Fact Sheet Date: 9/17/92

NEW YORK STATE
- HUMAN HEALTH FACT SHEET -

Ambient Water Quality Value for
Protection of Sources of Potable Water

SUBSTANCE: Acetone **CAS REGISTRY NUMBER:** 67-64-1

AMBIENT WATER QUALITY VALUE: 50 ug/L

BASIS: General Organic Guidance Value [6 NYCRR 702.15 (a)(1)(ii)]

SUMMARY OF INFORMATION

Introduction:

Acetone, or 2-propanone has the formula C_3H_6O and a molecular weight of 58.08 (Walter et al., 1975). It is widely used as an industrial and general laboratory solvent (Merck, 1983; as cited by NTP, 1991).

Pharmacokinetics:

Acetone is reported to be readily absorbed by oral, dermal and inhalation administration (Rowe and Wolf, 1963, Krasavage et al., 1982; both as cited by NTP, 1991). Following absorption, this highly water soluble substance is readily taken up by the blood and widely and quickly distributed throughout the tissues according to their water content and is metabolized or excreted unchanged (Haggard et al., 1944, Rowe and Wolf, 1963, Krasavage et al., 1982, Wigaeus et al., 1982; all as cited by NTP, 1991). Three gluconeogenic pathways of acetone metabolism have been described (Price and Rittenberg, 1950, Sakami, 1950, Mourkides et al., 1959, Casazza et al., 1984, Kosugi et al., 1986a,b; all as cited by NTP, 1991).

Large doses of acetone are predominantly removed by its elimination unmetabolized, but metabolism plays a greater role in the removal of small doses (Haggard et al., 1944; as cited by NTP, 1991).

Acute Toxicity:

Oral LD_{50} values for acetone include 3,000 mg/kg in the mouse, 5,340 mg/kg in the rabbit, and 5,800 mg/kg in the rat (RTECS, 1992). LD_{50} values by other routes include 1,297 mg/kg in the mouse (intraperitoneal), 5,500 mg/kg in the rat (intravenous) and 20 g/kg in the rabbit (skin). An LC_{50} of 50,100 mg/m^3/8 H in the rat was also reported.

Chronic Toxicity:

A 1986 U.S. EPA 90-day gavage study in rats is the basis for an oral reference dose (RfD) for acetone (IRIS, 1991). In this study, groups of albino rats (30 animals/sex/group) were dosed with acetone at 0, 100, 500 or 2,500 mg/kg/day. No effects were observed at 100 mg/kg/day. Female rats showed significantly increased kidney weights in the 500- and 2,500 mg/kg/day groups. Both sexes exhibited increased liver weight and liver/body weight ratios and increased kidney-to-body and brain weight ratios at the high dose. A marked increase in severity in tubular degeneration of the kidneys and hyaline drop accumulation was noted with increasing doses. This accumulation was significant in males at 500 mg/kg/day and in both sexes at the high dose. A NOEL and LOAEL of 100 and 500 mg/kg/day respectively were identified, based on nephrotoxicity and increased liver and kidney weights.

NTP (1991) conducted a 13-week drinking water study in rats and mice. Male and female F344/N rats (10/sex/group) and female $B6C3F_1$ mice (10/group) were exposed to acetone in drinking water at 0, 2,500, 5,000, 10,000, 20,000 or 50,000 ppm. Male $B6C3F_1$ mice (10/group) were exposed to drinking water containing acetone at 0, 1,250, 2,500, 5,000, 10,000 or 20,000 ppm.

Effects in rats shown by the NTP study include increases in relative organ weights. Statistically significant differences were noted at 2,500 ppm and 20,000 ppm and up in females and 50,000 ppm in males for increases in relative kidney weights; 20,000 ppm and up for both sexes for increases in relative liver weights, and 50,000 ppm in males for an increase in relative testis weight. Also at 50,000 ppm, male rats exhibited depressed sperm motility, caudal weight, and epididymal weight and an increase in the incidence of abnormal sperm ($p < 0.05$ compared to controls for each parameter). In addition, sperm motility was decreased ($p < 0.01$) at 2,500 ppm but not at 10,000 ppm. Effects on the blood were noted at several dose levels. Males at the two highest doses demonstrated a statistically significant leukocytosis, caused by an absolute increase in lymphocytes. Females at 50,000 ppm exhibited the same effect. Other statistically significant hematological changes in males include increases in both mean corpuscular hemoglobin and mean cell volume at 2,500 ppm and at 10,000 ppm and higher, and a decreased concentration of reticulocytes at 5,000 ppm and up. Also in males, hemoglobin and

erythrocytes were significantly different from controls (decreased) at 5,000, 20,000 and 50,000 ppm. The same was true for hematocrit at 5,000 and 20,000 ppm. Male rats also showed an increase in the incidence and severity of nephropathy with increased dose, a spontaneous, long-term progressive condition.

Effects in mice reported by NTP include decreased fluid intake in females only at all dose levels. The only significant and consistent organ weight changes were in females at the high dose, as increased liver and decreased spleen weights. Statistically significant changes in hematologic parameters included increased hemoglobin at and above 5,000 ppm in males and 20,000 ppm in females, increased mean corpuscular hemoglobin in males at 20,000 ppm and increased hematocrit in females at 50,000 ppm. Centrilobular hepatocellular hypertrophy, at a minimal degree of severity, was noted in 2/10 females at 50,000 ppm.

Male Wistar rats exposed to drinking water containing 0.5% acetone (the only dose tested) for six weeks were assessed for neurobehavioural toxicity (rotarod test) and peripheral nerve conduction velocity (NCV) (Ladefoged et al., 1989). No effect on balance time was noted in the rotarod test, but NCV was reduced compared to controls after 6 weeks (value significantly different from control, $p<0.05$).

Rengstorff and Khafagy (1985) reported that guinea pigs treated once daily with 0.5 ml acetone, applied to the skin 5 days/week for 6 weeks developed cataracts (12/40 animals) approximately 3 months after the end of treatment. None were seen in the ten saline controls, but no statistical determination was provided.

Rengstorff et al. (1972) dosed albino guinea pigs cutaneously with 0.5 ml acetone 3x/week for 3 weeks. Animals were followed for six months after the initial administration. Two of 12 animals showed a cataractous response, specifically extensive vacuolated areas that involved the entire periphery of the lens. None in a group of over 500 unexposed animals had cataracts. In a second study, two out of four guinea pigs given 1.0 ml acetone cutaneously twice a day, five days per week for eight weeks developed cataracts within six months. No lens abnormalities were found in eight control animals. No statistical evaluations were provided for these two experiments.

In workers exposed to 1,000 ppm for three hours per day over a period of "many" years, complaints included chronic inflammation of airways, stomach and duodenum, and dizziness (Anon., 1985).

Reproductive/Developmental Effects:

Mast et al. (1988) reported a NOEL of 2,200 ppm for developmental toxicity of acetone by inhalation in both the Sprague-Dawley rat and Swiss mouse. Animals were exposed for 6 hr/day on days 6-17 (mice) and 6-19 (rats) of gestation. Mice exposed to 6,600 ppm acetone (reduced from 11,000 ppm after one day) exhibited a statistically

significant reduction in fetal weight and a statistically significant increase in the percent incidence of late resorptions. In rats, fetal weights were significantly reduced at 11,000 ppm compared to controls.

Mast et. al. (1989; unclear if the same as the preceding study) exposed Sprague-Dawley rats to acetone vapors for 6 hr/day, 7 days/week on days 6-19 of gestation and reported significantly reduced fetal body weights at 11,000 ppm. In Swiss (CD-1) mice exposed for the same duration on days 6-17 of gestation, the 6,600 ppm level showed a significant reduction in fetal body weights and a significant increase in resorptions.

In another inhalation study (Nizyayeva, 1982, as cited by NTP, 1991) animals (unspecified) exposed to acetone at 0, 30 or 300 mg/m^3 on days 1-20 of gestation showed a statistically significant but not concentration-related decrease in the percentage of live embryos at both test concentrations.

In pregnant women exposed to acetone at approximately 30 mg/m^3 and 300 mg/m^3 embryotropic effects ranging from high lipid levels to embryotoxic effects, respectively, were reported (Nizyaeva, 1982, as cited by Walsh, 1990).

In a study where chicken eggs were injected with 0.1 ml acetone, the treated group showed decreased percentage hatchability and increased embryonic mortality in the first week of incubation. (Ameenuddin and Sunde, 1984). Acetone was shown to result in embryolethality and dysmorphogenesis in an in vitro rat embryo study (Kitchin and Ebron, 1984).

Genotoxicity:

In a number of studies, acetone did not show genotoxic effects (all as cited by IRIS, 1991):

- Salmonella typhimurium strains TA 98 and TA 100; Schizosaccharomyces pombe strain P1 with or without liver homogenates (McCann et al., 1975; Abbondandolo et al., 1980; Maron et al., 1981; Hallstrom et al., 1981).
- Cell transformation systems (Freeman et al., 1973; Rhim et al., 1974; Quarles et al., 1979 a, b).
- Assays for chromosomal aberrations and sister chromatid exchange (Norppa et al., 1981; Norppa, 1981; Tates and Kriek, 1981).
- DNA binding (Kubinski et al., 1981).

- Point mutation in mouse lymphoma cells (Amacher et al., 1980).

- Transfection of E. coli CR63 cells (Vasavada and Padayatty, 1981).

Results for acetone were negative in five strains (TA98, TA100, TA1535, TA1537, TA1538) in the Ames Salmonella reverse mutation assay (De Flora et al., 1984; as cited by HSDB, 1992).

Acetone was reported to result in chromosomal aberrations in a study by Kawachie et al. (1980; as cited by IRIS, 1991). It was found to induce a dose-dependent increase in the frequency of chromosomal malsegregation using Saccharomyces cerevisiae D61.M (Albertini, 1991).

Oncogenicity:

U.S. EPA classifies acetone as D: not classifiable as to human carcinogenicity, on the basis of a lack of data concerning carcinogenicity in humans or animals (IRIS, 1991).

NTP (1991) states that, "there is no evidence that exposure to acetone is associated with an increased incidence of cancer in humans." Furthermore, NTP states that "no reports are available in the literature on the long-term toxicity or carcinogenicity of acetone to animals" (Kawachi et al., 1980, Soderman, 1982; both as cited by NTP, 1991).

A study in which 0.1 ml acetone was applied to the skin of 20 ICR/Ha Swiss mice 3x/week for 365 days, followed by observation for 208 additional days, revealed no tumors of any kind (Van Duuren et al., 1971, as cited by Walter et al., 1975). No tumors were found when the cervical protio and os of virgin C3H/HeJ mice were painted with an unspecified amount of acetone for periods of up to 5 months (Park and Koprowska, 1968; as cited by Walter et al., 1975).

Interactions with Other Substances:

NTP (1991) notes that acetone interacts synergistically with and exacerbates the hepatorenal toxicity and/or mutagenicity of a wide variety of carcinogens and/or toxicants. It was shown in mice that oral treatment with acetone before the administration of chloroform, 1,1,2-trichloroethane or trichloroethylene increased the hepatotoxicity of the chlorinated hydrocarbons (Traiger and Plaa, 1974; as cited by Walter et al., 1975). Acetone has been shown to enhance the mutagenicity of N-methyl-N'-nitro-N-nitrosoguanidine (Gichner and Veleminsky, 1987).

The toxicity (presumably rat oral LD_{50}) of 50% mixtures of acetone with 25 solvents was reported to be additive, that of 50/50 acetone/acetonitrile was supra-additive (Smyth et al., 1969; as cited by Walter et al., 1975).

The acute toxicity of ethanol to rats was potentiated by pretreatment with acetone (Patty; as cited by HSDB, 1992). Acetone in drinking water was found to potentiate the effect of 2,5-hexanedione on both behavior and nerve conduction velocity of rats (Ladefoged et al., 1989). 2,5-Hexanedione in combination with acetone results in non-reversible infertility (Larsen et al., 1991). Acetone has also been shown to potentiate the testis injuring effect of 2,5-hexanedione in the rat. Elovaara et al. (1990) reported that the pulmonary toxicity of styrene is potentiated by pretreatment with acetone. Mikalsen et al. (1991) reported that acetone plus fasting results in induction of microsomal Cr(VI) metabolism and increases chromium toxicity. The administration of acetone increased the amount of cytochrome P-450 and the rates of metabolism of several substrates (Kobusch et al., 1989). A P-450 isoform that can activate N-nitrosodimethylamine to its carcinogenic product, is increased in rats after treatment with acetone (Hunt and Westerkam, 1989). Deethylation of diethylnitrosamine (DEN) is assumed to be the first step toward the formation of an active intermediate that leads to an oncogenic effect (Puccini et al., 1989). These investigators reported that acetone induces DEN deethylase of rat liver microsomes.

Other Standards and Guidelines:

Under New York State Department of Health regulations (10 NYCRR Part 5), acetone is an unspecified organic contaminant (UOC) with a maximum contaminant level (MCL) of 50 ug/L in drinking water (NYS DOH, 1990).

DERIVATION OF VALUE

Regulations [6 NYCRR 702.15(a)(1)] require that the ambient water quality value be the more stringent of the values derived using the procedures in sections 702.3 through 702.7 or a "general organic guidance value" of 50 ug/L.

From the NOEL of 100 mg/kg/day from the 90-day gavage study in rats, USEPA applied an uncertainty factor of 1,000 to derive an oral reference dose (RfD) of 0.1 mg/kg/day (IRIS, 1991). According to procedures in regulation (6 NYCRR 702.5), New York State would also derive an acceptable daily intake (ADI), equivalent to an RfD, of 0.1 mg/kg/day. A potential ambient water quality value based on this ADI would be 700 ug/L.

Values can also be derived from the 13-week rat and mouse studies described above. In the male rat, considering the hematological changes at 2,500 ppm to be a LOAEL, a potential water quality value of 140 ug/L can be derived using 702.5. From a daily acetone consumption level of 200 mg/kg (as described by NTP) and an uncertainty factor of 10,000 (comprised of 1,000 for a less than long-term animal study, and 10 because a NOAEL is not available) an ADI of 20 ug/kg/day is derived, which yields a potential water quality value of 140 ug/L.

In the male mouse, the hematological change at 5000 ppm represents a LOAEL, and the next lower value of 2500 ppm a NOAEL. From an acetone dose of 1,353 mg/kg/day (described by NTP) and a uncertainty factor of 1000 for a NOEL from a less than chronic animal study, an ADI of 1.4 mg/kg/day and potential water quality value of 9800 ug/L are calculated.

A value can also be derived from the study by Ladefoged et al. (1989). Taking the only dose tested (0.5%) as the LOAEL, using those authors' experimentally reported water consumption data and an uncertainty factor of 10,000 for a LOAEL from a less than long-term animal study, an ADI of 0.07 mg/kg/day and potential water quality value of 490 ug/L is calculated.

Although the available non-oncogenic data on acetone yield a value less stringent than 50 ug/L, substantial data gaps exist for both chronic oral toxicity and oncogenicity. These gaps include the lack of an adequate lifetime drinking water study and acetone's classification as "D: not classifiable" based on a lack of data with respect to carcinogenicity in animals or humans. Accordingly, there are not adequate and sufficient data available to justify values greater than 50 ug/L based on both oncogenic and non-oncogenic effects as described in 702.15(a)(1)(ii). The appropriate ambient water quality guidance value for acetone, therefore, is 50 ug/L, based on the "general organic guidance value" [702.15 (a)(1)(ii)].

REFERENCES:

Abbondandolo, A., S. Bonatti, C. Corsi, et al. 1980. The use of organic solvents in mutagenicity testing. Mutation Research 79:141-150.

Albertini, S. 1991. Reevaluation of the 9 compounds reported conclusive positive in yeast Saccharomyces cerevisiae aneuploidy test systems by the Gene-Tox Program using strain D61.M of Saccharomyces cerevisiae. Mutation Research 260:165-180.

Amacher, D. E., S. C. Paillet, G. N. Turner, V. A. Ray and D. S. Salsburg. 1980. Point mutations at the thymidine kinase locus in L5178Y mouse lymphoma cells. 2. Test validation and interpretation. Mutation Research 72:447-474.

Ameenuddin, S. and M. L. Sunde. 1984. Sensitivity of chick embryo to various solvents used in egg injection studies. Proceedings of the Society for Experimental Biology and Medicine 175:176-178.

Anon. 1985. Acetone. Safety Practitioner 3(2):6-7.

Casazza, J. P., M. E. Felver and R. L. Veech. 1984. The metabolism of acetone in rat. Journal of Biological Chemistry 259:231-236.

DeFlora, S. et al. 1984. Mutation Research 133(3):161-198.

Elovaara, E., H. Vainio and A. Aitio. 1990. Pulmonary toxicity of inhaled styrene in acetone-, phenobarbital- and 3-methylcholanthrene- treated rats. Archives of Toxicology 64:365-369.

Freeman, A. E., E. K. Weisburger, J. H. Weisburger, R. G. Wolford, J. M. Maryak and R. J. Huebner. 1973. Transformation of cell cultures as an indication of the carcinogenic potential of chemicals. Journal of the National Cancer Institute 51(3):799-808.

Gichner, T. and J. Veleminsky. 1987. The organic solvents acetone, ethanol and dimethylformamide potentiate the mutagenic activity of N-methyl-N'-nitro-N-nitroso-guanidine, but have no effect on the mutagenic potential of N-methyl-N-nitrosourea. Mutation Research 192:31-35.

Haggard, H. W., L. A. Greenberg and J. M. Turner, 1944. The physiological principles governing the action of acetone together with determination of toxicity. Journal of Industrial Hygiene and Toxicology 26:133-151.

Hallstrom, I., A. Sundvall, U. Rannug, R. Grafstrom and C. Ramel. 1981. The metabolism of drugs and carcinogens in isolated subcellular fractions of Drosophila melangaster. I. Activation of vinyl chloride, 2-amnioanthrecene and benzo(a)pyrene as measured by mutagenic effects in Salmonella typhimurium. Chemico-Biological Interactions 34:129-143.

Hunt, C.M. and W.R. Westerkam. 1989. Differential induction of rat hepatic, renal, and pancreatic cytochrome P-450IIE1 specific N-nitrosodimethylamine activity by ethanol, acetone and fasting. Gastroenterology 96(5 part 2):A223.

Integrated Risk Information System (IRIS) Database. November, 1991. U.S. Environmental Protection Agency, Washington, D.C.

Kawachi, T., T. Yahagi, T. Kada et al. 1980. Cooperative programme on short-term assays for carcinogenicity in Japan. In: Molecular and Cellular Aspects of Carcinogen Screening Tests. R. Nontesano, ed. WHO, IARC, Lyon, France. P. 323-330.

Kitchin, K. T. and M. T. Ebron. 1984. Further development of rodent whole embryo culture: Solvent toxicity and water insoluble compound delivery system. Toxicology 30:45-57.

Kobusch, A.B., G.L. Plaa and P. DuSouich. 1989. Effects of acetone and methyl n-butyl ketone on hepatic mixed-function oxidase. Biochemical Pharmacology 38(20):3461-3467.

Kosugi, K., R. F. Scofield, V. Chandramouli, K. Kumaran, W. C. Schumann and B. R. Landau. 1986a. Pathways of acetone's metabolism in the rat. Journal of Biological Chemistry 261:3952-3957.

Kosugi, K., V. Chandramouli, K. Kumaran, W. C. Schumann and B. R. Landau. 1986b. Determinants in the pathways followed by the carbons of acetone in their conversion to glucose. Journal of Biological Chemistry 261:13179-13181.

Krasavage, W. J., J. L. O'Donoghue and G. D. DiVincenzo. 1982. Ketones. Clayton, G. D. and Clayton, F. E., Eds.: Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2C. Toxicology. New York: John Wiley and Sons, Inc. pp. 4709-4727.

Kubinski, H., G. E. Gutzke and Z. O. Kubinski. 1981. DNA - cell - binding (DCB) assay for suspected carcinogens and mutagens. Mutation Research 89:95-136.

Ladefoged, O., U. Hass and L. Simonsen. 1989. Neurophysiological and behavioural effects of combined exposure to 2,5-hexanedione and acetone or ethanol in rats. Pharmacology and Toxicology 65:372-375.

Larsen J-J., M. Lykkegaard and O. Ladefoged. 1991. Infertility in rats induced by 2,5-hexanedione in combination with acetone. Pharmacology and Toxicity 69:43-46.

Mast, T.J., J.J. Evanoff, R.L. Rommereim, K.H. Stoney, R.J. Weigel, and R.B. Westerberg. 1988. Inhalation Developmental Toxicity Studies: Teratology Study of Acetone in Mice and Rats. Final Report No. NIH-YOI-ES-70153.

Mast, T.J., R.L. Rommerein, R.J. Wiegel, R.B. Westerberg, B.A. Schwetz and R.E. Morrissey. 1989. Development toxicity study of acetone in mice and rats. Teratology 39(5):468.

Maron, D., J. Katzenellenbogen and B. N. Ames. 1981. Compatibility of organic solvents with the Salmonella/microsome test. Mutation Research 88:343-350.

McCann, J., E. Choi, E. Yamasaki and B. N. Ames. 1975. Detection of carcinogens as mutagens in the Salmonella/microsome test: Assay of 300 chemicals. Proceedings of the National Academy of Sciences 72(12): 5135-5139.

The Merck Index. 1983. 10th Ed. Rahway, NJ: Merck & Co., Inc. p. 10.

Mikalsen, A., J. Alexander, R.A. Andersen and M. Ingelman-Sundburg. 1991. Effect of in vivo chromate, acetone and combined treatment on rat liver in vitro microsomal chromium (VI) reductive activity and on cytochrome P-450 expression. Pharmacology and Toxicology 68:456-463.

Mourkides, G. A., D. C. Hobbs and R. E. Koeppe. 1959. The metabolism of acetone-2-C^{14} by intact rats. Journal of Biological Chemistry 234:27-30.

National Toxicology Program (NTP). 1991. NTP Report on the Toxicity Studies of Acetone in F344/N Rats and B6C3F_1 Mice (Drinking Water Studies). January, 1991. NIH Publication No. 91-3122. PB91-185975.

New York State Department of Health (NYSDOH). 1990. 10 NYCRR Part 5, Drinking Water Supplies (Statutory Authority: Public Health Law Section 225) Subpart 5-1. January 19, 1990.

Nizyayeva, I. V. 1982. On hygienic assessment of acetone. Gigiena Truda i Professional nye Zabolevaniia pp. 24-28.

Norppa, H. 1981. The in vitro induction of sister chromatid exchanges and chromosome aberrations in human lymphocytes by styrene derivatives. Carcinogenesis 2(3):237-242.

Norppa, H., K. Hemminki, M. Sorsa and H. Vainio. 1981. Effect of monosubstituted epoxides on chromosome aberrations and SCE in cultured human lymphocytes. Mutation Research 91:243-250

Park, H. Y. and I. Koprowska. 1968. A comparative in vitro and in vivo study of induced cervical lesions of mice. Cancer Research 28(8):1478-1489.

Patty. Indus. Hyg. and Tox. 3rd ed. Vol 2A, 2B, 2C 1981-1982, p. 4727.

Price, T. D. and D. Rittenberg. 1950. The metabolism of acetone. I. Gross aspects of catabolism and excretion. Journal of Biological Chemistry 185:449-459.

Puccini, P., R. Fiorio, V. Longo and P. G. Gervasi. 1989. High affinity diethylnitrosamine-deethylase in liver microsomes from acetone-induced rats. Carcinogenesis 10(9):1629-1634.

Quarles, J. M., M. W. Sega, C. K. Schenley and W. Lijinsky. 1979a. Transformation of hamster fetal cells by nitrosated pesticides in a transplacental assay. Cancer Research 39:4525-4533.

Quarles, J. M., M. W. Sega, C. K. Schenley and R. W. Tennant. 1979b. Rapid screening for chemical carcinogens: Transforming activity of selected nitroso compounds detected in a transplacental host-mediated culture system. National Cancer Institute Monograph 51:257-263.

Registry of Toxic Effects of Chemical Substances (RTECS). On-line database. October, 1991.

Rengstorff, R. H. and H. I. Khafagy. 1985. Cutaneous acetone depresses aqueous humor ascorbate in guinea pigs. Archives of Toxicology 58:64-66.

Rengstorff, R. H., J. P. Petrali and V. M. Sim. 1972. Cataracts induced in guinea pigs by acetone, cyclohexanone, and dimethyl sulfoxide. American Journal of Optometry and Archives of American Academy of Optometry 49:308-319.

Rhim, J. S., D. K. Park, E. K. Weisburger and J. H. Weisburger. 1974. Evaluation of an in vitro assay system for carcinogens based on prior infection of rodent cells with nontransforming RNA tumor virus. Journal of the National Cancer Institute 52(4):1167-1173.

Rowe, V. K. and M. A. Wolf. 1963. Ketones. Patty, F. A., Ed.: Industrial Hygiene and Toxicology, 2nd rev. ed., Vol. II. New York: John Wiley and Sons, Inc., pp. 1719-1731.

Sakami, W. 1950. Formation of formate and labile methyl groups from acetone in the intact rat. Journal of Biological Chemistry 187:369-378.

Smyth, H. F., Jr., C. S. Weil, J. S. West and C. P. Carpenter. 1969. Exploration of joint toxic action of twenty-seven industrial chemicals intubated in rats in all possible pairs. Toxicology and Applied Pharmacology 14(2):340-347.

Soderman, J. V., Ed. 1982. CRC Handbook of Identified Carcinogens and Noncarcinogens: Carcinogenicity-Mutagenicity Database, Vol. I. Chemical Class File. Boca Raton, FL: CRC Press, Inc., pp. vi, vii, x, 11, 211.

Tates, A. D. and E. Kriek. 1981. Induction of chromosomal aberrations and sister-chromatid exchanges in Chinese hamster cells in vitro by some proximate and ultimate carcinogenic arylamide derivatives. Mutation Research 88:397-410.

Traiger, G. J. and G. L. Plaa. 1974. Chlorinated hydrocarbon toxicity. Potentiation by isopropyl alcohol and acetone. Archives of Environmental Health 28(5):276-278.

Van Duuren, B. L., A. Sivak, C. Katz and S. Melchionne. 1971. Cigarette smoke in carcinogenesis: Importance of tumor promoters. Journal of the National Cancer Institute 47(1):235-240.

Vasavada, H. A. and J. D. Padayatty. 1981. Rapid transfection assay for screening mutagens and carcinogens. Mutation Research 91:9-14.

Walsh, D. 1990. Chemical Safey Data Sheets. Vol. I: Solvents. Royal Society of Chemistry. England.

Walter, P., A. Craigmill and A. Dukick. 1975. Methyl Ketone Toxicity (Acetone, Methyl Ethyl Ketone, Diacetone Alcohol, Methyl Isobutyl Ketone and Methyl n-Butyl Ketone). A Monograph. Prepared for Consumer Product Safety Commission, Bureau of Biomedical Science, Bethesda, Maryland, under Contract CPSC-C-75-0100, FIRL 80G-C4225-02. PB-280 472.

Wigaeus, E., A. Lof and M. Nordqvist. 1982. Distribution and elimination of 2-[^{14}C]-acetone in mice after inhalation exposure. Scandanavian Journal of Work, Environment and Health 8:121-128.

SEARCH STRATEGY:

The following databases were searched:

TOXLINE. October, 1991
NTIS. October, 1991
Hazardous Substances Data Bank (HSDB). January, 1992
Integrated Risk Information System (IRIS). November 12, 1991
Registry of Toxic Effects of Chemical Substances (RTECS). January, 1992

CSS/SS
September, 1992