, **79**, 204–211

Parodi, S., De Flora, S., Cavanna, M., Pino, A., Robbiano, L., Bennicelli, C. & Brambilla, G. (1981) DNA-damaging activity *in vivo* and bacterial mutagenicity of sixteen hydrazine derivatives as related quantitatively to their carcinogenicity. *Cancer Res.*, **41**, 1469–1482

Rogan, E.G., Walker, B.A., Gingell, R., Nagel, D.L. & Toth, B. (1982) Microbial mutagenicity of selected hydrazines. *Mutat. Res.*, **102**, 413–424

Rogers, A.M. & Back, K.C. (1981) Comparative mutagenicity of hydrazine and 3 methylated derivatives in L5178Y mouse lymphoma cells. *Mutat. Res.*, **89**, 321–328

Sagelsdorff, P., Lutz, W.K. & Schlatter, C. (1988) DNA methylation in rat liver by daminozide, 1,1-dimethylhydrazine, and dimethylnitrosamine. *Fundam. appl. Toxicol.*, **11**, 723–730

Sina, J.F., Bean, C.L., Dysart, G.R., Taylor, V.I. & Bradley, M.O. (1983) Evaluation of the alkaline elution/rat hepatocyte assay as a predictor of carcinogenic/mutagenic potential. *Mutat. Res.*, **113**, 357–391

Suzuki, Y., Shimizu, H., Ishikawa, T., Sakaba, H., Fukumoto, M., Okonogi, H. & Kadokura, M. (1994) Effects of prostaglandin E2 on the micronucleus formation in mouse bone-marrow cells by various mutagens. *Mutat. Res.*, **311**, 287–293

Tarr, M.J., McKown, B.J. & Olsen, R.G. (1988) Enhancement of murine mixed lymphocyte response by 1,1-dimethylhydrazine: Characterisation and possible mechanisms. *Cancer Detect. Prev.*, **12**, 573–581

Tosk, J., Schmeltz, I. & Hoffmann, D. (1979) Hydrazines as mutagens in a histidine-requiring auxotroph of *Salmonella typhimurium*. *Mutat. Res.*, **66**, 247–252

Tyson, C.K. & Mirsalis, J.C. (1985) Measurement of unscheduled DNA synthesis in rat kidney cells following in vivo treatment with genotoxic agents. *Environ. Mutag.*, **7**, 889–899

United States National Library of Medicine (1997) *Hazardous Substances Data Bank (HSDB)*, Bethesda, MD [Record No. 528]

Verschueren, K. (1996) *Handbook of Environmental Data on Organic Chemicals*, 3rd Ed., New York, Van Nostrand Reinhold, pp. 824–825

Vogel, E.W. & Nivard, M.J. (1993) Performance of 181 chemicals in a *Drosophila* assay predominantly monitoring interchromosomal mitotic recombination. *Mutagenesis*, **8**, 57–81

Von Wright, A. & Tikkanen, L. (1980) The comparative mutagenicities of hydrazine and its mono- and di-methyl derivatives in bacterial test systems. *Mutat. Res.*, **78**, 17–23

Wargovich, M.J., Goldberg, M.T., Newmark, H.L. & Bruce, W.R. (1983) Nuclear aberrations as a short-term test for genotoxicity to the colon: evaluation of nineteen agents in mice. *J. natl Cancer Inst.*, **71**, 133–137

WHO (1993) *Guidelines for Drinking Water Quality*, 2nd Ed., Vol. 1, *Recommendations*, Geneva

Wyrobek, A.J. & Bruce, W.R. (1975) Chemical induction of sperm abnormalities in mice. *Proc. natl Acad. Sci. USA*, **72**, 4425–4429

Zijlstra, J.A. & Vogel, E.W. (1988) Influence of inhibition of the metabolic activation on the mutagenicity of some nitrosamines, triazenes, hydrazines and seniciphylline in *Drosophila melanogaster*. *Mutat. Res.*, **202**, 251–267