N,N-Dimethylacrylamide

NAME OF SUBSTANCE N,N-DIMETHYLACRYLAMIDE
CAS REGISTRY NUMBER 2680-03-7

No specific toxicological information found.

1,4-Dimethylpiperazine

NAME OF SUBSTANCE **1,4-DIMETHYLPIPERAZINE**
CAS REGISTRY NUMBER 106-58-l

No specific toxicological information found.

N,N-Dimethylbenzylamine

NAME OF SUBSTANCE	N,N-DIMETHYLBENZYLAMINE
CAS REGISTRY NUMBER	103-83-3

No specific toxicological information found.

N,N-Dimethylacetamide

NAME OF SUBSTANCE N,N-DIMETHYLACETAMIDE
CAS REGISTRY NUMBER 127-19-5

o REFERENCE: [Rumack BH & Spoerke DG: POISINDEX(R) Information System. Micromedex Inc., Denver, CO, 1994; CCIS CD-ROM Volume 80, edition exp May,1994.] **PEER REVIEWED"

MEDICAL SURVEILLANCE

The determination of urinary N-monomethylacetamide in the end of shift urine sample was used to monitor exposure to dimethylacetamide. Five workers were observed followed for 4 consecutive weeks. Airborne dimethylac:etamide appeared to account for the greatest amount of urinary N-monomethylacetamide detected and, at the exposure concentrations encountered (0.5 to 2 ppm), a relationship of 10 ppm urinary N-monomethylacetamide inhaled was observed. Interindividual variation was small and no evidence of build-up in N-monomethylacetamide urinary levels was seen in these subjects. Mean airborne dimethylacetamide concentrations were somewhat higher by the end of the week, but magnitude was such that the differences were not statistically significant. It is concluded that changes in dimethylacetamide exposures can be quantitatively reflected by urinary N-monomethylacetamide. [Kennedy GL Jr, Sherman H; Drug Chem Toxicol 9 (2): 147-70 (II 986)] **PEER REVIEWED**

MEDICAL SURVEILLANCE

A study of occupational exposure to dirnethylactamide was conducted using both biological and environmental monitoring techniques. Personal and area air samples were analyzed for ciimeihylacetamide at a facililty manufacturing prefabricated synthetic products. Spot urine samples were collected from eight exposed and four unexposed workers for 5 consecutive work days and on the following Monday. These were analyzed for N-methylacetamide, a dimethylacetamide metabolite. Area air dimethylacetamide concentrations were generally constant, ranging from 11.81 to 17.24 ppm with a mean of 14.74 ppm. Personal dimethylacetamide concentrations showed a wide variability. The concentrations were distributed log normally with arithmetic and geometric means of 14.0 and 6.0 ppm, respectively. Urinary N-methylacetamide concentrations were not correlated with personal air dimethylacetamide concentrations. Six of the exposed workers excreted about 18% of the inhaled dimethylacetamide dose, calculated as the 8 hr time weighted average exposure, as N-methylacetamide. The other two exposed workers excreted about 30 percent of the inhaled dose as N-methylacetamide. Urinary N-methylacetamide concentrations the Monday following exposure were negligible or had returned to their preexposure values. Based on these results the half life for urinary excretion of N-methylacetamide was calculated to be 16 hours. The authors conclude that for dimethylacetamide and similar substances that are easily absorbed through the skin, biological monitoring is superior to airborne exposure monitoring for determining total uptake and evaluating potential health risks. [Bonn PJA et al; J Occup Med 29 (11): 898-903 (1987)] **PEER REVIEWED"

HUMAN TOXICITY EXCERPTS

CERTAIN N-SUBSTITUTED AMIDES . . . . DIMETHYL ACETAMIDE, MAY PRODUCE CHRONIC

LIVER OR RENAL DAMAGE. [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , p. 17753 **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS
JAUNDICE HAS BEEN OBSERVED . . . IN WORKERS EXPOSED REPEATEDLY AT . . . 20-25 PPM . . . SKIN PENETRATION UNDOUBTEDLY CONTRIBUTED TO THIS EFFECT. [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 1986. , p. 205] '*PEER REVIEWED**

HUMAN TOXICITY EXCERPTS
GIVEN TO HUMANS IN DAILY DOSES OF 400 MG/KG FOR 3 OR MORE DAYS . . . DEPRESSION, LETHARGY, CONFUSION & DISORIENTATION ENSUED. IN SOME . . . VISUAL & AUDITORY HALLUCINATIONS, PERCEPTUAL DISTORTIONS, DELUSIONS, EMOTIONAL DETACHMENT & AFFECTIVE BLUNTING . . . . [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984. Ii-2003 "PEER REVIEWED**

HUMAN TOXICITY EXCERPTS
DIZZINESS, SLEEPINESS, & WEAKNESS RESULTED FROM DMA CONCN OF 109.5-337 MG/CU M IN AIR OF METAL SURFACE FINISHING PROCESSES. [STUDIES ON THE MAX ALLOWABLE CONCN OF N,N-DIMETHYLACETAMIDE; CHUNG-HUA YU FANG I HSUEH TSA CHIH 13 (1): 29 (1979)] '*PEER REVIEWED**

HUMAN TOXICITY EXCERPTS
DIMETHYLACETAMIDE (NOT DILUTED OR MIXED WITH OTHER SUBSTANCES) DID NOT INDUCE EPIDERMAL HYPERPLASIA WHEN APPLIED TO THE UPPER BACKS OF ADULT MALES FOR TIME PERIODS UP TO 96 HR. [FISHER LB, MAIBACH HI; CONTACT DERMATITIS 1: 273 (1975)] **PEER REVJEWED"

HUMAN TOXICITY EXCERPTS
ACTION: HALLUCINOGEN; HUMAN DOSE: 40 MG/KG ORALLY [Usdin, E., and D.H. Efron. Psychotropic Drugs and Related Compounds 2nd. ed. U.S., Department of Health, Education, and Welfare, Publication (HSM) 72-9094. Washington, DC: U.S. Government Printing Office, 1972. , p. 425] "PEER REVIEWED'"

HUMAN TOXICITY EXCERPTS
SOMEWHAT LESS TOXIC THAN DIMETHYLFORMAMIDE . . . . [Sax, N.I. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold, 1984. , p. 1105] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS
N,N-DIMETHYLACETAMIDE /HAS/ ... TENDENCY TO /INDUCE/ CUMULATIVE EFFECTS. [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Jnterscience Publishers, 1963. , p. 1834] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS
IT IS ESPECIALLY IMPORTANT TO RECOGNIZE POSSIBILITY OF SIGNIFICANT SKIN ABSORPTION & TO PREVENT REPEATED OR PROLONGED SKIN CONTACT WITH CONCN ... SOLN. EXPOSED PERSONS SHOULD BE UNDER ADEQUATE MEDICAL SUPERVISION .... [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II:. Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , p. 1835] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS
DERMAL ABSORPTION FROM CUTANEOUSLY APPLIED DMA . . . RESULTED IN INJURY AT ... 0.1ML/KG/DAY. DERMAL FACTOR IS CONSIDERED IN PRACTICE TO BE SO SIGNIFICANT THAT NO AIR CONCN, HOWEVER LOW, WILL PROVIDE PROTECTION IF SKIN CONTACT WITH DMA (LIQUID) IS PERMITTED. [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 1986. , p. 205] "PEER REVIEWED**

HUMAN TOXICITY EXCERPTS
N,N-dimethylacetamide/ is capable of producing systemic injury when inhaled or absorbed through the skin in sufficient quantities over a prolonged period of time.
/N,N-dimethylacetamide/ has a low order of acute toxicity when swallowed or upon brief contact of the liquid or vapor with the eyes or skin. [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes l-26. New York, NY: John Wiley and Sons, 1978-1984. VI 169] "PEER REVIEWED"

HUMAN TOXICITY EXCERPTS
A study of 4-l workers /who/ had been exposed to dimethylacetamide from 2 to 10 years revealed the occurrence of disorders reflecting liver damage. Retention of bromosulfophthalein was increased in 9 /of/ 10 workers who had been exposed to dimethylacetamide for 7 to 10 years, and in 10 /of/ 20 workers who had been exposed to dimethylacetamide for 2 to 7 years. Other parameters of hepatic function which were altered in the exposed individuals include proteinemia, cholesterolemia, activities of hepatic transaminases and alkaline phosphatase in serum, and bilirubinemia. Hepatomegaly was diagnosed in 14 workers. [Snyder, R. (ed.). Ethyl Browning's Toxicity and Metabolism of Industrial Solvents. 2nd ed. Volume II: Nitrogen and Phosphorus Solvents. Amsterdam-New York-Oxford: Elsevier, 1990. , p. 146] **PEER REVIEWED"

HUMAN TOXICITY EXCERPTS
Retinoic acid induces the differentiation of NTERA-2 cl. D1 human embryonal carcinoma cells into neurons, cells permissive for the replication of human cytomegalovirus, and other cell types that cannot as yet be classified but are distinguishable from the stem cells. We tested several additional agents for their ability to induce the differentiation of these embryonal carcinoma cells- No differentiation was induced by butyrate, cyclic AMP, cytosine arabinoside, the tumor promoter 12-O-tetradecanoylphorbol 13-acetate, or the chemotherapeutic agent cis-diaminedichloroplatinum, although morphological changes were detected at the highest concentrations of these agents that permitted cell survival. However, retinal, retinol, 5-bromouracil 2'deoxyribose, 5-iodouracil 2'deoxyribose, hexamethylene bisacetamide,

dimethylacetamide, and dimethylsulfoxide all induced some neuronal differentiation, but to a lesser extent than retinoic acid. Also, 5-bromouracil 2'deoxyribose, 5-iodouracil 2'deoxyribose, hexamethylene bisacetamide, and dimethylacetamide induced the appearance of many cells permissive for the replication of human cytomegalovirus. Differentiation was, in all cases, accompanied by the lose of SSEA-3, a globoseries glycolipid antigen characteristically expressed by human embryonal carcinomas cells. However, another glycolipid antigen, A2B5, which appears in 60%-80% of differentiated cells 7 days following retinoic acid induction, was detected in less than 20% of the cells induced by the other agents studied. This implies that the human cytomegalovirus permissive cells induced by retinoic acid are not identical to those induced by 5-bromouracil 2'deoxyribose, 5-iodouracil 2'deoxyribose, and dimethylacetamide. [Andrews PW et al; Differentiation 31 (2): 119-26 (1986)] *'PEER REVIEWED**

HUMAN TOXICITY EXCERPTS Dimethylformamide and dimethylacetamide are widely used for their superior solvent properties. A series of single and multiple dose experiments in rodents were conducted to determine the target organs, and to establish doses which, under various routes of administration, produced those changes. Dimethylformamide produced moderate irritation in the rabbit eye, with the corneal response clearing in 2 to 4 weeks. Dimethylacetamide produced only mild, quickly reversible conjunctival irritation. Oral doses of dimethylformamide to the rat of 2,250 mg/kg or greater produced lethality which was associated with liver damage. Lethality occurred following oral doses of 4,500 mg/kg dimethylacetamide with LD50's for male and female rats of 5,809 and 4,930 mg/kg, respectively. The 1 hour LC50 by inhalation for dimethylacetamide in the rat was 2,475 ppm or greater. Sensory irritation was produced in the mouse at concentrations of 1,658 ppm or greater for dimethylformamide. Repeated oral doses of 450 mg dimethylformamide/kg to rats produced reduced body weight gain and liver injury with both changes' being reversible. Dimethylacetamide tested similarly produced body weight effects, liver injury, and testicular changes in the rat with all changes again being readily reversible. Dermal doses of 2,000 mg/kg of either dimethylformamide or dimethylacetamide were poorly tolerated by rabbits. Dimethylacetamide was slightly more toxic with all treated rabbits dying of acute hepatic necrosis. Repeated inhalation of 2,000-2,500 ppm produced mortality in rats exposed to dimethylformamide but not dimethylacetamide. Liver injury was seen with dimethylformamide, testicular changes with dimethylacetamide. Dimethylformamide and dimethylacetamide both produced slight anemia and leukocytosis in rats during 90 days of feeding. Liver weights were elevated in rats fed dimethylformamide, but not dimethylacetamide, at a level of 1,000 ppm. The "no-observed effect level" in rats fed dimethylformamide for 90 days was 200 ppm. The overall toxicologic profiles of both dimethylacetamide and dimethylformamide are similar with the target organ being the liver. [Kennedy GL Jr, Sherman H; Drug Chem Toxicol9 (2): 147-70 (1986)] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
ANIMAL STUDIES SHOWED THAT 50 PPM . . . INHALED BY RABBITS & CATS FOR 30 WK PRODUCED NO INJURIOUS EFFECTS . . . 40 PPM . . . BY INHALATION FOR 6 HR/DAY, 5 DAYS/WK FOR 6 MO RESULTED IN NO LIVER DAMAGE TO DOGS & RATS. LIVER INJURY BY DMA JNCURRED @ HIGHER CONCN CONSISTS OF CORD-CELL DEGENERATION, OBSERVABLE BY ALTERATION IN SULFOBROMOPHTHALEIN RETENTION TIME . . . RECOVERY WITH NO RESIDUAL /EFFECTS/ OCCURS IN . . . 4-6 MO. [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: American Conference of Governmental

industrial Hygienists, 1986. , p. 205] "PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
MARKED WEIGHT LOSS OCCURRED IN RATS WITH REPEATED IP INJECTIONS . . . LIVER DAMAGE IN SOME RATS & DOGS EXPOSED TO REPEATED INHALATION . . . OF 100-200 PPM. [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Inter-science Publishers, 1963. , p. 1834] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
GIVING PREGNANT RATS 1.5 MUKG ON GESTATIONAL DAY 4 OR 7 LED TO OVER 60% RESORPTIONS. SURVIVORS WERE STUNTED BUT NO DEFECTS WERE FOUND. PAINTING THE TAILS FOR WEEKLY PERIODS CAUSED NO EFFECT ON THE LITTERS. [Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986. , p. 208] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
UNDILUTED DMA APPLIED TO RABB'IT EYE . . . /CAUSED A/ SMALL AREA OF CORNEAL NECROSIS. [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 1986. , p. 205] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
WHEN AQ SOLN WAS ADMIN BY STOMACH TUBE TO PREGNANT RABBITS FROM THE 6TH TO THE 18TH DAY PAST INSEMINATION, EMBRYOTOXIC EFFECTS FROM DIMETHYLACETAMIDE OCCURRED ONLY WITH MATERNALLY TOXIC DOSES. [MERKLE J, ZELLER H; ARZNEIM-FORSCH 30 (9): 1557 (1980)] **PEER REVIEWED*"
NON-HUMAN TOXICITY EXCERPTS SC OR ORAL ADMIN OF 2.2 G/KG N,N-DIMETHYLACETAMIDE (DMA) TEERMINATED PREGNANCY IN HAMSTERS GIVEN THE CMPD AROUND NIDATION (DAYS 4-5 OF PREGNANCY). [MILLER WL ET AL; PROC SOC EXP BIOL MED 166 (2): 199 (1981)] **PEER REVIEWED"

NON-HUMAN TOXICITY EXCERPTS
ELEVATION OF BLOOD SUGAR OCCURRED IN RATS AFTER SINGLE ORAL (I MUKG) OR IP (1 ML/KG) DOSE OF DIMETHYLACETAMIDE. [GRANT AM; TOXICOL LETT (AMST) 3 (5): 259 (1979)] **PEER REVIEWED"

NON-HUMAN TOXICITY EXCERPTS
Dimethylacetamide was administered orally by gavage to pregnant female Charles River COBS CD (Charles River Breeding Laboratories, Portage, MI) rats (25/group) to determine its teratogenic potential. Dimethylacetamide was administered in single daily dose of 0 (deionized water), 65, 160, and 400 mg/kg at a constant volume of 10 ml/kg body weight on gestation days 6 through 19. Survival was 100% in all groups. The animals were sacrificed on gestation day 20, examined, and the fetuses removed for teratologic evaluation. There was a statistically significant reduction in maternal body weight at the 400 mg/kg/day treatment level. There was no significant difference in the mean numbers of viable fetuses, corpora lutea, total implantations or fetal sex distribution among the groups. A significant increase in

postimplantation loss/dam was observed at the 400 mglkglday dose. A dose related pattern of decreased mean fetal body weight that reached statistical significance at 400 mg/kg/day was observed. An increase in the number of malformations, particularly heart and/or vessel anomalies (33 fetuses, 18 litters), and in the number of litters with malformations was observed at the 400 mglkglday level. Tlhe increased number of developmental variations in the high dose treatment group . seemed to correspond with reduced fetal body weights of the group. No teratogenic effects were observed at or below a 160 mglkglday treatment. [Johannsen FR et al; Fundam Appl Toxicol 9 (3): 550-6 (1987)] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
Groups of 12 male Sprague-Dawley rats were exposed to N,N-dimethylacetamide 6 hr/day, 5 days/wk, and mated to untreated virgin females after 43 exposure days. Mean analytical exposure concn were 40, 116, and 386 ppm, respectively. A control group was exposed to air containing no N,N-dimethylacetamide. A total of 69 days of exposure to DMAC at these levels produced treatment related effects of increased liver wt and liver/body wt ratios in the high (I 16 ppm) and medium (386 ppm) exposure groups of male rats. No clinical signs of toxicity were seen. Clinical chemistry analyses indicated no significant differences between any of the treatment groups and the control group. Reproductive data indicated no treatment related effects on copulation efficiency or efficiency in effecting pregnancy, and there were no detectable treatment related effects on preimplantation loss, postimplantation loss, embryotoxicity, or fetotoxicity in litters of females mated to males exposed to N,N-dimethylacetamide. [Wang GM et al; J Toxicol Environ Health 27 (3): 297-305 (1989)] "PEER REVIEWED*'

NON-HUMAN TOXICITY EXCERPTS
... Rated 3 on rabbit eyes, /on a scale of 1 to IO with IO being the most severe/. [Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. , p. 1031] **PEER REVIEWED"

NON-HUMAN TOXICITY EXCERPTS
Dimethylacetamide was embryotoxic in rats when a single dose of 2 g/kg was administered via the intraperitoneal route on days 4 and 14 of gestation. This dose produced the resorption of all litters. Daily oral administration of dimethylacetamide (0.4 g/kg) to rats from day 6 to day 19 of gestation caused fetal malformations accompanied by toxicity to the maternal organism. Reproduction in rats was not influenced by repeated exposure to dimethylacetamide vapors up to 300 ppm. In rabbits, daily oral doses of 0.09 g/kg from day 6 to 19 gestation had no adverse effect; at 0.29 g/kg fetal resorption was observed, together with weight loss in the mothers. Repeated administration of 0.47 g/kg was very toxic to the mothers and caused total resorption in the surviving animals. [Snyder, R. (ed.). Ethyl Browning's Toxicity and Metabolism of Industrial Solvents. 2nd ed. Volume II: Nitrogen and Phosphorus Solvents. Amsterdam-New York-Oxford: Elsevier, 1990. , p. 146] **PEER REVIEWED"

NON-HUMAN TOXICITY EXCERPTS
One month after ip administration of a near lethal dose of dimethylacetamide to mice, damage to hepatocytes was observed together with necrotic pancreatitis and severe necrosis of splenic lymphocytes. Testicular atrophy was also seen four days post treatment. Post mortem examination of rats which had received the LD50 of dimethylacetamide via the oral route

revealed generalized hemorrhage in several organs and necrosis in the liver and kidneys. Dermal doses of 2 g/kg caused death of rabbits from acute hepatic necrosis. [Snyder, R. (ed.). Ethyl Browning's Toxicity and Metabolism of Industrial Solvents. 2nd ed. Volume 11: Nitrogen and Phosphorus Solvents. Amsterdam-New York-Oxford: Elsevier, 1990. , p. 146] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
Repeated administration of 0.5 g/kg orally to rats daily for 1 month did not cause pathological lesions detectable by microscopy. At 1.9 g/kg applied dermally to rats on IO consecutive days, death occurred between the sixth and tenth dose; in this study, severe inflammation and irritation of the stomach and the lung was recorded. Cutaneous application of dimethylacetamide at 4 g/kg/day for 5 days/week for 6 weeks killed dogs after they had experienced weakness, ataxia, diarrhea, loss of weight and jaundice. Hepatic damage was indicated by increase in the bromosulphothalein retention time and the activity of serum alkaline phosphatase and was confirmed by histopathology. In contrast, the dogs survived this treatment for 6 months when the dose was only 1 g/kg and toxicity was not observed except for pale coloration and fatty degeneration in the livers. The central nervous system of rabbits which received 0.25 to 2 g/kg given by different routes for 21 days or longer was affected as evidenced by variable electroencephalographic changes, dysrhythmias and electrographic seizures at the higher doses. In this species, dimethylacetamide caused mild irritation when applied undiluted to the belly. [Snyder, R. (ed.). Ethyl Browning's Toxicity and Metabolism of Industrial Solvents. 2nd ed. Volume II: Nitrogen and Phosphorus Solvents. Amsterdam-New York-Oxford: Elsevier, 1990. , p. 145] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
Rats and dogs: inhalation: liver damage: 100-200 ppm, repeated. [Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983. , p. 543] "PEER REVIEWED*"

NON-HUMAN TOXICITY EXCERPTS
Relatively high single doses to various species following oral, dermal, ip, iv, or inhalation exposures generally are required to produce mortality. The liver is the primary target following acute high level exposure, but massive doses can also produce damage to other organs and tissues. Repeated sublethal treatment by various routes also shows the liver to be the target organ with the degree of damage being proportional to the amount absorbed. [Kennedy GL Jr; Crit Rev Toxic01 17 (2): 129-82 (1986)] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
Dimethylacetamide is a widely used industrial solvent. It has been reported to be teratogenic when given to rats by injection or following dermal application. Most of these studies employed large single doses and did not examine both the fetal and the maternal response. In this study, groups of pregnant Crl:CD rats were exposed to 32, 100, or 282 ppm dimethylacetamide by inhalation for 6 hr/day from Days 6 through 15 of gestation (day on which copulation plug was detected was termed Day 1G). A control group of chambered pregnant rats was exposed simultaneously to air only. All female rats were euthanized on Day 21G. At 282 ppm, both maternal weight gain during the exposure period and fetal weight were significantly decreased

and accompanied by a significant dose response trend. These effects were not seen in rats inhaling either 32 or 100 ppm. Fetal resorptions were not increased in any of the groups exposed to dimethylacetamide. Fetal incidences of external, visceral, or skeletal variations and malformations were similar between the test and control groups. Therefore, both fetal and maternal toxicity were noted at 282 ppm and the no observed adverse effect level under these experimental conditions was 100 ppm for both the dam and the conceptus. Dimethylacetamide was not demonstrated to produce malformations in the rat fetus even at a level that was toxic to the dam. [Solomon HM et al; Fundam Appl Toxicol 16 (3): 414-22 (1991)] **PEER REVIEWED"

NON-HUMAN TOXICITY EXCERPTS
It was found that monolayer cultures of F9 cells induced to differentiate with trans-retinoic acid contain two major subpopulations of cells. These two cell types can be distinguished by their cellular morphology, their pattern of laminin accumulation, and their ability to undergo further differentiation in response to N6-O2-dibutyryl adenosine 3':5' cyclic monophosphoric acid. Furthermore, the developmental pathway induced by trans-retinoic acid appears to lead to two alternative pathways, and differentiation at the branch point is either directly or indirectly controlled by cyclic monophosphoric acid. Differentiation along one branch of this pathway can be induced by 5-bromodeoxyuridine, whereas differentiation along an unrelated pathway is induced by N'-N'-dimethylacetamide. In all cases, differentiation is closely paralleled by suppression of the tumorigenic phenotype indicating that these two processes are tightly linked and probably share a common step. [Moore EE et al; Differentiation 31 (3): 183-90 (1986)] "PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
Possible damage to the reproductive system of rats from dimethylacetamide was explored by exposing male and female Crl:CD(SD)BR rats to vapors of the chemical at concentrations of 0, 30,100 or 300 ppm. The rats were exposed for periods of 6 hours/day, 5 days/week for 10 weeks. Following this, they were exposed for 7 days/week for 7 to 8 weeks. For female rats no exposure was permitted from gestation day 21 through postpartum day four. Changes in body weight and survival, or clinical signs of distress were not noted in parental rats as a result of exposure to dimethylacetamide. The ratio of liver weight to body weight increased in groups where both males and females were exposed to 300 ppm. Such finding did not occur when only males or only females were exposed: to this dose level. Mating performance, fertility, length of gestation, progeny numbers, structure and viability of progeny were not changed as a result of exposure to dimethylacetamide. Body weights of pups at 21 postpartum days were lower among those derived from matings where both parental rats or the female parental rat had been exposed to 300 ppm dose levels. Dimethylacetamide did not cause any gross pathologic changes nor was there any significant change in liver and gonad weights. The /results conclude/ that repeated inhalation exposure to dimethylacetamide at dose levels up to 300 ppm 'is not harmful to the reproductive function in rats. [Ferenz RL, Kennedy GL JR; Fundam Appl Toxicol 7 (1): 132-137 (1986)] "PEER REVIEWED"

NON-HUMAN TOXICITY VALUES
LD50 Rat oral 5.4 ml/kg [Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989. , p. 509] **PEER REVIEWED**

NON-HUMAN TOXICITY VALUES
LD50 Mouse ip 3240 mg (3.4 ml)/kg [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984. II-200] -PEER REVIEWED*'

NON-HUMAN TOXICITY VALUES
LD50 Rat male oral 5,809 mg/kg [Kennedy GL Jr, Sherman H; Drug Chem Toxicol 9 (2): 147-70 (1986)] "PEER REVIEWED**

NON-HUMAN TOXICITY VALUES
LD50 Rat female oral 4,390 mg/kg [Kennedy GL Jr, Sherman H; Drug Chem Toxicol 9 (2): 147-70 (1986)] **PEER REVIEWED**

2-Methyleneglutaronitrile

NAME OF SUBSTANCE 2-METHYLENEGLUTARONITRILE
CAS REGISTRY NUMBER 1572-52-7

No specific toxicological information found.

2,6-Di-*tert*-butyl-4-methylphenol

NAME OF SUBSTANCE 2,6-DI-T-BUTYL-P-CRESOL
CAS REGISTRY NUMBER 128-37-0

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The following Overview, • ** BUTYLATED HYDROXYTOLUENE ***,
is relevant for this HSDB record chemical.

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o CLINICAL EFFECTS :

SUMMARY

o The clinical manifestations of acute overdose are not well known. Ingestion of 4 grams produced gastritis, dizziness, confusion, and temporary loss of consciousness in an adult. BHT dust is irritating if in contact with the eyes, nose or throat. Chronic toxicity in animals is related to potassium depletion.

HEENT

o BHT dust is irritating to the eyes, nose, and throat.

NEUROLOGIC

o Weakness, dizziness, and brief loss of consciousness have been reported in an adult who ingested 4 grams.

o Hallucinations, ataxia, and dysarthria were seen in an adult who ingested 80 grams.

GASTROINTESTINAL

o Epigastric pain and vomiting have been reported in overdose.

FLUID-ELECTROLYTE

o Hypokalemia may be noted.

MUSCULOSKELETAL

o Muscle weakness may be noted in conjunction with potassium depletion.

o REFERENCE

[Rumack BH: POISINDEX(R) Information System. Micromedex Inc., Englewood, CO, 1995; CCIS CD-ROM Volume 87, edition exp Feb, 1996. Hall AH & Rumack BH (Eds): TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 1995; CCIS CD-ROM Volume 87, edition exp Feb, 1996.]

**PEER REVIEWED"

NON-HUMAN TOXICITY EXCERPTS

AT 500 MG/KG/DAY LIVER ENLARGEMENT IN RAT WAS SEEN TO BE REVERSIBLE. [GILBERT, GOLBERG; FOOD COSMET TOXICOL 3:417 (1965)] **PEER REVIEWED'*

NON-HUMAN TOXICITY EXCERPTS;

NEW EVIDENCE INDICATED FEEDING MICE THE DRUG @ /A LEVEL/ 5-10 TIMES THAT IN PROCESSED FOODS CAUSED SIGNIFICANT BRAIN & BEHAVIORAL CHANGES.

TREATED MICE FOUGHT MORE & SLEPT LESS THAN UNTREATED CONTROLS. [Rossoff, I.S. Handbook of Veterinary Drugs. New York: Springer Publishing Company, 1974. , p. 58] '*PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

ADMIN IN FEED OF RATS & MICE OF BOTH SEX @ 3000 OR 6000 PPM; IN RATS 105 WK & 107 OR 108 WK IN MICE. NO TUMORS OCCURRED IN EITHER SEX OF RATS & MICE. [CARCINOG TEST PROGRAM, BETHESDA, REPORT, DHEW/PUB/NIH-79-1706, NCI-CG-TR-150, PB-298539, 113 (1979)] **PEER REVIEWED"

METABOLISM/METABOLITES

BIOTRANSFORMATION...IN RATS AFFORDED 3,5-DI-T-BUTYL-4-HYDROXYBENZOIC ACID &THE CORRESPONDING ESTER GLUCURONIDE VIA 2, 6-DI-T-BUTYL-4-HYDROXY(14C)METHYLPHENOL & S-(3,5-DI-T-BUTYL-4-HYDROXYBENZYL)-N-ACETYLCYSTEINE. [The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 1: A Review of the Literature Published Between 1 960 and 1969. London: The Chemical Society, 1970, , p. 259] **PEER REVIEWED**

Benzothiazole

NAME OF SUBSTANCE BENZOTHIAZOLE
CAS REGISTRY NUMBER 95-16-9

No specific toxicological information found.

2-Ethylhexanoic acid

NAME OF SUBSTANCE **2-ETHYLHEXANOIC** ACID
CAS REGISTRY NUMBER **149-57-5**

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The following Overview, *** ACIDS ***,
is relevant for this HSDB record chemical.

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o CLINICAL EFFECTS :

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

o INGESTION: Oral ingestion may produce mild to moderately severe oral and esophageal **burns** with *more* severe bums occurring in the stomach. Perforations are rare but may occur. The **pyloric** end of the stomach is most severely affected and is the site of delayed stricture *occurring* generally at 3 weeks after the ingestion.

1. Initial signs and symptoms may not reliably predict the extent of injury to the gastrointestinal tract.

o DERMAL: Severe dermal bums may occur with dermal exposure. Complications seen with dermal bums include cellulitis, sepsis, contractures, osteomyelitis, and systemic toxicity from absorbed acid. Chromic acid bums can result in systemic toxicity.

o INHALATION: Inhalation of acid vapors, mists or aerosols may result in dyspnea, pleuritic chest pain, pulmonary edema, hypoxemia, bronchospasm, pneumonitis, tracheobronchitis and persistent pulmonary function abnormalities. Pulmonary dysfunction similar to asthma has been reported.

o EYE **Irritation** may develop after exposure to mists, aerosols or vapors. Splash contact may cause **corneal** erosions.

HEENT

0.2.4.1 ACUTE EXPOSURE

o Eye exposure may result in pain, swelling, **corneal** erosions and blindness.

CARDIOVASCULAR

0.2.5.1 ACUTE EXPOSURE

o Cardiovascular collapse may develop soon after severe poisonings. Cardiac ischemia may occur after several hours of uncorrected circulatory collapse.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

o Exposure to acids may produce dyspnea, pleuritic chest pain, pulmonary edema, hypoxemia, bronchospasm, pneumonittis, and persistent pulmonary function abnormalities. Airway **hyperreactivity** has also been reported.

4. The onset of respiratory symptoms may be delayed for several hours.

GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

o Ingestion of acids may result in bums, gastrointestinal bleeding, gastritis, perforations, **dilation,** edema, necrosis, vomiting, stenosis, **fistula,** and **duodenal/jejunal** injury.

HEPATIC

0.2.9.1 ACUTE EXPOSURE

o Systemic toxicity may result in acute hepatic injury. Hepatic injury has been reported following chronic exposure to chromic acid.

GENITOURINARY

0.2.10.1 ACUTE EXPOSURE

o Renal failure is a rare complication of severe poisonings. Hemoglobinuria may develop secondary to hemolysis. Nephritis may develop after hydrochloric acid ingestion.

ACID-BASE

0.2.11 .I ACUTE EXPOSURE

o Metabolic acidosis may be noted following significant acid ingestion and may be due to systemic absorption of acid. Acidosis may also be secondary to severe chemical burns and shock.

FLUID-ELECTROLYTE

0.2.12.1 ACUTE EXPOSURE

o Massive fluid and electrolyte shifts may occur with extensive dermal or gastrointestinal bums. Hyperkalemia may occur with hemolysis. Hyperphosphatemia, hypocalcemia and hyperchloremia have been reported.

HEMATOLOGIC

0.2.13.1 ACUTE EXPOSURE

o Hemolysis may occur following significant acid ingestion. Disseminated intravascular coagulation has been reported.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

o Chemical bums to the skin are often associated with concurrent thermal burns and trauma. Complications seen with thermal burns including cellulitis, sepsis, contractures, osteomyelitis, may occur as well as systemic toxicity from absorbed acid. Deep or extensive bums may require grafting.

0.2.14.2 CHRONIC EXPOSURE

o Prolonged or repeated exposure to chromic acid mist can result in dermatitis. Ulcerations may also occur.

IMMUNOLOGIC

0.2.1 9.1 ACUTE EXPOSURE

o fiypersensitivity has been reported.

OTHER

0.2.23.1 ACUTE EXPOSURE

o Injury to the spleen: gallbladder, diaphragm, and peritoneum has been noted with significant acid ingestions (Wu & Lai, 1993).

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o REFERENCE

[Rumack BH: POISINDEX(R) Information System. Micromedex Inc., Englewood, CO, 1995; CCIS CD-ROM Volume 87, edition exp Feb, 1996. Hall AH & Rumack BH (Eds): TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 1995; CCIS CD-ROM Volume 87, edition exp Feb, 1996.]

"PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

...CASE OF CORNEAL INJURY, WITH PROMPT HEALING, HAS BEEN REPORTED. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 4925] "'PEER REVIEWED"

NON-HUMAN TOXICITY EXCERPTS

MALE RATS FED 2% 2-ETHYLHEXANOIC ACID IN THE DIET FOR 3 WK DISPLAYED NO CHANGES IN BODY WT GAIN COMPARED TO CONTROLS, BUT SHOWED HEPATOMEGALY.

THE LIVER-TO-BODY WT RATIO INCREASED BY 50%. [Clayton, G. D. and F. E. Clayton (eds.). Patty's industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 4925] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

RATS FED 2-ETHYLHEXANOIC ACID (2%) FOR 3 WK SHOWED DECR SERUM TRIGLYCERIDE....AND A LARGE INCR IN HEPATIC PEROXISOMES. . ..HAS A MARKED EFFECT ON LIPID METAB, IN VIVO AND IN VITRO, CAUSING INHIBITION OF TRIGLYCERIDE BIOSYNTHESIS IN INTESTINAL MUCOSA. THIS LEADS TO CHANGES IN ABSORPTION OF FATTY ACIDS & CHOLESTEROL. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 4925] "'PEER REVIEWED*'

INTERACTIONS

OLEIC ACID WAS INCORPORATED MAXIMALLY INTO RAT EVERTED INTESTINAL SAC TRIGLYCERIDE WHEN THE SACS WERE INCUBATED IN 0.154 MOLAR PHOSPHATE BUFFER PH 7.0. 2-ETHYL-N-CAPROIC ACID INHIBITED THE OLEIC ACID INCORPORATION BY 25-50 WHEN THE RATIO OF 2-ETHYL-N-CAPROATE TO OLEATE IN THE MEDIUM WAS 20:1 OR GREATER. [VAHOUNY GV ET AL; INHIBITION OF TRIGLYCERIDE SYNTHESIS IN EVERTED INTESTINAL SACS; PROC SOC EXP BIOL MED 128(2) 495 (1968)] "PEER <REVIEWED**

4-Phenylcyclohexene

NAME OF SUBSTANCE 4-PHENYLCYCLOHEXENE
CAS REGISTRY NUMBER 49944 6-5

No specific toxicological information found.

1,3-Dichloro-2-propanol

NAME OF SUBSTANCE 1,3-DICHLORO-2-PROPANOL
CAS REGISTRY NUMBER 96-23-l

TOXIC HAZARD RATING
4(?). 4= VERY TOXIC: PROBABLE ORAL LETHAL DOSE (HUMAN) 50-500 MG/KG, BETWEEN 1 TEASPOON & 1 OZ FOR 70 KG PERSON (150 LB). SIMILAR TO CARBON TETRACHLORIDE POISONING, BUT IRRITANT ACTIONS (EG HEMORRHAGIC GASTRITIS, PHARYNGITIS, ETC) MAY BE EVEN MORE SEVERE. [Gosselin, R.E., H.C. Hodge, R.P. Smith, and M.N. Gleason. Clinical Toxicology of Commercial Products. 4th ed. Baltimore: Williams and Wilkins, 1976. II-119] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS
MODERATELY TOXIC BY INHALATION AND INGESTION. [Hawley, G.G. The Condensed Chemical Dictionary. 9th ed. New York: Van Nostrand Reinhold Co., 1977. , p. 280] **PEER REVIEWED*"
NON-HUMAN TOXICITY EXCERPTS
1,3-DICHLORO-2-PROPANOL TESTED ON RABBIT EYES IS VERY IRRITATING AND HAS CAUSED MODERATELY SEVERE DAMAGE, GRADED 8 ON A SCALE OF 1 TO 10. [Grant, W. M. Toxicology of the Eye. 2nd ed. Springfield, Illinois: Charles C. Thomas, 1974. , p. 374] "PEER REVIEWED*'
METABOLISM/METABOLITES
METAB OF 1,3-DICHLOROPROPAN-2-OL BY RATS RESULTED IN 2 MERCAPTURIC ACID METABOLITES IN URINE, N,N'-BIS(ACETYL)-S,S'-[1,3-BIS(CYSTEINYL)] PROPAN-2-OL & N-ACETYL-S-(2,3-DIHYDROXYPROP'YL)CYSTEINE. ALSO PRODUCED BETA-CHLOROLACTATE AS OXIDATIVE METABOLITE. [JONES AR, FAKHOURI G; XENOBIOTICA; 9(10) 595 (1979)] **PEER REVIEWED"

1-Dodecanol

NAME OF SUBSTANCE 1-DODECANOL ,
CAS REGISTRY NUMBER 112-53-8

TOXIC HAZARD RATING
2(?). 2= SLIGHTLY TOXIC: PROBABLE ORAL LETHAL DOSE (HUMAN) 5-15 G/KG; BETWEEN 1 PINT & 1 QUART FOR 70 KG PERSON (150 LB). (?)= TOXICITY RATINGS FOLLOWED BY INTERROGATION POINTS ARE BASED ON OBVIOUSLY INADEQUATE DATA; SOME REPRESENT NO MORE THAN GUESSES. [Gosselin, R.E., H.C. Hodge, R.P. Smith, and M.N. Gleason. Clinical Toxicology of Commercial Products. 4th ed. Baltimore: Williams and Wilkins, 1976. II-118] '"PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
SEVEN RATS & SEVEN RABBITS, WHICH SURVIVED.../AN ORAL DOSE/ OF EITHER 24 OR 36 ML OF TECHNICAL LAURYL ALCOHOL/KG OF BODY WT, DEMONSTRATED NO SIGNIFICANT GROSS OR MICROSCOPIC CHANGES. [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , p. 1469] "PEER REVIEWED"

NON-HUMAN TOXICITY EXCERPTS
SEE ALCOHOLS, HIGHER. . ..RAT ASPIRATION TEST SUGGESTS THAT...MELTED DODECYL (LAURYL) ALCOHOLS ARE DANGEROUS IF THEY ENTER THE TRACHEA. ...EVEN A SMALL QUANTITY (0.2 ML) BEHAVES LIKE THE HYDROCARBON SOLVENTS (SUCH AS KEROSENE) IN CAUSING DEATH FROM PULMONARY EDEMA. /ALCOHOLS, HIGHER/ [Gosselin, R.E., H.C. Hodge, R.P. Smith, and M.N. Gleason. Clinical Toxicology of Commercial Products. 4th ed. Baltimore: Williams and Wilkins, 1976. II-I 18] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
LAURYL ALCOHOL CAUSED PRACTICALLY NO SKIN IRRITATION IN GUINEA PIGS. /FROM TABLE/ [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , p. 1469] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
N-DODECYL ALCOHOL WAS TOXIC TO RATS BY ASPIRATION ROUTE. AS CHAIN LENGTH OF N-PRIMARY ALCOHOL INCR (C11-C13) MORTALITY RATIO DID NOT CHANGE BUT ANIMALS SURVIVED LONGER & THEN DIED OF PULMONARY EDEMA & HEMORRHAGE. [GERARDE HW ET AL; ARCH ENVIRON HEALTH 13(4) 457 (1966)] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
LAURYL ALCOHOL INDUCED NUTRITIONAL ENCEPHALOMALACIA WHEN FED TO I-DAY-OLD CHICKS FOR 3 WEEKS. MEDIAN LETHAL DIETARY LEVEL WAS 18%. [YOSHIDA M ET AL; EFFECT OF ALCOHOLS, ALDEHYDES & THEIR DERIV TO INDUCE NUTRITIONAL ENCEPHALOMALACIA IN STARTING CHICKS; AGR BIOL CHEM 35(10) 1610 (1971)] "PEER REVIEWED**

ε-Caprolactam

NAME OF SUBSTANCE **CAPROLACTAM**
CAS REGISTRY NUMBER 105-60-2

o CLINICAL EFFECTS :

SUMMARY

o Caprolactam exposure causes eye, skin, and mucous membrane irritation. Respiratory irritation and coughing may be seen following inhalation exposure. Respiratory sensitization with bronchospasm was demonstrated in one group of occupationally-exposed workers. 1. One case has been reported of a worker who developed dermatitis, seizures, fever, and leukocytosis after caprolactam exposure. 2. Direct contact with the hot liquid can cause burns of the eyes and skin. Prolonged and confined skin contact with the material can also cause dermal bums, especially if the liquid is spilled into footwear. 3. Contact dermatitis and eczema have been noted in chronically exposed workers. Hypersensitivity dermal reactions may occur. The lesion is most often a tightening and reddening of the skin, similar to the appearance of a sunburn. Skin that is severefy affected may peel, but seldom blisters. The nails may become brittle.

o Experimental animals exposed to caprolactam have developed convulsions and liver and kidney injuries. Respiratory stimulation and mild hypotension occurred in experimental animals given large oral doses. A decreased respiratory rate *was* noted in rats with inhalational exposure to caprolactam dust. 1. With small oral doses, mild hypertensive effects were seen. An intravenous dose of 500 mg/kg caused brief periods of cardiac arrest with hypotension in dogs. 2. The convulsant activity of caprolactam in experimental animals seems to occur by antagonism of gamma-aminobutyric acid (GABA)-mediated central nervous system inhibition.

o Caprolactam is mutagenic in insects, microbial assay systems, rodent cells, and human lymphocytes. However, in the majority of mutagenicity tests, caprolactam SHOWED NO ACTIVITY.

o An IARC Cancer Review found no evidence of carcinogenesis in animals. The NTP Carcinogenesis Bioassay found no evidence of carcinogenesis in mice and rats. The 1986 EPA GENETOX Program found no carcinogenicity in mice and rats.

o Caprolactam has caused adverse effects on spermatogenesis in rats following inhalation exposure. Female rats exposed to caprolactam had estrous cycle disturbances and decreased fecundity. Transplacental transfer of caprolactam has been shown in mice. Caprolactam was not teratogenic or embryotoxic in rats and rabbits at oral doses of 100 to 1,000 mg/kg per day for 9 to 22 days of gestation.

o Dyspermia has been noted with increased incidence in a group of workers exposed to caprolactam, cyclohexanone, and dinil.

o One group of Soviet women with occupational caprolactam exposure in the textile industry were reported to have an increased incidence of a variety of complications of pregnancy, oligodysmenorrhea, and hypermenorrhea. Children born to these workers were noted to be normal.

VITAL SIGNS

o Fever, increased respiratory rates, hypertension, hypotension, and tachycardia have been noted in either exposed humans or experimental animals.

HEENT

o Caprolactam is an irritant of the eyes, nose and throat. Dry nasal mucosa and epistaxis may be noted in workers. Direct contact with the liquid can cause corneal burns.

CARDIOVASCULAR

o Hypotension and hypertension have been seen in poisoned experimental animals. Workers with chronic exposure have complained of chest discomfort and palpitations, and have had a tendency to develop tachycardia and mild hypotension.

o EKG changes were noted in a group of workers with chronic exposure, including sinus bradycardia, sinus arrhythmia, flattening of the P wave, and prolongation of the PR interval.

RESPIRATORY

o Exposed workers have complained of coughing and respiratory tract irritation. Respiratory sensitization and bronchospasm has been described in some caprolactam-exposed workers. An increased incidence of bronchial asthma and bronchitis was noted in a group of Soviet workers with chronic caprolactam exposure.

o Respiratory stimulation and mild hypotension occurred in experimental animals given large oral doses. A decreased respiratory rate was noted in rats with inhalational exposure to caprolactam dust.

NEUROLOGIC

o One worker acutely overexposed to caprolactam developed generalized tonic-clonic seizures, fever, and leukocytosis. Caprolactam has caused convulsions in experimental animals. 1. The convulsant activity of caprolactam in experimental animals seems to occur by antagonism of gamma-aminobutyric acid (GABA)-mediated central nervous system inhibition.

o Chronically exposed workers have complained of headaches and a variety of nervous disorders.

GASTROINTESTINAL

o Anorexia, nausea, epigastric discomfort, flatulence, and a bitter taste in the mouth have been described in chronically-exposed workers.

HEPATIC

o Exposed experimental animals have developed hepatotoxicity. This effect has not been reported in exposed humans.

GENITOURINARY

o Exposed experimental animals have developed a variety of kidney lesions. These effects have not been reported in exposed humans.

TEMPERATURE REGULATION

o Fever was seen in one acutely poisoned worker.

XEMATOLOGIC

o Leukocytosis was seen in one acutely poisoned worker. Lymphocytosis has occurred with chronic occupational exposure.

DERMATOLOGIC

o Direct contact with the hot liquid can cause dermal bums. Prolonged and confined skin contact with the material can also cause dermal bums, especially if the liquid is spilled into footwear.

o Contact dermatitis and eczema have been noted in chronically exposed workers. The lesion is most often a tightening and reddening of the skin, similar to the appearance of a sunburn. Skin that is severely affected may peel, but seldom blisters. Hyperkeratosis or fissuring of the skin may occur in some occupational exposures. The nails may become brittle or deformed,

o Hypersensitivity dermal reactions may occur.

PREGNANCY/BREAST MILK

o female rats exposed to caprolactam had estrous cycle disturbances and decreased fecundity. Transplacental transfer of caprolactam has been shown in mice. Caprolactam was not teratogenic or embryotoxic in rats and rabbits at oral doses of 100 to 1,000 mg/kg per day for 9 to 22 days of gestation.

o One group of Soviet women with occupational caprolactam exposure in the textile industry were reported to have an increased incidence of a variety of complications of pregnancy, oligodysmenorrhea, and hypermenorrhea. Children born to these workers were noted to be normal.

CARCINOGENICITY

o An IARC Cancer Review found no evidence of carcinogenesis in animals. The NTP Carcinogenesis Bioassay found no evidence of carcinogenesis in mice and rats. The 1986 EPA GENETOX Program found no carcinogenicity in mice and rats.

GENOTOXICITY .

o Caprolactam is mutagenic in insects, microbial assay systems, rodent cells, and human lymphocytes. However, in the majority of mutagenicity tests, caprolactam SHOWED NO ACTIVITY,

Lirnonene (Dipentene)

NAME OF SUBSTANCE LIMONENE
CAS REGISTRY NUMBER 138-86-3

o CLINICAL EFFECTS :

SUMMARY

o Limonene is most likely of low toxicity. Mild dermal irritation and skin sensitization may occur. Hematuria and albuminuria might occur if large amounts are ingested. Somnolence and hypothermia have been noted in mice. Gastric epithelial irritation was caused by oral administration in mice. Cats completely wetted with a limonene-containing insecticidal dip developed skin excoriation, hypersalivation, transient blepharospasm in directly exposed eyes, hypothermia, muscle tremors, and ataxia.

RESPIRATORY

o Aspiration might produce lipoid pneumonitis.

GENITOURINARY

o Hematuria and albuminuria might occur in large ingestions.

DERMATOLOGIC

o Dermal irritation and sensitization are seen. Percutaneous absorption may occur.

HUMAN TOXICITY EXCERPTS

NO TOXIC REACTIONS HAVE BE DESCRIBED OTHER THAN MILD LOCAL IRRITATION & SKIN SENSITIZATION, BUT ALBUMINURIA & HEMATURIA ARE PROBABLE IF INGESTED IN SUFFCIENT QUANTITY. [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984. II-259] **PEER REVIEWED"

HUMAN TOXICITY EXCERPTS

DIPENTENE TESTED /AS IRRITATION TEST/ AT 20% IN PETROIATUM PRODUCED NO IRRITATION AFTER A 48 HR CLOSED PATCH TEST IN 25 HUMAN SUBJECTS. A MAXIMIZATION TEST . . . WAS CARRIED OUT ON 25 VOLUNTEERS. THE MATERIAL WAS TESTED @ CONCN OF 20%, IN PETROLATUM & PRODUCED NO SENSITIZATION REACTIONS. [Opdyke, D.L.J. (ed.). Monographs on Fragrance Raw Materials. New York: Pergamon Press, 1979. , p. 333) **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

FOLLOWING DENTAL SURGERY, PATIENT PRESENTED WITH INTENSE SWELLING OF HIS TONGUE, LIPS, & GINGIVAL MUCOSA. TESTING REVEALED HYPERSENSITIVITY TO PEPPERMINT OIL (A DENTAL PREPN), DUE TO SENSITIZING PROPERTIES OF INGREDIENTS SUCH AS LIMONENE. [DOOMS-GOOSSENS A ET AL; CONTACT DERMATITIS 3 (6): 304 (1977)] **PEER REVIEWED"

HUMAN TOXICITY EXCERPTS

THREE CASES OF ALLERGIC CONTACT DERMATITIS FROM DIPENTENE IN SAME BRAND OF HONING OIL REPORTED. MANUFACTURER HAS SINCE REPLACED IT WITH AN ALTERNATIVE. [RYCROFT R JG; CONTACT DERMATITIS 6 (5): 325 (1980)] **PEER REVIEWED"

HUMAN TOXICITY EXCERPTS
The toxicokinetics of d-limonene were studied in human volunteers exposed by inhalation (2 hr, work load 50 W) in an exposure chamber on three different occasions. The exposure concn were approximately 10, 225, and 450 mg/cu m d-limonene. The relative pulmonary uptake was high, approximately 70% of the amount supplied. A decrease in vital capacity was observed after exposure to d-limonene at a high exposure level. The subjects did not experience any irritative symptoms or symptoms related to the CNS. [Falk-Filipsson A et al; J Toxicol Environ Health 38 (1): 77-88 (1993)] **PEER REVIEWED'*
NON-HUMAN TOXICITY EXCERPTS
D-LIMONENE SOLUTION INJECTED AS BOLUS INTO BILIARY TRACT OF CATS PRODUCED HEPATOBILIARY TISSUE DAMAGE, DEPENDING ON CONTACT TIME, VOLUME AND FLOW DIRECTION OF THE SOLUTION. /D-LIMONENE/ [SCHENK J ET AL; Z GASTROENTEROL 18 (7): 389 (1980)] "PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
STUDY OF CHROMATOGRAPHIC DATA OF GLC PROFILES FROM TOTAL PARTICULATE MATTER OF 8 EXPTL CIGARETTES. D-LIMONENE WAS 1 PEAK IDENTIFIED THAT CORRELATED WITH CARCINOGENIC ACTIVITY WHEN PAINTED ON MICE SKIN. D-LIMONENE IS BEST INDICATOR THUS FAR OF TOBACCO SMOKE BIOLOGICAL ACTIVITY, /D-LIMONENE/ [HO CH ET AL; ANAL CHEM 48 (14): 2223 (1976)] **PEER REVIEWED"
NON-HUMAN TOXICITY EXCERPTS
2363 MG/KG GIVEN ORALLY TO MICE FOR 6 DAYS FROM DAY 7 TO DAY 12 OF GESTATION DECR BODY WT GAIN & INCR INCIDENCE OF ABNORMAL BONE FORMATION IN FETUSES. ALSO DECR BODY WT GAIN IN MALE OFFSPRING. TOXICITY WAS NOT SEVERE. [KODAMA R ET AL; OYO YAKURI 13 (6): 863 (1977)] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
ADMIN TO DOGS @ 1.2-3.6 ML/KG/DAY FOR 6 MONTHS CAUSED FREQUENT VOMITING & NAUSEA & DECR IN BODY WT, BLOOD SUGAR & CHOLESTEROL. NO SIGNIFICANT CHANGE OBSERVED IN ORGANS EXCEPT IN THE KIDNEY. [TSUJI M ET AL; OYO YAKURI 9 (5): 775 (1975)] "*PEER REVIEWED*'
NON-HUMAN TOXICITY EXCERPTS
AMINOPYRINE DEMETHYLASE & ANILINE HYDROXYLASE INCR 26 & 22% BY REPEATED ORAL ADMIN OF 400 MG/KG FOR 30 DAYS TO RATS. DECR PLASMA & LIVER CHOLESTEROL & ALTERED FATTY ACIDS OF LIVER PHOSPHOLIPIDS. ENZYMES NOT AFFECTED AFTER SINGLE DOSE OF 200-1200 MG/KG. [ARIYOSHI T ET AL; XENOBIOTICA 5 (I): 33 (1975)] "PEER REVIEWED"
NON-HUMAN TOXICITY EXCERPTS
ORALLY 227-1385 MG/KG/DAY CAUSED SLIGHT DECR IN BODY WEIGHT, LITTLE OR NO CHANGE IN WATER & FOOD CONSUMPTION IN RATS, NO HISTOPATHOLOGICAL CHANGES, EXCEPT GRANULAR CASTS IN KIDNEY OF SOME MALE RATS. [TSUJI M ET AL; OYO YAKURI 9 (3): 403 (1975)] "PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
LIMONENE WAS INHIBITORY /HEPATIC HMGCoA (HYDROXY-3-METHYLGLUTARYL-CoA) REDUCTASE/ WHEN ADMIN INTRAGASTRICALLY @ 3 MMOL/KG TO RATS. [CLEGG RJ ET AL; BIOCHEM PHARMACOL 29 (15): 2125 (1980)] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS

Naturally occurring compounds belonging to two hemicagroups were studied for their capacities to inhibit N-nitrosodiethylamine-induced carcinogenesis in female A/ mice. One group consisted of D-limonene and D-carvone. . . . Test compounds were given orally either 15 min or 1 hr prior to NDEA. Under these conditions, D-limonene and D-carvone reduced forestomach tumor formation by about 60% and pulmonary adenoma formation by about 35%. /D-limonene/ [Wattenberg LW et al; Cancer Res 49 (10): 2689-92 (1989)] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
Adult male and female Sprague Dawley rats were given single oral doses of 0, 0.1, 0.3, 1, or 3 mmol d-limonene/kg (0, 14, 41, 136, or 409 mg/kg) in corn oil. A dose response relationship for acute exacerbation of hyaline droplets by d-limonene treatment was observed. Hyaline droplets were graded according to size, eosinophilic intensity, and the number of tubules loaded with droplets. Control rats received a mean score of 3. At 3 mmol/kg, admin of d-limonene resulted in a score of 10. At 0.1 mmol/kg, no effect on hyaline droplet accumulation was seen in male rats. 24 hr after admin of 3 mmol d-limonene/kg, the renal concentration of d-limonene equivalents was approximately 2.5 times higher in male rats than in female rats. Equilibrium dialysis in the presence or absence of sodium dodecyl sulfate indicated that approximately 40% of the d-limonene equivalents in male rat kidney associated with proteins in a reversible manner, whereas no significant association was observed between d-limonene equivalents and female rat kidney proteins. Gel filtration HPLC indicated that d-limonene in male rat kidney is associated with a protein fraction having a mol wt of approximately 20,000. Using reverse phase HPLC, d-limonene was shown to be associated with alpha-2u-globulin which was identified by amino acid sequencing. The major metabolite associated with alpha-2u-globulin was d-limonene-1,2-oxide. Parent d-Uimonene was also identified as a minor component in the alpha-2u-globulin fraction. /D-limonene/ [Lehman McKeeman LD et al; Toxicol Appl Pharmacol 99 (2): 250-9 (1989)] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
d-Limonene was not mutagenic in four strains of Salmonella typhimurium (TA98, TA100, TA1535, or TA1537), did not significantly increase the number of trifluorothymidine resistant cells in the mouse L5178Y/TK + or - assay, and did not induce chromosomal aberrations or sister chromatid exchanges in cultured Chinese hamster ovary cells. All assays were conducted in the presence and absence of exogenous metabolic activation (S9). [DHHS/NTP; Toxicology and Carcinogenesis Studies of d-Limonene (gavage Studies) p. 3 (1990) Technical Rpt Series No. 347 NIH Pub No. 90-2802] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS)
Inhibition of cholesterol biosynthesis occurred in the small intestine of rats after administration of d-limonene for 7 days, but no significant effect on the secretion of radiolabeled cholesterol into bile and feces was observed. d-Limonene increased the perfusion pressure of the sphincter of Oddi in dogs when injected iv or directly into the common bile duct. d-Limonene has also been used successfully for the postoperative dissolution of retained cholesterol gallstones. ID-limonenel [DHHS/NTP; Toxicology and Carcinogenesis Studies of d-Limonene (Gavage Studies) p. 13 (1990) Technical Rpt Series No. 347 NIH Pub No. 90-2802] **PEER REVIEWED"
NON-HUMAN TOXICITY EXCERPTS
There is a diverse group of hydrocarbons that induce a specific spectrum of nephropathic alterations. Examples include d-limonene, an aromatic hydrocarbon. Only male rats develop kidney alterations upon exposure, Other mammals such as female rats, 'mice, guinea pigs, dogs

and monkeys evidently are refractory to kidney injury upon exposure. The male rat hydrocarbon nephropathy should not be predictive of a normal human renal response. [Alden CL; Toxicol Pathol 14 (1): 109-I 1 (1986)] **PEER REVIEWED"

NON-HUMAN TOXICITY EXCERPTS

The role of alpha2-microglobulin in xenobiotic induced nephropathy was examined in rats. Male NCI Black Reiter rats were administered various cmpd including 1650 mg/kg d-limonene by gavage daily for 4 days. Twenty four hours after the last dose, the animals were killed and the kidneys were removed and sectioned. Nephrotoxicity was assessed by examining the sections for the presence of hyaline droplets and other histological changes. The sections were assayed for alpha2-microglobulin using a histochemical technique. Lindane induced hyaline droplet formation in male, but' not female, F344 rats. d-Limonene did not induce hyaline droplet formation or alpha2-microglobulin production in male NCI Black Reiter rats. It was concluded that the presence of alpha2-microglobulin is necessary for the development of kidney disease in male rats exposed to d-limonene. [Dietrich DR, Swenberg JA; Fund Appl Toxicol 16 (4): 749-62 (1991] "PEER REVIEWED*'

NON-HUMAN TOXICITY EXCERPTS

The monocyclic monoterpenoid compounds limonene and sobrerol have anticarcinogenic activity when fed during the initiation stage of dimethylbenz(a)anthracene induced rat mammary carcinogenesis. The potential roles of hepatic glutathione-S-transferase and uridine diphosphoglucuronosyl transferase were studied in monoterpene-mediated chemoprevention. Diets containing the isoeffective anticarcinogenic terpenes, 5% limonene or 1% sobrerol, elevated hepatic glutathione-S-transferase activity > 2 fold when measured using the general substrate I-chloro-2,4-dinitrobenzene and 3,4-dichloronitrobenzene for the glutathione-S-transferase dimer 3-3. However, there were no significant changes in hepatic glutathione-S-transferase activity when 1,2-epoxy-3-(p-nitrophenoxy)propane was used. Liver glutathione-S-transferase subunit 3 had the greatest increase followed by 1 and 4 with no change in subunit 2. Both terpene diets significantly increased the activity of the methylcholanthrene inducible and the phenobarbital inducible uridine diphosphoglucuronosyl transferase isozymes. It was proposed: that much of the anticarcinogenic activity of these monocyclic monoterpenes during the initiation phase of dimethylbenz[a]anthracene carcinogenesis is mediated through the induction of the hepatic detoxification enzymes glutathione-S-transferase and uridine diphosphoglucuronosyl transferase. [Elegbede JA et al; Carcinogenesis 14 (6): 1221-3 (1993)] "PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

The nephrotoxicity of d-limonene was studied in rats and mice. Kidney sections taken from male rats, strain not specified, that had been part of a 91 day oral dosing study of limonene in rats and mice, were examined by light microscopy. The study showed that renal alterations were induced only in male rats. Dose related decreases in absolute weight gain and relative weight gain (expressed as a percentage of the control weight gain) also occurred. The 2400 mg/kg dose killed nine of ten female rats. Kidney sections of male rats showed that limonene caused cytoplasmic basophilia of proximal convoluted tubule cells, tubular hyperplasia or atrophy, fibrosis of Bowman's capsule, and an interstitial fibrolymphocytic response. The severity of the lesions was dose related except in rats given 2400 mglkg limonene. The severity of the Jesions in the 2400 mg/kg group was similar to those seen in rats given 150 mglkg. Occasional foci of proximal convoluted tubule epithelial cell necrosis of degeneration were seen in all treated rats, Granular casts were seen in the outer medulla of animals that survived to the end

of the study except for one rat in the 2400 mg/kg group. No hyaline droplet accumulation within the cytoplasm of proximal convoluted tubule epithelial cells was seen. Except for the absence of hyaline droplet formation, the changes induced by limonene are similar to those seen in male rats exposed to decalin. [Kanerva RL, Alden CL; Food Chem Toxicol 25 (5): 355-8 (1987)]
"PEER REVIEWED-
NON-HUMAN TOXICITY EXCERPTS
The allergenic potential of d-limonene oxidation products was examined. Samples of d-limonene were exposed to air or unexposed in a preliminary experiment. The concn of d-limonene decreased after 8 wk air exposure. Carvone, cis and trans limonene oxide, and cis and trans carveal were the major oxidation products detected. Only slight decomposition was seen in nonexposed d-limonene. Dunkin-Hartley guinea pigs were induced by topical application of (+)-limonene oxide, (R)-(-)-carvone, (-)-carveal, or air exposed d-limonene. (+)-Limonene oxide and (-)-carveal consisted of mixtures of cis and trans isomers of the two compounds. The sensitizing potential of the compounds was assessed by the Freund complete adjuvant test after challenge with (+)-limonene oxide. Other guinea pigs were induced with air exposed d-Jimonene. The sensitizing potential of air exposed or nonexposed d-limonene, (+)-limonene oxide, or (R)-(-)-carvone was evaluated by the guinea pig maximization test. Air exposed d-limonene was a strong sensitizer in both the Freund complete adjuvant test and guinea pig maximization test. d-Limonene that was not air exposed exhibited no sensitizing potential. (+)-Limonene oxide and R-(-)-carvone, but not (-)-carveal, were potent sensitizers. Air oxidation of d-limonene is necessary for its sensitizing potential. Air oxidation produces potent allergens such as limonene oxide and carvone. [Karlberg AT et al; Contact Dermatitis 26 (5): 332-40 (1992)] '*PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
d-Limonene, a monocyclic monoterpenoid with known insecticidal properties, was assayed (by a standard method of cutaneous exposure) for general lethality effects as well as neurotoxic effects on escape reflex pathways in earthworms, Eisenia fetida (Savigny). Neurotoxicity was assessed by noninvasive electrophysiological techniques involving (a) quantification of the impacts of chronic and acute sublethal exposures on impulse conduction in the worms medial and lateral giant nerve fiber pathways, (b) determination of whether such effects were generalized or localized within various body regions, and (c) determination of the reversibility of neurotoxic effects. The LD50 value for d-limonene alone was 6.0 ppm, and the LT50 value for exposure to 12.6 ppm was 4.9 hr. Effects on lethality were not synergized significantly by either piperonyl butoxide or sesame oil. Generally, chronic and acute intoxication involved a rapid and predictable cascade of behavioral and morphological symptoms, including increased mucus secretion, writhing, clitellar swelling, and elongation of the body. In addition, chronic d-limonene exposures induced significant weight loss, but there was no effect on median giant nerve fiber and lateral giant nerve fiber conduction velocities, even though abnormal rebounding of median giant nerve fiber impulses and spontaneous lateral giant nerve fiber spiking were often evident. Acute exposures, however, induced significant decreases in conduction velocity in both the median giant nerve fiber and lateral giant nerve fiber, but the effects were regionally specific; for example, lateral giant nerve fiber velocities were significantly reduced in the posterior half of the body but not in the anterior half. The magnitude of conduction velocity decreases was directly related to both concn and duration of exposure. Decreases in conduction velocities after acute exposures were reversed once d-limonene exposure ceased. [Karr LL et al; Pestic Biochem Physiol 36 (2): 175-86 (1990)] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS
The anticarcinogenic effects of monocyclic monoterpenes such as limonene were demonstrated when given during the initiation phase of 7,12-dimethylbenz[a]anthracene induced mammary cancer in Wistar-Furth rats. The possible mechanisms for this chemoprevention activity including limonene's effects on 7,12-dimethylbenz(a)anthracene-DNA adduct formation and hepatic metabolism of 7,12-dimethylbenz[a]anthracene were investigated. Twenty four hours after carcinogen administration, there were approx 50% decreases in 7,12-dimethylbenz(a)anthracene-DNA adducts found in control animals formed in the liver, spleen, kidney and lung of limonene fed animals. While circulating levels of 7,12-dimethylbenz(a)anthracene and/or its metabolites were not different in control and limonene fed rats, there was a 2.3 fold increase in 7,12-dimethylbenz(a)anthracene and/or 7,12-dimethylbenz(a)anthracene derived metabolites in the urine of the limonene fed animals. Limonene and sobrerol, a hydroxylated monocyclic monoterpenoid with increased chemoprevention activity, modulated cytochrome p450 and epoxide hydrolyase activity. The 5% limonene diet increased total cytochrome p450 to the same extent as phenobarbital treatment, while 1% sobrerol (isoeffective in chemoprevention to 5% limonene) did not. However, both 5% limonene and 1% sobrerol diets greatly increased the levels of microsomal epoxide hydrolyase protein and associated hydrating activities towards benzo[a]pyrene 4,5-oxide when compared to control and phenobarbital treatment. These changes also modified the rate and regioselectivity of in vitro microsomal 7,12-dimethylbenz(a)anthracene metabolism when compared to phenobarbital treatment or control. Identification of the specific isoforms of cytochrome p450 induced by these terpenoids was performed with antibodies to cytochrome p450 isozymes in Western blot analysis and inhibition studies of microsomal 7,12-dimethylbenz(a)anthracene metabolism. Five percent limonene was more effective than 1% sobrerol at increasing the levels of members of the cytochrome p450 2B and 2C families but was equally effective at increasing epoxide hydrolyase. Furthermore, both terpenoid diets caused increased formation of the proximate carcinogen, 7,12-dimethylbenz(a)anthracene 3,4-dihydrodiol. [Maltzman TH et al; Carcinogenesis 12 (11): 2081-7 (1 991)] **PEER REVIEWED"
NON-HUMAN TOXICITY VALUES
LD50 Mouse oral 5.6-6.6 g/kg [DHHSINTP; Toxicology and Carcinogenesis Studies of d-Limonene (Gavage Studies) p.13 (1990) Technical Rpt Series No. 347, NIH Pub No. 90-2802] "PEER REVIEWED**
NON-HUMAN TOXICITY VALUES
LD50 Mouse ip 1.3 g/kg [DHHS/NTP; Toxicology and Carcinogenesis Studies of d-Limonene (Gavage Studies) p.13 (1990) Technical Rpt Series No. 347, NIH Pub No. 90-2802] **PEER REVIEWED"
NATIONAL TOXICOLOGY PROGRAM REPORTS
Two year studies of d-limonene /more than 99% pure/ were conducted by administering 0, 75, or 150 mg/kg d-limonene in corn oil by gavage to groups of 50 F344/N male rats, 5 days per week for 103 weeks; groups of 50 female F344/N rats were administered 0, 300, or 600 mg/kg. Mean body weights of rats dosed with d-limonene were similar to those of vehicle controls throughout the studies. Survival of the high dose female rats after week 39 and of the vehicle control male rats after week 81 was significantly reduced (survival at week 104--male: vehicle control, 29/50; low dose, 33/50; high dose, 40/50; female: 42/50; 40/50; 26/50). The kidney was confirmed as the primary target organ for chemically related lesions. No lesions were

observed in female rats. For males, the nonneoplastic lesions included exacerbation of the age-related nephropathy, linear deposits of mineral in the renal medulla and papilla, and focal hyperplasia of the transitional epithelium overlying the renal papilla. Uncommon tubular cell adenomas and adenocarcinomas of the kidney also occurred in dosed male rats, and this effect was supported by a dose-related increased incidence of tubular cell hyperplasia. . . . There was clear evidence of carcinogenic activity of d-limonene for male F344/N rats, as shown by increased incidences of tubular cell hyperplasia, adenomas, and adenocarcinomas of the kidney, There was no evidence of carcinogenic activity of d-limonene for female F344/N rats that received 300 or 600 mg/kg. /D-Limonene/ [DHHS/NTP; Toxicology and Carcinogenesis Studies of d-Limonene (Gavage Studies) p. 3 (1990) Technical Rpt Series No. 347 NIH Pub No. 90-2802] "PEER REVIEWED**

NATIONAL TOXICOLOGY PROGRAM REPORTS

Groups of 50 male B6C3F1 mice were administered 0, 250, 500 mg/kg, . . . /5 days per week for 103 weeks/; groups of 50 female B6C3FI mice were administered 0, 500, or 1000 mg/kg. Mean body weights of dosed and vehicle control male mice were similar throughout the studies. Mean body weights of high dose female mice were notably lower than those of the vehicle controls after week 28. Survival of the low dose group-of male mice was significantly lower than that of vehicle controls at the end of the study (33150; 24/50; 39150). No difference in survival was observed between vehicle control and dosed female mice (43/50; 44/50; 43/50). . . . No chemically related increases in neoplasms were observed. The incidence of neoplasms of the anterior pituitary gland in high dose female mice was lower than that in vehicle controls (adenomas or carcinomas, combined: vehicle control, 12/49; high dose, 2/48). Cells with an abnormal number of nuclei (8/49; 32/50) and cytomegaly (23149; 38150) were observed in the liver of high dose male mice. There was no evidence of carcinogenic activity of d-limonene for male B6C3FI mice that received 250 or 500 mg/kg. There was no evidence of carcinogenic activity of d-limonene for female B6C3FI mice that received 500 or 1000 mg/kg. [DHHS/NTP; Toxicology and Carcinogenesis Studies of d-Limonene (gavage Studies) p. 3 (1990) Technical Rpt Series No. 347 NIH Pub No. 90-2802] **PEER REVIEWED**

2-Methylnaphthalene

NAME OF SUBSTANCE 2-METHYLNAPHTHALENE
CAS REGISTRY NUMBER 91-57-6

HUMAN TOXICITY EXCERPTS
IN CONTRAST TO NAPHTHALENE, THE ONLY REPORTED EFFECTS OF METHYLATED NAPHTHALENE IN MAN ARE SKIN IRRITATION AND SKIN PHOTOSENSITIZATION. /METHYLATED NAPHTHALENE/ [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984. III-309] **PEER REVIEWED"
NON-HUMAN TOXICITY EXCERPTS
EXPOSURE OF THE DUNGENESS CRAB (C MAGISTER) LARVAE TO SEAWATER SOLN OF THE WATER SOL FRACTION (WSF) OF COOK INLET CRUDE OIL SHOWED THAT THE CONCN OF AROMATIC HYDROCARBONS IN WSF WAS INVERSELY RELATED TO THE DEGREE OF ALKYLATION IN NAPHTHALENE FAMILY, BUT THE ACUTE TOXICITY OF THE AROMATIC CMPD WAS DIRECTLY RELATED TO THE DEGREE OF ALKYL SUBSTITUTION. THE SEAWATER CONCN OF 2-METHYLNAPHTHALENE IN WATER SOL FRACTION OF COOK INLET CRUDE OIL WAS 0.03 + or - 0.001 MG/L. [CALDWELL ET AL; FATE EFF PET HYDROCARBONS MAR ECOSYST ORG, PROC SYMP, 1977, 210-20] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
2-Methylnaphthalene /admin orally at concn 5.00 mg/kg/ is lethal to /rats/. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 3338] **PEER REVIEWED'*
NON-HUMAN TOXICITY EXCERPTS
TOBACCO SMOKE CONDENSATES, 239 CMPD REPRESENTATIVE OF THE GASEOUS & SEMIVOLATILE PHASE OF TOBACCO SMOKE, WERE ASSAYED FOR MUTAGENICITY TOWARDS 4 HISTIDINE REQUIRING MUTANTS OF SALMONELLA TYPHIMURIUM. I- & 2-METHYLNAPHTHALENE WERE TESTED QUANTITATIVELY USING TA98 AND TA100 WITH AND WITHOUT S9 FROM 3-METHYLCHOLANTHRENE INDUCED RATS THE CONCN USED WERE 3 UMOL/PLATE. 1- & 2-METHYLNAPHTHALENE WERE NOT MUTAGENIC. [FLORIN I ET AL; TOXICOL 15 (3): 219-32 (1980)] **PEER REVIEWED**

Adiponitrile

NAME OF SUBSTANCE ADIPONITRILE
CAS REGISTRY NUMBER 111-69-3

TOXIC HAZARD RATING
CLASSIFICATION: D; not classifiable as to human carcinogenicity. BASIS FOR CLASSIFICATION: No human and no animal cancer data were available. Adiponitrile was negative for mutagenicity in Salmonella with and without activation. HUMAN CARCINOGENICIN DATA: None. ANIMAL CARCINOGENICITY DATA: None. [U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Adiponitrile (I 1 l-69-3) from the National Library of Medicine's TOXNET System, March 28, 1994) [CITATION] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS
A CASE HISTORY OF HUMAN EXPOSURE . . . REPORTED THE EFFECTS OF DRINKING ,,A FEW MILLILITERS" OF ADIPONITRILE BY AN 18 YR OLD MALE. ABOUT 20 MIN AFTER INGESTION HE EXPERIENCED TIGHTNESS IN THE CHEST, HEADACHE, WEAKNESS WITH DIFFICULTY IN STANDING, & VERTIGO. HE BECAME CYANOTIC, RESPIRATIONS WERE RAPID, & HE HAD LOW BLOOD PRESSURE & TACHYCARDIA. THE PUPILS WERE DILATED & BARELY REACTED TO LIGHT. HE EXHIBITED MENTAL CONFUSION & TONIC-CLONIC CONTRACTIONS OF LIMBS & FACIAL MUSCLES. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 4881] **PEER REVIEWED""
HUMAN TOXICITY EXCERPTS
... HUMAN SKIN EXPOSURES TO ADIPONITRILE RESULT IN SKIN IRRITATION & INFLAMMATION . . . ONE CASE IN WHICH ADIPONITRILE CAUSED MASSIVE DESTRUCTION OF THE SKIN ON ONE FOOT. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 4881] "PEER REVIEWED**
HUMAN TOXICITY EXCERPTS
HIGHLY TOXIC BY INGESTION, INHALATION & SKIN ABSORPTION. IT PRODUCES DISTURBANCES OF RESPIRATORY & CIRCULATORY SYSTEMS. [National Fire Protection Guide. Fire Protection Guide on Hazardous Materials. 10 th ed. Quincy, MA: National Fire Protection Association, 1991. 49-20] **PEER REVIEWED**
HUMAN TOXICITY EXCERPTS
POISONING BY ADIPONITRILE RESEMBLES POISONING WITH HYDROCYANIC ACID . . . [Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. , p. 108] **PEER REVIEWED"
HUMAN TOXICITY EXCERPTS
/Symptoms of/ human toxicity of adiponitrile . . . /include/ deep anesthesia, headache, vertigo, vomiting, cyanosis of the skin and mucosa, tachypnea, tachycardia, hypotension, mydriasis, and clonic convulsions of the limbs. [Snyder, R. (ed.). Ethyl Browning's Toxicity and Metabolism of Industrial Solvents. 2nd ed. Volume II: Nitrogen and Phosphorus Solvents. Amsterdam-New York-Oxford: Elsevier, 1990. , p. 327] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS
A case of cyanide poisoning resulting from exposure to propionitrile was decribed. A 55 year old male employed at a chemical facility suffered dermal and respiratory exposure while attempting to repair a pump leaking propionitrile. Although he was wearing gloves, he did not have any other protective equipment. He rapidly lost consciousness and was taken to the infirmary. Upon arrival at the infirmary, he was comatose and unresponsive. He was administered oxygen at the rate of 5 l/min and transferred to the intensive care unit of a hospital. Clinical studies showed evidence of respiratory alkalosis and mild metabolic acidosis. The patient received 4 g hydroxycobalamin and 8 g sodium thiosulfate iv over 30 minutes. The symptoms completely cleared up over the next hr. Blood cyanide and thiocyanate concentrations were monitored. Before receiving the hydroxycobalamin and thiosulfate treatment, his blood cyanide concn was 5.71 ug/ml. The thiocyanate concn was negligible. After the cyanide/thiosulfate infusion was completed, the blood cyanide concn had decreased to 0.93 ug/ml and the thiocyanate had increased to 21.1 ug/ml. The thiocyanate concentrations returned *to* the baseline value 5 hr after treatment. . . . Propionitrile can release cyanide and produce serious poisoning after skin or inhalation exposure. The combination of sodium thiosulfate and hydroxycobalamin is an effective antidote. /Propionitrile/ [Bismuth C et al; J Emer Med 5 (3): 191-5 (1987)] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
A 2 YR DRINKING WATER EXPOSURE OF WISTAR RATS AT 0.5, 5.0, & 50 PPM ADIPONITRILE PRODUCED SIGNIFICANT ADRENAL DEGENERATION IN FEMALE RATS AT ALL 3 CONCN & AT 50 PPM IN MALE RATS. ALL BODY WT & ORGAN WT RATIOS OF SPLEEN, LIVER, & KIDNEY WERE WITHIN NORMAL RANGES. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982., p. 4880] **PEER REVIEWED*'
NON-HUMAN TOXICITY EXCERPTS
EXPOSURES OF PREGNANT SPRAGUE DAWLEY RATS AT 10,100, & 500 PPM IN DRINKING WATER DID NOT CHANGE FERTILITY, GESTATION, OR VIABILITY OF OFFSPRING. EXPOSURE OF MONGREL DOGS TO APPROX 10, 100, 500, & 1000 PPM ADIPONITRILE IN THE DIET RESULTED IN GREATLY DECR FOOD INTAKE & VOMITING AT 1000 PPM. NO HEMATOLOGIC ABNORMALITIES WERE FOUND. KIDNEY & LIVER FUNCTION WERE NORMAL AT 500 PPM & BELOW. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-l 982., p. 4881] '"PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
MEDIAN LETHAL CONCN WAS 1.71 MG/L FOR ACUTE (4 HR) INHALATION OF ADULT MALE CHR-CD RATS. RATS WERE EXPOSED TO 0 (CONTROL), 0.03, 0.1 OR 0.3 MG VAPORIZED ADIPONITRILE/L FOR 10 6-HR PERIODS (5 EXPOSURE DAYS, 2 REST DAYS, 5 EXPOSURE DAYS). CLINICAL SIGNS DURING EXPOSURE INCL IRREGULAR RESPIRATION & MILD SALIVATION. AT 0.3 MG/L RATS SHOWED WT LOSS DURING 1ST 5 EXPOSURES FOLLOWED BY NORMAL RATE OF WT GAIN. AFTER 10 EXPOSURES, RATS IN THIS GROUP SHOWED INCR BLOOD GLUCOSE, UREA NITROGEN, CREATININE & URINE GLUCOSE; DECR ERYTHROCYTES COUNT, HEMOGLOBIN, LEUKOCYTE COUNT, RELATIVE NUMBER OF EOSINOPHILS, & URINE OSMOLALITY. RATS EXPOSED TO 0.1 MG/L HAD INCR UREA NITROGEN & LYMPHOCYTES & DECR NUMBER OF NEUTROPHILS & EOSINOPHILS. RATS FROM ALL 'GROUPS HAD NORMAL VALUES 14 DAYS AFTER LAST

EXPOSURE. [SMITH LW, KENNEDY GL JR; TOXICOL APPL PHARMACOL 65 (2): 257 (1982)] "PEER REVIEWED*'
NON-HUMAN TOXICITY EXCERPTS
Adiponitrile was evaluated for embryotoxic and teratogenic potential in rats. Mated Sprague Dawley rats were administered adiponitrile by gavage on gestation days 6-19, inclusive. Daily dosage levels (mg/kg body wt) were 0, 20, 40, and 80. There was evidence of maternal toxicity in the high dose group. Some maternal effects also were seen at the middle dosage. Slight fetotoxicity was observed at the highest dosage. No teratogenic effects were observed at any dosage level. [Johannsen FR et al; Fundam Appl Toxicol7 (I): 33-40 (1986)] **PEER REVIEWED"
NON-HUMAN TOXICITY EXCERPTS
Rats were exposed 6 hr/day, 5 day/wk for 4 or 13 wk to atmospheres containing a range of adiponitrile concentrations and observed for signs of toxicity. A fertility assessment was also included as a component of the 13 wk study. Mortality and reduced weight gain were observed within 1 wk only in rats exposed to 493 mg/sq m. Evidence of slight anemia was present in rats exposed to 99 mg/sq m and above. There was no histopathological evidence of organ toxicity in about 30 tissues from both sexes exposed up to 99 mg/cu m, the highest concentration tested, for 13 wk. In addition, fertility, as monitored by reproductive performance and litter parameters, was normal in both males and females similarly exposed. [Short RD et al; J Toxicol Environ Health 30 (3): 199-208 (1990)] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
No effect was seen in the blood of guinea pigs dosed repeatedly with 3-30 mg/kg sc doses of adiponitrile 6 days/wk for 40-70 days. [Snyder, R. (ed.). Ethyl Browning's Toxicity and Metabolism of Industrial Solvents. 2nd ed. Volume II: Nitrogen and Phosphorus Solvents. Amsterdam-New York-Oxford: Eisevier, 1990. , p. 326] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
Exposure of mongrel dogs to approximately 10, 100, 500 and 1000 ppm adiponitrile in the diet resulted in greatly decreased food intake and vomiting at 1000 ppm. No hematological abnormalities were found. Kidney and liver function were normal at 500 ppm and below. [Snyder, R. (ed.). Ethyl Browning's Toxicity and Metabolism of Industrial Solvents. 2nd ed. Volume II: Nitrogen and Phosphorus Solvents. Amsterdam-New York-Oxford: Elsevier, 1990. , p. 326] "PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
Rats were exposed to 0, 0.03, 0.1 or 0.3 mg/l of vaporized adiponitrile for ten 6 h periods (5 exposure days, 2 rest days, 5 exposure days). Clinical signs during exposure included irregular respiration and mild salivation. At 0.3 mg/l rats showed weight loss during the first 5 exposures followed by a normal rate of weight gain. Rats in this group exhibited increased blood glucose, urea nitrogen creatine and urinary glucose; decreased erythrocyte and leucocyte counts and hemoglobin values. Some blood abnormalities also were seen in the 0.1 mg/l exposure group. Rats in all groups had normal values 14 days after the last exposure. [Snyder, R. (ed.). Ethyl Browning's Toxicity and Metabolism of Industrial Solvents. 2nd ed. Volume II: Nitrogen and Phosphorus Solvents. Amsterdam-New York-Oxford: Elsevier, 1990. , p. 326] **PEER REVIEWED"
NON-HUMAN TOXICITY VALUES
LD50 Guinea pig sc 50 mg/kg [Verschueren, K. Handbook of Environmental Data of Organic Chemicals, 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983. , p. 166] **PEER

REVIEWED"'
NON-HUMAN TOXICITY VALUES
LD50 Rat oral 300 **mg/kg** [Snyder, R. (ed.). Ethyl Browning's Toxicity and Metabolism of industrial Solvents. 2nd ed. Volume II: Nitrogen and Phosphorus Solvents. Amsterdam-New York-Oxford: Elsevier, 1990. , **p. 326]** '"PEER REVIEWED** .
NON-HUMAN TOXICITY VALUES
LD50 Mouse ip 40 **mg/kg** [Snyder, R. (ed.). Ethyl Browning's Toxicity and Metabolism of Industrial Solvents. 2nd ed. Volume II: Nitrogen and Phosphorus Solvents. Amsterdam-New York-Oxford: Elsevier, 1990. , p. **326]** "PEER REVIEWED**
NON-HUMAN TOXICITY VALUES
LC50 Rat inhalation 1.71 **mg/l/4** hr [Snyder, R. (ed.). Ethyl Browning's Toxicity and Metabolism of Industrial Solvents. 2nd ed. Volume II: Nitrogen and Phosphorus Solvents. Amsterdam-New York-Oxford: Elsevier, 1990. , p. **326]** **PEER REVIEWED'*

Octamethylcyclotetrasiloxane

NAME OF SUBSTANCE OCTAMETHYLCYCLOTETRASILOXANE
CAS REGISTRY NUMBER 556-67-2

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The following Overview, *** SILICONES ***,
is relevant for this HSDB record chemical.

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o CLINICAL EFFECTS :

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

o Silicones have a low reactivity. Reactions occur almost exclusively when silicone is injected or implanted. There is considerable evidence that injected silicone may evoke a foreign body granulomatous reaction. After injection, vacuoles have been found in lungs, liver, brain, kidney, spleen and pancreas.

1. Severe reactions to injection include fever, pneumonitis, ARDS, and rarely death.

o Silicones, such as simethicone, are nontoxic when ingested orally.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

o Silicone injection has been associated with the development of fatal pulmonary edema, pneumonitis, pleural effusion, ARDS and dyspnea.

HEPATIC

0.2.9.1 ACUTE EXPOSURE

o Granulomatous hepatitis has occurred following silicone injection.

GENITOURINARY

0.2.10.1 ACUTE EXPOSURE

o Renal failure was reported in one patient after augmentation mammoplasty.

DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

o Hypopigmentation and peau d'orange skin changes have been reported after silicone injection or implantation.

CARCINOGENICITY

0.2.21.2 HUMAN OVERVIEW

o Two large studies have not found an increase in cancer among patients with silicone breast implants (Petit et al, 1994; Duffy and Woods, 1994).

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o RANGE OF TOXICITY :

o Silicones have a very low oral toxicity. Several rat studies have shown no or minimal toxicity even when given chronically in their diet.

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o REFERENCE :

[Rumack BH: POISINDEX(R) Information System. Micromedex Inc., Englewood, CO, 1995; CCIS CD-ROM Volume 87, edition exp Feb, 1996. Hall AH & Rumack BH (Eds): TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 1995; CCIS CD-ROM Volume 87, edition exp Feb, 1996.]

NON-HUMAN TOXICITY EXCERPTS

Low molecular weight organosiloxane cmpd, at 0.01-l 00 mglkglday orally in female /ovariectomized/ rats, increased uterine weight . . . produced uterine hyperemia, and changed uterine morphology. . . . Several compounds were estrogenic in character and were more potent orally than parenterally. Biological activity was correlated with stereospecificity, and cyclosiloxanes were more active than their corresponding linear siloxanes. /Organosiloxanes/. [Hayden JF, Barlow SA; Toxicol Appl Pharm 21: 68-79 (1972)] "PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

The clastogenic activity of several organosilicon compounds was investigated using in vivo cytogenetic tests. The test compounds included methyltrichlorosilane, dimethyldichlorosilane, trimethylchlorosilane, trimethylsilanol, hexamethyldisiloxane, and hexamethylcyclotrisiloxane. Male Sprague Dawley rats received ip injections of the test chemicals, and bone marrow samples were collected at 6, 24, and 48 hr. Chromosomes were prepared using standard air drying methods. Confirmatory bone marrow chromosome assays and the dominant lethal test were used to evaluate the in-vivo clastogenic potential of trimethylsilanol. Chromosomes were harvested after intraperitoneal injections of the agent at concn of 300,400, and 500 mg/kg, and a 9 wk dosing schedule prior to mating was used for the dominant lethal study. No significant, dose related increase in chromosome damage was observed for any of the agents tested. Simple chromatid gaps and breaks were the predominant type of damage. Neither the bone marrow chromosome assay nor the dominant lethal test revealed any clastogenic activity for trimethylsilanol. It was concluded that all the agents tested lack clastogenic activity. [Isquith A et al; Food Chem Toxicol26 (3): 263-6 (1988)] "PEER REVIEWED**

Nonanal

NAME OF SUBSTANCE NONANAL
CAS REGISTRY NUMBER 124-19-6

No specific toxicological information found.

Phenyl Ether

NAME OF SUBSTANCE **DIPHENYL** ETHER
CAS REGISTRY NUMBER **101-84-8**

HUMAN TOXICITY EXCERPTS
IT IS ONLY SLIGHTLY IRRITATING TO SKIN AND OCCASIONAL BRIEF CONTACT DOES NOT **HAVE** ANY EFFECT. IRRITATION OCCURS ONLY **AFTER** REPEATED & PROLONGED CONTACT. ODOR IS EXTREMELY UNPLEASANT. [International **Labour** Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill Book Co., 1971. , p. **392]** "PEER REVIEWED'*
HUMAN TOXICITY EXCERPTS
AT CONCN OF **7-10** PPM /OF DOWTHERM/, VAPOR CAUSES BURNING OF EYES, **IRRITATION** OF RESPIRATORY TRACT & SEVERE NAUSEA. REPEATED & PROLONGED CONTACT CAN CAUSE IRRITATION OF SKIN. **/DOWTHERM/** [International **Labour** Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill %ook Co., 1971. , p. **392]** **PEER REVIEWED**
HUMAN TOXICITY EXCERPTS
ACUTE INTOXICATION /BY **DOWTHERM/** IS POSSIBLE FROM ACCIDENTAL INGESTION, RESULTING IN SEVERE DEGENERATIVE LESIONS IN LIVER & KIDNEYS, WHICH ARE IRREVERSIBLE IF DOSE IS VERY LARGE. **/DOWTHERM/** [International **Labour** Office. Encyclopedia of Occupational Health and Safety. Volumes I and II. New York: McGraw-Hill %ook Co., 1971. , p. 392) **PEER REVIEWED*'
HUMAN TOXICITY EXCERPTS
...DOES NOT PRESENT AN APPRECIABLE HAZARD TO HEALTH AS ORDINARILY USED. **[Patty, F.** (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , **p. 1700]** **PEER REVIEWED**
HUMAN TOXICITY EXCERPTS
...VAPOR CONCN THAT CAN OCCUR AT ORDINARY ROOM TEMP PRESENT NO HAZARD OF SYSTEMIC INJURY. . **..DISAGREEABLE ODOR.../AT** SUCH **CONCN/.** [Patty, F. (ed.). **Industrial** Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, **1963.** , p. **1700]** **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
-INJURY TO LIVER, SPLEEN, KIDNEY, THYROID, & INTESTINAL **TRACT.../WAS** OBSERVED IN RATS SURVIVING ORAL **ADMIN** OF 3.99 G/KG/. [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, **1963. , p. 1700]** **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
SKIN **IRRITATION TESTS.../ON/** RABBITS INDICATE THAT UNDILUTED MATERIAL IS... **IRRITATING IF** EXPOSURES ARE PROLONGED OR REPEATED.
EFFECTS...ARE...ERYTHEMA & EXFOLIATION, WHICH CLEARS PROMPTLY UPON CESSATION OF EXPOSURE. [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , p. **1700]** **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS,
WHEN.../PHENYL ETHER/ WAS GIVEN IN SINGLE DOSES **BY...STOMACH** TUBE /TO RATS

& GUINEA PIGS/, DOSES OF 4.0 G/KG WERE REQUIRED TO PRODUCE DEATH OF ALL ANIMALS OF BOTH SPECIES... DOSES OF 1.0 G/KG WERE SURVIVED BY GUINEA PIGS AND DOSES OF 2.0 G/KG WERE SURVIVED BY ALL RATS TREATED. [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volurne II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , p. 1700] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
...SOME EXPT ON MATERIALS THAT CONSISTED LARGELY OF.../DIPHENYL ETHER/ INDICATED THAT VAPOR CONCN THAT CAN OCCUR @ ORDINARY ROOM TEMP PRESENT NO HAZARD OF SYSTEMIC INJURY. [Patty, F. (ed.). Industrial Hygiene and Toxicology. Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , p. 1700] "PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
WHEN.../DIPHENYL ETHER/ IS DILUTED, AS IN PERFUME COMPOSITIONS, IT DOES NOT APPEAR TO PRESENT ANY HAZARD OF SKIN IRRITATION. [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , p. 1700] **PEER REVIEWED**

2-Phenylphenol

NAME OF SUBSTANCE 0-PHENYLPHENOL
CAS REGISTRY NUMBER 90-43-7

TOXIC HAZARD RATING

No data are available in humans. Inadequate evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 3: The agent is not classifiable as to its carcinogenicity to humans. [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World . Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). S7 70 (1987)] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

WHEN TESTED ON 200 . . . SUBJECTS AS A 5.0% SOLN IN SESAME OIL & AS A 0.1% AQ SOLN OF THE SODIUM SALT, 0-PHENYLPHENOL FAILED TO CAUSE EITHER PRIMARY SKIN IRRITATION OR SKIN SENSITIZATION. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1 981-1982. , p. 2617] ● *F'EER REVIEWED**

HUMAN TOXICITY EXCERPTS

MAY CAUSE CORNEAL INJURY (NECROSIS), ESP THE SODIUM SALT. [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984. II-1891 **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

A POSITIVE MUTAGENIC DOSE RESPONSE RELATION WAS PROVED BETWEEN THE NUMBER OF ABERRATIONS OF HUMAN DIPLOID FIBROBLASTS CULTIVATED WITH OPP FOR 24 HR AND THE CONCENTRATION OF OPP IN CULTURE MEDIUM RANGING FROM 0.1 TO 1.0 UG/ML WITH SIGNIFICANCE ABOVE 0.2 UG/ML. [TAKAHASHI K; MUTAT RES 54 (2): 255 (1978)) *'PEER REVIEWED*"

HUMAN TOXICITY EXCERPTS

A fatal oral dose of 10 g was reported., and toxic effects on the urothelium of the bladder were observed in two humans exposed to o-phenylphenol. [DHHS/NTP; Toxicology and Carcinogenesis Studies of ortho-Phenylphenol alone andwith 7,12-Dimethylbenz(a)anthracene in Swiss CD-1 Mice (Dermal Studies) p.15 (1986) Technical Rpt Series No. 301 NIH PUb No. 86-2557) "PEER REVIEWED"

HUMAN TOXICITY EXCERPTS

In humans, o-phenylphenol is moderately toxic when ingested or inhaled. [DHHS/NTP; Toxicology and Carcinogenesis Studies of ortho-Phenylphenol alone and with 7,12-Dimethylbenz(a)anthracene in Swiss CD-1 Mice (Dennal Studies) p. 14 (1986) Technical Rpt Series No. 301 NIH PUb No. 86-2557] **PEER REVIEWED*

NON-HUMAN TOXICITY EXCERPTS

MALE & FEMALE RATS . . . MAINTAINED FOR 2 YR ON DIETS CONTAINING 0.02 OR 0.2% ... SHOWED NO ADVERSE EFFECTS AS JUDGED BY GROSS APPEARANCE, GROWTH, HEMATOLOGY, RATE OF MORTALITY, ORGAN WT & HISTOPATHOLOGICAL CHANGES IN ... TISSUES. SIMILAR GROUPS /MALE & FEMALE/ RATS MAINTAINED FOR 2 YR ON DIET CONTAINING 2% . . . DEVIATED FROM CONTROLS BY EXHIBITING SLIGHT RETARDATION

OF GROWTH, HISTOPATHOLOGICAL KIDNEY CHANGES (MARKED TUBULAR DILATION) & PRESENCE OF SMALL AMT OF 0-PHENYLPHENOL IN TISSUES OF KIDNEY. DOGS THAT RECEIVED ORAL DOSES OF 0.02, 0.2 & 0.5 G/KG/DAY . . . FOR . . . 1 YR SHOWED NO ADVERSE EFFECTS AS JUDGED BY BODY WT, HEMATOLOGICAL VALUES, ORGAN WT & HISTOPATHOLOGICAL CHANGES IN VARIOUS TISSUES. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. , p. 2617] "PEER REVIEWED*'

NON-HUMAN TOXICITY EXCERPTS

IN RATS INGESTION CAUSES DEATH FROM NERVOUS DEPRESSION, AS DOES PHENOL. ... IN CATS ORAL LETHAL DOSES . . . IN AQ SUSPENSIONS CAUSE HEMORRHAGIC GASTROENTERITIS & HEMORRHAGES IN LIVER, LUNG & MYOCARDIUM. [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984. II-189] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

NONTUMORIGENIC WHEN ADMIN ORALLY TO MICE @ 35-100 MG/KG/DAY. /FROM TABLE/ [Hayes, W. J., Jr. Toxicology of Pesticides Baltimore: Williams & Wilkins, 1975. , p. 192] "PEER REVIEWED*'

NON-HUMAN TOXICITY EXCERPTS

IN DOMINANT LETHAL STUDIES, OPP INDUCED NO DOMINANT LETHAL MUTATIONS @ ANY STAGE OF SPERMATOGENESIS IN C3H MALE MICE AFTER ORAL ADMIN OF DAILY DOSES OF 100 OR 500 MG/KG FOR 5 DAYS. IN CYTOGENETIC STUDIES, OPP PRODUCED NO STRUCTURAL & NUMERICAL ABERRATIONS @ ANY DOSE TESTED IN 4 WK OLD WISTAR MALE RATS AFTER ORAL ADMIN OF DAILY DOSES OF 50,100, 200,400 & 800 MG/KG FOR 5 DAYS OR SINGLE DOSES OF 250, 500, 1000, 2000 & 4000 MG/KG. NEG RESULTS OBTAINED IN ALL MICTOBIOL STUDIES USING RECOMBINATION ASSAY FOR BACILLUS SUBTILIS, REVERSION ASSAYS WITH AND WITHOUT METABOLIC ACTIVATION IN ESCHERICHIA COLI AND HOST MEDIATED ASSAY WITH SALMONELLA TYPHIMURIUM AND 7 WK OLD MALE MICE. [SHIRASU Y ET AL; MUTAT RES 54 (2): 227 (1978)] "PEER REVIEWED"

NON-HUMAN TOXICITY EXCERPTS

0-Phenylphenol was evaluated for the induction of sex-linked recessive lethal mutations in Drosophila melanogaster by the National Toxicology Program. Canton-S wild type males were treated with concentrations of OPP that result in approximately 30% mortality. Following treatment males were mated individually to 3 harems of Basc virgin females to produce 3 broods for analysis. The concentrations of OPP tested by injection (500 ppm) or feeding (250 ppm) were negative in this assay. [Woodruff RC et al; Environ Mutagen 7: 677-702 (1985)] "'PEER REVIEWED"

NON-HUMAN TOXICITY EXCERPTS

o-Phenylphenol was weakly mutagenic in strain Ta1535 of Salmonella typhimurium only in the absence of rat liver S9; it was not mutagenic in strains TA1 537, TA98, or TA1 00. It was mutagenic in the mouse lymphoma L5178Y/TK+ or - assay in the presence or absence of Aroclor 1254 induced male F344 rat liver S9. o-Phenylphenol did not induce sex-linked recessive lethal mutations in Drosophila melanogaster. o-Phenylphenol induced sister chromatid exchanges in Chinese hamster ovary (CHO) cells only in the absence of Aroclor 1254 induced male Sprague-Dawley rat liver S9. [DHHS/NTP; Toxicology & Carcinogenesis Studies of ortho-Phenylphenol Alone and with 7,12-Dimethylbenz(a)anthracene in Swiss CD-1 Mice

(Dermal Studies) Technical Report Series No. 301 (1986) NIH Publication No. 86-2557]
"PEER REVIEWED*'
NON-HUMAN TOXICITY EXCERPTS
o-Phenylphenol, administered orally to 9 pregnant mice at doses ranging from 1.45 to 2.0 g/kg, produced maternal toxicity and delayed fetal development but not teratogenicity. . . . In another study, o-phenylphenol was found to be fetotoxic but not teratogenic when administered to pregnant rats in daily doses of 600 mg/kg, on days 6 through 15 gestation . . . . o-Phenylphenol was not embryotoxic or teratogenic to Sprague-Dawley rats at doses up to 700 mg/kg per day administered on gestation days 6 through 15. [DHHS/NTP; Toxicology and Carcinogenesis Studies of ortho-Phenylphenol alone andwith 7,12-dimethylbenz(a)anthracene in Swiss CD-l Mice (Dermal Studies) p.14 (1986) Technical Rpt Series No. 301 NIH Pub No. 86-2557] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
o-Phenylphenol does not induce changes in immune function in mice following short term oral administration. This finding was confinned . . . in studies in which B6C3F1 mice were administered oral doses of o-phenylphenol (up to 200 mg/kg day) for 10 days and then examined for a variety of immune functions. [DHHSINTP; Toxicology and Carcinogenesis Studies of ortho-Phenylphenol alone and with 7,12-Dimethylbenz(a)anthracene in Swiss CD-l Mice. (Dermal Studies) p.14 (1986) Technical Rpt Series No. 301 NIH Pub No. 86-2557]
"PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
An increased incidence of neoplasms of the urinary bladder in F344/DuCrj rats administered sodium o-phenylphenate in the diet. In a 13 week study, urinary bladder papillomas or transitional cell carcinomas developed in 1/1 0 male rats fed 1% sodium o-phenylphenate, 9/10 male rats fed 2%, 1/10 male rats fed 4%, and 2/10 female rats fed 4%. In a 91-week study, transitional cell carcinomas of the urinary bladder, renal pelvis, or renal papilla developed in 1/21, 7/21, 20/21, and 17/21 male rats fed sodium o-phenylphenate in the diet at concentrations of 0.5%, 1%, 2%, or 4%, respectively. /Sodium o-phenylphenate/ [DHHS/NTP; Toxicology and Carcinogenesis Studies of ortho-Phenylphenol alone andwith 7,12-Dimethylbenz(a)anthracene in Swiss CD-l Mice (Dermal Studies) p.15 (1986) Technical Rpt Series No. 301 NIH PUb No. 86-2557] **PEER REVIEWED**
NON-HUMAN TOXICITY VALUES
LD50 Cat oral 500 mg/kg [DHHS/NTP; Toxicology and Carcinogenesis Studies of ortho-Phenylphenol alone and with 7,12-Dimethylbenz(a)anthracene in Swiss CD-1 Mice. (Dermal Studies) p.14 (1986) Technical Rpt Series No. 301 NIH Pub No. 86-2557] **PEER REVIEWED**
NON-HUMAN TOXICITY VALUES
LD50 Rat single oral dose >1 g/kg [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984. II-189] **PEER REVIEWED"
NON-HUMAN TOXICITY VALUES
LD50 Rat oral 2.7 g/kg [Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983. , p. 993] **PEER REVIEWED"
NON-HUMAN TOXICITY VALUES
LD50 Guinea pig single oral 3500 mg/kg [Verschueren, K. Handbook of Environmental Data of

Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983. , p. 993] **PEER REVIEWED*"
NON-HUMAN TOXICITY VALUES
LD50 White rat single oral 2480 mg/kg [Verschueren, K. Handbook of Environmental Data of Organic Chemicals. 2nd ed. New York, NY: Van Nostrand Reinhold Co., 1983. , p. 993] **PEER REVIEWED"
NON-HUMAN TOXICITY VALUES
LD50 Mice oral 2000 mg/kg [Hartley, D. and H. Kidd (eds.). The Agrochemicals Handbook. 2nd ed. Lechworth, Herts, England: The Royal Society of Chemistry, 1987. A440/Aug 87] **PEER REVIEWED**
NON-HUMAN TOXICITY VALUES
LD50 Mice ip 50 mg/kg [Sax, N.I. Dangerous Properties of Industrial Materials. 6th ed. New York, NY: Van Nostrand Reinhold, 1984. , p. 434] *"PEER REVIEWED**

NATIONAL TOXICOLOGY PROGRAM REPORTS
Carcinogenesis studies were conducted to determine whether o-phenylphenol was a complete carcinogen for skin or a promoter in a two stage initiation/promotion skin paint model. Groups of 50 Swiss CD-1 mice of each sex were used for up to 102 wk. Five dose groups were used: an acetone vehicle control group; a positive control group initiated with 7,12-dimethylbenz(a)anthracene and promoted with 12-O-tetradecanoylphorbol-13-acetate; an initiator control group that received DMBA plus acetone; a group that received repeated applications of o-phenylphenol; and a promotion group that was initiated with 7,12-dimethylbenz(a)anthracene and received repeated applications of o-phenylphenol. The following doses were applied dermally to a clipped area on the dorsal interscapular region 3 days/wk: o-phenylphenol 55.0 mg/0.1 ml acetone; or 12-O-tetradecanoylphorbol-13-acetate 0.005 mg/0.1 ml acetone. 7,12-Dimethylbenz(a)anthracene was administered as a single dose at a concn of 0.05 mg/0.1 ml acetone. 7,12-Dimethylbenz(a)anthracene was administered as a single dose at a concn of 0.05 mg/0.1 ml acetone to the dorsal interscapular region. . . . Under the conditions of these 2 yr dermal application studies, there was no evidence of carcinogenicity in male or female Swiss CD-1 mice administered o-phenylphenol alone or as a promoter following initiation with 7,12-dimethylbenz(a)anthracene. . . . [DHHS/NTP; Toxicology & Carcinogenesis Studies of ortho-Phenylphenol Alone and with 7,12-Dimethylbenz(a)anthracene in Swiss CD-l Mice (Dermal Studies) p.7 Technical Report Series No. 301 (1986) NIH Publication No. 86-2557] **PEER REVIEWED** .
IARC SUMMARY AND EVALUATION
No data are available in humans. Inadequate evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 3: The agent is not classifiable as to its carcinogenicity to humans. [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). S7 70 (1987)] **PEER REVIEWED**

NAME OF SUBSTANCE **DECAMETHYLCYCLOPENTASILOXANE**
CAS REGISTRY NUMBER **541-02-6**

NON-HUMAN TOXICITY EXCERPTS
Low molecular weight organosiloxane compds, at 0.01-100 **mg/kg/day** orally in female fovariectomizedl rats, increased uterine weight . . . produced uterine hyperemia, and changed uterine morphology. . . . Several compounds were estrogenic in character and were more potent orally than parenterally. Biological activity was correlated with stereospecificity, and cyclosiloxanes were more active than their corresponding linear siloxanes. **/Organosiloxanes/ [Hayden** JF, Barlow SA; Toxicol Appl **Pharm** 21: 68-79 **(1972)]** **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
Decamethylcyclopentasiloxane rated I on rabbit eyes /tested externally, according to the degree of injury observed after 24 hours, have been rated on a scale of **1** to **10/.** [Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. , p. **1028]** "PEER REVIEWED*"
NON-HUMAN TOXICITY EXCERPTS
The clastogenic activity of several organosilicon compounds was investigated using in vivo **cytogenetic** tests. The test **compounds** included methyltrichlorosilane, dimethyldichlorosilane, trimethylchlorosilane, trimethylsilanol, hexamethyidisiloxane, and hexamethylcyclotrisiloxane. Male Sprague Dawley rats received intraperitoneal injections of the test chemicals, and bone marrow samples were collected at 6, 24, and 48 hr. Chromosomes were prepared using standard air drying methods. Confirmatory bone marrow chromosome assays and the dominant lethal test were used to evaluate the in vivo clastogenic potential of trimethylsilanol. Chromosomes were harvested after intraperitoneal injections of the agent at **concn** of 300, 400, and 500 **mg/kg,** and a 9 wk dosing **schedule** prior to mating was used for the dominant lethal study. No significant, dose related increase in chromosome damage was observed for any of the agents tested. Simple **chromatid** gaps and breaks were the predominant type of damage. Neither the bone marrow chromosome assay nor the dominant lethal test revealed any clastogenic activity for trimethylsilanol.. The authors conclude that all the agents tested lack clastogenic **activity. [Isquith** A et al; Food Chem **Toxicol** 26 (3): 263-66 **(1988)]** **PEER REVIEWED"

Vinyl acetate

NAME OF SUBSTANCE VINYL ACETATE
CAS REGISTRY NUMBER 108-05-4

TOXIC HAZARD RATING

Classification of carcinogenicity: '1) evidence in humans: inadequate; 2) evidence in animals: insufficient. Overall summary evaluation of carcinogenic risk to humans is Group 3: The agent is not classifiable as to its carcinogenicity to humans. /From table/ [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). S7 73 {I 987)] **PEER REVIEWED"

o CLINICAL EFFECTS :

SUMMARY

o Vinyl acetate is irritating to the eyes, skin, mucous membranes, and respiratory tract. Chronic industrial exposure has been reported to cause CNS symptoms, chronic bronchitis, cardiovascular symptoms, liver function changes, and hepatic enzyme induction.

HEENT

0 Reversible corneal injury may occur.

CARDIOVASCULAR

o Cardiac effects are not well documented. Chronic exposure has resulted in arrhythmias, chest pain, and syncope.

RESPIRATORY

o Respiratory tract irritation (cough, hoarseness) has been reported after exposure to 22 ppm. Chronic bronchitis and impaired ventilating function have been associated with industrial exposure.

NEUROLOGIC

o Chronic exposure is reported to cause fatigue, irritability, insomnia, encephalopathy, vertigo, weakness, and polyneuritis.

HEPATIC

o liver function changes and hepatic enzyme induction may occur after chronic exposure.

DERMATOLOGIC

o Severe skin irritation with blister formation may occur.

HUMAN TOXICITY EXCERPTS

... 15 YR INDUSTRIAL EXPERIENCE WITH 21 CHEM OPERATORS . . . AT LEVELS FROM 5 TO 10 PPM INDICATED THAT VINYL, ACETATE IS NOT A SIGNIFICANT UPPER RESPIRATORY TRACT IRRITANT AT 10 PPM, BUT AROUND 22 PPM SLIGHT IRRITATION WAS OBSERVED IN THE FORM OF COUGH & HOARSENESS. . . . OLFACTORY FATIGUE MAY OCCUR IN ... A FEW MIN @ LEVELS AROUND 20 PPM. RECOVERY IS RAPID . . . [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 1986. , p. 621] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS
ONE CASE OF BURN OF A HUMAN CORNEA HAS BEEN LISTED AS RETURNED TO NORMAL IN LESS THAN FORTY-EIGHT HOURS. [Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. , p. 978] **PEER REVIEWED**
HUMAN TOXICITY EXCERPTS
FACTORY WORKERS EXPOSED TO VINYL ACETATE SHOWED GRADUAL DETERIORATION OF HEART MUSCLES, ARRHYTHMIAS, AMPLITUDE DECR IN ECG, & RECOGNIZED MYOCARDIUM DYSTROPHIES, FAINTING SPELLS, PAIN AROUND THE HEART AREA, & A SENSATION OF DYING. [AGARONYAN ZP, AMATUNI VA; KROVOOBRASHCHENIE 13 (4): 31-6 (1980)] *'PEER REVIEWED**
HUMAN TOXICITY EXCERPTS
CHANGES IN VITAL FUNCTION CAPACITY & MAX VENTILATION CAPACITY WERE FOUND IN PERSONS EMPLOYED IN PRODUCTION OF VINYL ACETATE. DISTURBANCES OF PULMONARY FUNCTIONS DEPEND ON THE INTENSITY & DURATION OF THE EFFECT OF THE CHEM CMPD. [AMATUNI VG, AGARONYAN ZP; ZH EKSP KLIN MED 19 (4): 72-8 (1979)] "PEER REVIEWED**
HUMAN TOXICITY EXCERPTS
IN A VINYL RESIN PLANT 456 WORKERS (313 MEN & 143 WOMEN) WERE EXAMINED FOR THE PRESENCE OF CHRONIC NONSPECIFIC DISEASES OF THE RESP TRACT (CNDRT). THE % OF CHRONIC BRONCHITIS WAS HIGHER IN VINYL CHLORIDE & VINYL ACETATE DEPT. [JEDRYCHOWSKI W ET AL; PRZEGL LEK 36 (9): 679-82 (1979)] **PEER REVIEWED*'
HUMAN TOXICITY EXCERPTS
Two vinyl monomers, styrene and vinyl acetate, were tested for their ability to induce chromosome aberrations in cultured human lymphocytes. The effects of a 24 hr treatment (48 hr after culture initiation) were studied both in whole blood cultures (with 2X10+8 erythrocytes/ml) and in isolated lymphocytes (with 4000 erythrocytes/ml). Vinyl acetate (0.125-2 mM), the more potent clastogen of the two monomers tested, induced a distinct dose dependent increase in chromatid type aberrations and a slight elevation in chromosome type breaks in both culture types. The lowest concentration giving a positive result was 0.25 mM. The clastogenic effects of vinyl acetate were somewhat more pronounced in isolated lymphocytes than in whole blood. Vinyl acetate is known to be rapidly hydrolyzed in vitro to acetaldehyde, which probably explains the positive result. [Jantunen K et al; Mutat Res 159 (1-2): 109-16 (1986)] **PEER REVIEWED**
HUMAN TOXICITY EXCERPTS
A Texas (USA) petrochemical plant had elevated standardized mortality ratios for neoplasms of the brain. A case-control study examined possible associations between gliomas of the brain and job title, departmental employment history, chemical exposure history, geographic location within plant, dates of employment and residence. The greatest apparent risks were associated: with exposure to carbon dioxide, diethyl sulfate, diethylene glycol, ethanol, ethylene, isopropanol, methane, tetraethylene glycol, and vinyl acetate; with first employment in the 1940s or early 1950s; and with residence in La Marque, Texas. No significant differences between cases and controls were apparent in duration of exposure to any of these chemicals. [Leffingwell SS et al; Neuroepidemiology 2 (3-4): 179-95 (1984)] **PEER REVIEWED**
HUMAN TOXICITY EXCERPTS
ABNORMAL PREGNANCIES WERE RELATED TO CHEM POLLUTANTS PRESENT IN

WORKING ATMOSPHERE IN THE PRODUCTION OF ACETYLENE & VINYL ACETATE. [TALAKINA El ET AL; GIG TR PROF ZABOL (3): 46-7 (1977)] **PEER REVIEWED**
HUMAN TOXICITY EXCERPTS
INDUST EXPERIENCE HAS REVEALED SEVERE IRRITATION OF SKIN WITH BLISTER FORMATION. [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 1986. , p. 621] **PEER REVIEWED**
HUMAN TOXICITY EXCERPTS
The frequency of sister chromatid exchange (SCE) was studied in cultures of human lymphocytes exposed to vinyl acetate or acetaldehyde for various time periods and in different phases of the cell cycle. Equimolar concn (0.1-2.4 mM) of vinyl acetate and acetaldehyde induced very similar, dose-dependent increases of sister-chromatid exchange. The sister-chromatid exchange frequency in cells treated with vinyl acetate increased linearly with exposure times up to 24 hr. Cells exposed to vinyl acetate or acetaldehyde in the late Gl-phase of the cell cycle showed a two-fold higher sister-chromatid exchange frequency than cells exposed in early Gl. Cultures treated with vinyl acetate in the first Gl-phase showed a significant increase of sister-chromatid exchange during 3 subsequent cell cycles. Thus, (I) acetaldehyde is likely to be responsible for the sister-chromatid exchange induction /noted/ in vinyl acetate treated cells, (2) the sister-chromatid exchange inducing activity of acetaldehyde persists for several cell cycles in vitro, and (3) removal of sister-chromatid exchange inducing acetaldehyde damage occurs during G1. Taken together, the data suggest that acetaldehyde has slow turn-over in human lymphocytes in vitro, and may accumulate in the cells, possibly by forming reversible Schiff bases, and when release gives rise to sister-chromatid exchange inducing DNA cross-links. [He SM, Lambert B; Mutat Res 158 (3): 201-8 (1985)] **PEER REVIEWED"
HUMAN TOXICITY EXCERPTS
Human leukocytes were incubated in the presence of vinyl acetate or acetaldehyde (IO-20 mM) for 4 hr at 37 degrees C in vitro. DNA damage was analysed by alkaline elution. None of the compounds induced a detectable increase in the frequency of DNA strand breaks. Cells exposed to 5 Gy of X-ray immediately after treatment and before alkaline elution showed a clear, dose-dependent retardation of the elution rate in comparison with X-irradiated control cells. These results demonstrate that both vinyl acetate and acetaldehyde induce DNA cross-links in human cells. [Lambert B et al; Mutat Res 146 (3): 301-3 (1985)] **PEER REVIEWED"
HUMAN TOXICITY EXCERPTS
A 48 hr treatment with vinyl acetate (0.05-l mM) induced a drastic increase in sister chromatid exchanges (SCEs) and (in first division cells) structural chromosome aberrations in cultured human lymphocytes. The effects were more pronounced in cultures of isolated lymphocytes than in whole-blood cultures. Gas chromatographic analysis of human whole-blood lymphocyte cultures treated for 10 seconds to 20 min with vinyl acetate (5.4 mM) revealed a rapid degradation of vinyl acetate and formation of acetaldehyde. During the 20 min observation period, no degradation of vinyl acetate or formation of acetaldehyde were observed in complete culture medium without blood, which suggested that the reaction was enzymatic. Acetaldehyde induced SCEs in human whole-blood lymphocyte cultures at concentrations (0.125-2 mM) comparable to those used for vinyl acetate. The results indicate that vinyl acetate induces chromosome damage in cell cultures through enzyme-mediated hydrolysis to

acetaldehyde. [Norppa H et al; Cancer Res 45 {IO): 4816-21 (1985)] **PEER REVIEWED**
HUMAN TOXICITY EXCERPTS
... Effects on the clastogenic activity of styrene and vinyl acetate human lymphocytes were investigated. Lymphocytes were cultured with heparinized whole blood or with purified lymphocytes alone. Cultures were treated with 0.5 to 6.0 mM concentrations of styrene, 0.125 to 2.0 mM concentrations vinyl acetate, or 10.0 mM acetone as a vehicle control. In whole blood lymphocyte cultures, styrene induced a dose dependent increase in the number of chromatid breaks and gaps at 2mM concentrations or greater. The two highest concentrations had toxic effects decreasing the frequency of mitotic cells. In cultures of isolated lymphocytes, styrene increased the frequency of chromatid aberrations, mostly breaks, in a dose dependent manner starting from the lowest concentration tested. No significant effect was apparent in chromosome type aberrations. At and above 2 mM, styrene reduced the mitotic frequency and at 6 mM no analyzable metaphases were found. At 4 mM styrene in whole blood cultures, compared to isolated lymphocytes, a statistically significant response for chromatid breaks, gaps, and total aberration frequencies were seen. Vinyl acetate in whole blood cultures showed a clear dose dependent response in total chromosome aberrations which increased from 3.5 to 86.8/100 cells with increasing doses. In purified lymphocyte cultures, the dose dependent increase was also apparent. Up to 0.5 mM, the clastogenic effects of vinyl acetate were somewhat more pronounced in isolated lymphocytes than in whole blood. At 0.25 and 0.5 mM this difference was significant for chromatid breaks, gaps, total chromatid aberrations, and for total aberrations. The differences between culture types were smaller, but still apparent, when results were viewed on the basis of aberrant cells rather than aberrations/cell. The authors conclude that the clastogenic effect of styrene is greater in the whole blood system than in isolated cells, while the opposite is true for vinyl acetate. The presence of erythrocytes provides additional targets for reactive molecules, which results in slight inactivation in the case of viny1 acetate. [Jantunen K et al; Mutation Research 159 (I-2): 109-16 (1986)] **PEER REVIEWED"
NON-HUMAN TOXICITY EXCERPTS
DOGS EXPOSED 6 HR DAILY FOR SEVERAL WK @ CONCN STARTING WITH AN AVG OF 91 PPM & ENDING AFTER . . . 11 WK @ 186 PPM SHOWED NO CIRCULATORY ABNORMALITIES OR EVIDENCE OF ALTERED METABOLISM. THE DOMINANT RESPONSE ... WAS IRRITATION OF THE EYES WITH LACRIMATION. . . . RATS EXPOSED . . . /AT 106 PPM/ EXHIBITED NORMAL GROWTH & BEHAVIOR AFTER 15 DAILY 6 HR EXPOSURES, BUT EXPOSURES AT TWO AND ONE-HALF TIMES THIS LEVEL SHOWED RETARDED GROWTH IN FEMALES. NO HEMATOLOGIC OR PATHOLOGIC ABNORMALITIES ATTRIBUTABLE TO EXPOSURES AS HIGH AS 630 PPM WERE FOUND. [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: American Conference of Governmental Industrial. Hygienists,, 1986. , p. 621] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
VINYL ACETATE IS A LOW EYE IRRITANT, BUT INJURIES HAVE BEEN OBSERVED TO HEAL WITHIN 48 HR. IT DEFATS THE SKIN & IS . . . /A CNS DEPRESSANT/ IN HIGH CONCN. CHRONIC 24 HR INHALATION OF 2.4 MGICU M VINYL ACETATE BY RATS RESULTED IN SUBTLE HEPATIC CHANGES OF ENZYME RHYTHMS, BUT WERE MORE PRONOUNCED WITH 13.2 & 68 MG/CU M. [Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons,

1981-1982. , p. 2279] "PEER REVIEWED"
NON-HUMAN TOXICITY EXCERPTS
A GROUP OF 96 SPRAGUE-DAWLEY RATS (SEX NOT SPECIFIED) WERE EXPOSED FOR 4 HR/DAY ON 5 DAYS/WK FOR 52 WK TO MAX TOLERATED CONCN, 8.8 G/CU M (2500 PPM) VINYL ACETATE IN AIR NO TUMORS WERE REPORTED TO HAVE OCCURRED DURING 135 WK. EARLY MORTALITY WAS HIGH: 49 ANIMALS SURVIVED FOR 26 OR MORE WK. (THE WORKING GROUP NOTED THAT THE TIME OF DEATH OF ANIMALS THAT LIVED LONGER THAN 26 WK WAS NOT INDICATED) [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). V19 345 (1979)] "PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
CONTINUOUS 4 MO INHALATION BY RATS & MICE OF 13.2 OR 68.0 MG VINYL ACETATE/CU M CAUSED CONCN DEPENDENT EMPHYSEMA & LUNG ATELECTASIS, & DISTURBED BLOOD CIRCULATION IN OTHER ORGANS. THE FUNCTIONS OF CNS, HYPOPHYSIS, &ADRENAL GLAND WERE DISTURBED. [RUMYANTSEV AP ET AL; KHIM PROM-ST, SER: TOKSIKOL SANIT KHIM PLASTMASS (2): 20-2 (1979)] *'PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
Vinyl acetate was tested in the Ames Salmonella test with Salmonella typhimurium strains TA1 537, TA1538, TA1 535, TA98, and TA1 00 with and without rat or hamster S9 mix from animals pretreated with Arocior 1254. The cmpd was not mutagenic and was not toxic to the ceils at doses up to 1000 uglpiate. [Lijinsky W; Teratog Carcinog Mutagen 1: 259-67 (1980)] "PEER REVIEWED"
NON-HUMAN TOXICITY EXCERPTS
Groups of 20 female Fischer F344 rats, 7 to 8 wk of age, received 0 (controls), 1000 or 2500 mg/l vinyl acetate (with no significant impurities) in drinking water for 100 wk & were then observed for the rest of their lifetime (max, 130 wk). At that time, survival in males & females was: controls, 7/20 & 5/20; 1000 mg/l, 8/20 & 1 1/20; 2500 mg/l, 1/6 & 1 1/20, respectively. Increases in incidence of liver neoplastic nodules (0 control, 4 low-dose & 2 high dose males; 0 control, 0 low dose & 6 high dose females (p< 0.01), of uterine adenocarcinomas (0 control, 1 low dose & 5 high dose females) (p< 0.024) & poipys (0 control, 3 low dose, & 5 high dose females), & thyroid C-cell adenomas (0 control, 2 low dose & 5 high dose females) (p= 0.024) were observed in treated groups. No malignant neoplasm was found in liver. (The Working Group noted the small number of animals used, that histopathological exam was limited to gross lesions & major organs only, that the animals received less than nominal doses of the cmpd due to the instability of vinyl acetate in drinking-water, & lack of characterization of the decmposed products). [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). V39 121 (1986)] "PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS1
The content of free non-protein thiols (-SH) was investigated in the livers of guinea pigs, rats, and mice after ip injection of vinyl acetate. A rapid change of the hepatic non-protein thiols level was found in guinea pigs after injection of 500 mg/kg, resulting in a 50% decr in non-protein thiols content. In mice, the decr was slower and amounted to only 23% 4 hr after injection of 300 mg/kg. Rats responded to a single dose of 450 mg/kg with only a 10% redn of liver

non-protein thiols content. An approx 20% decr was observed after chronic intermittent exposure (5 hr/day for 6 mo) to 10, 100 or 500 mg/cu m vinyl acetate. [Holub I, Tarkowski S; Int Arch Occup Environ Health 51 (2): 185-9 (1982)] **PEER REVIEWED"
NONHUMAN TOXICITY EXCERPTS
The questioning of results of carcinogenicity of vinyl acetate resulted in the conducting of a DNA binding assay in vivo in rats, using (14)C-labelled vinyl acetate. After administration of (14)C-vinyl acetate to male and female Fischer-344 rats, either orally (1 mCi) or by inhalation (0.45-0.75 ml injected into the gas phase of the exposure chamber), no specific hepatic DNA adducts, known to occur after administration of labeiied vinyl halides or vinyl carbamates, could be detected. [Simon P et al; Toxicol Lett 27 (l-3): 115-20 (1985)] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
A distinct dose-dependent induction of sister chromatid exchanges occurred in Chinese hamster ovary ceils after a 24 hr vinyl acetate treatment (0.125-1 mM). A pulse treatment of Chinese hamster ovary cells for 4 hr also yielded a clear increase in sister-chromatid exchanges, but at higher concentrations (0.3-5 mM). The presence of rat liver S9 mix enhanced the sister-chromatid exchange inducing effect of vinyl acetate in Chinese hamster ovary ceils. [Norppa H et al; Cancer Res 45 (10): 4816-21 (1985)] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
following exposure for 6 hr on 5 dayslwk over a 4 wk period, signs of irritation of the respiratory tract were observed in mice exposed to concn of 520 mg/cu m (150 ppm) & in rats exposed to 1760 mg/cu m (500 ppm). Exposure of both species to 3500 mg/cu m (1000 ppm) for 6 hr/day on 6 dayslwk over 3 mo caused retardation in wt gain; no specific damage to parenchymal organs was noted. [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). V36 122 (1986)] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
VINYL ACETATE IS A LIQUID OF RATHER LOW TOXICITY WHEN TAKEN ORALLY. . . . THE FATAL DOSE LD50 IS 2.92 G/KG BODY WEIGHT FOR RATS. VERY SMALL AMT OF HYDROQUINONE ARE ADDED TO IT BUT THEY ARE NOT ENOUGH TO AFFECT ITS INTRINSIC TOXICITY (AMT NEEDED TO ACT AS AN INHIBITOR IS AT THE MOST 15 PPM). [Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. , p. 327] '*PEER REVIEWED"
NON-HUMAN TOXICITY EXCERPTS
Micronuclei induction by vinyl acetate was investigated in mouse bone marrow cells. . . . Vinyl acetate was given intraperitoneally in doses of 250, 500, 1000, or 2000 mg/kg body weight to 10 to 15 week old male C57Bl/6 mice. Animals were sacrificed 30 hours later. The effect of vinyl acetate on the incidence of micronucleated polychromatic erythrocytes was dose dependent, being statistically significant at doses of 1000 and 2000 mg/kg. A decrease was noted in the ratio of polychromatic to normochromatic cells with increasing doses of vinyl acetate and was significantly lower than the control value at 500 mg/kg and higher doses, indicating a toxic effect of vinyl acetate on bone marrow cells. . . . The increase of micronucleated lymphocytes was statistically significant in cultures treated with 0.5 and 1 mM. At 1 mM however, the incidence of micronuclei was at the same level as with 0.5 mM, in spite of the two fold increase in dose. It was suggested that the observed induction of micronuclei in mouse bone marrow is probably brought about by acetaldehyde as vinyl acetate is rapidly hydrolyzed into acetaldehyde in numerous in vitro systems. [Maki-Paakkanen J, Norppa H; Mutation Research 190 (I): 41-45

(1987)] "PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
The effects of oral administration of vinyl acetate to rats were investigated. The dose levels used were 2500 and 1000 mg/l of water. Both solutions were administered as drinking water to groups of 20 male and 20 female F344 rats. The animals were caged in groups of four with an allotment of 80 milliliters of vinyl acetate solution per day to each cage, 5 days/week. The other 2 days/week, unlimited tap water was available. An elevated incidence of adenocarcinomas of the uterus, C-cell neoplasms of the thyroid, and neoplastic nodules in the liver among female rats given 2500 ppm doses suggested a carcinogenic effect of vinyl acetate. Possible activity of several vinyl derivatives was investigated in F344 rats and hamsters. Rats received the compounds in drinking water, and hamsters were treated by gavage. Acrolein, acrolein oxime, acrolein diethylacetal and allyl alcohol showed similar weak carcinogenic properties. Except for the tumors of the adrenal cortex in female rats given acrolein itself, there was no neoplasm showing an increased statistically significant incidence by any of the compounds in rats or hamsters. [Lijinsky W; Annals of the New York Academy of Sciences 534: 246-54 (1988)]
"PEER REVIEWED"
NON-HUMAN TOXICITY EXCERPTS
Chronic and reproductive toxicology studies were performed for vinyl acetate. Inhalation studies using rats and mice were conducted, with animals being exposed to 50, 200, or 600 ppm vinyl acetate in air. A small percentage of early deaths in mice, attributable to respiratory lesions, was possibly associated with inhalation of 600 ppm vinyl acetate. Body weight gain was lower in both species at higher concentrations. In the nasal cavity, atrophy of the olfactory epithelium with replacement with different cell types was noted in both species at 200 and 600 ppm. Epithelial hyperplasia of the trachea was noted at 200 and 600 ppm in mice only. In the lungs in both species, foamy histiocytes, epithelial exfoliation and fibroepithelial tags were noted at 600 ppm. Mice demonstrated epithelial hyperplasia at 600ppm and fibroepithelial tags were noted at 200 ppm. Changes were noted at 53 weeks into the study and showed little progression for the remainder of the time. Eleven tumors was found in the nasal cavities of rats at the 600 ppm exposures; eight were benign papillonnas of various cell types and three were squamous carcinomas, There was no evidence that vinyl acetate exposure caused adverse systemic effects and 50ppm was a clear no observable effect level. A chronic 2 year toxicity/carcinogenicity study following1 in-utero exposure in rats via drinking water exposure was undertaken. Dose related reductions in water and food intake, and body weight gain were seen. An increase in relative kidney weight in high dose males was the only treatment related organ effect. A two generation reproduction study was conducted in rates exposed via drinking water. A decrease in fertility was seen in the 5000 ppm group, attributable to males. Results of other studies on the toxicity of vinyl acetate were reviewed. [Clary JJ; Annals of the New York Academy of Sciences 534: 255-60 (1988)] "PEER REVIEWED"
NON-HUMAN TOXICITY EXCERPTS
In view of divergent opinions concerning MAC value for vinyl acetate, a study on acute and chronic inhalatory toxic effect of this compound on animals was carried out. The scope of the study included determination of CL50 value after Litchfield and Wilcoxon and lo-month exposure of animals to vinyl acetate at concentrations 10, 100 and 500 mg/m3, 5 days weekly, 5 hours daily. During IO-month experiment the animals were observed and body weight controlled. In addition, periodically some hematological examinations and biochemical of blood serum as well as histopathological examinations of inner organs were carried on. Post-mortally

the weight of inner organs was determined. CL50 value determined on rats has amounted to 4100 ppm. In the study on chronic effect, the prevalence and the degree of intensity of the changes of the used by us indicators was the least in the group of animals exposed to vinyl acetate at concentration of 10 mg/m3. These changes were transient not involved reticulopenia and animals' body weight decrease. Histopathological examinations revealed some inflammatory changes in respiratory system both in control and exposed animals. Only planoepithelial metaplasia of bronchi was found exclusively in animals exposed to vinyl acetate at all concentrations used. The changes within liver were found only in animals exposed to vinyl acetate at concentration of 100 and 500 mg/m3. These changes involved fatty degeneration of hepatic parenchyma, proliferation and extension of smooth endoplasmatic reticulum and the changes within the biliary canaliculi. 'Taking the above results into account it seems that the lowest of the recommended in the world MAC value-10 mg/m3 may be accepted as the upper limit of the maximum admissible concentration for vinyl acetate. [Crajkowska T et al; Med Pr 37 (I): 26-36 (1986)] **PEER REVIEWED"

NON-HUMAN TOXICITY EXCERPTS

The testicular genotoxic effects of vinylacetate (VA) and its hydrolysis product, acetaldehyde (AA), were studied in mice by analyzing the induction of morphologically abnormal sperm and meiotic micronuclei. VA significantly increased the frequency of sperm abnormalities at 500 mglkglday while lower doses were ineffective. AA did not induce abnormal sperm. Neither of the compounds influenced the frequency of meiotic micronuclei. VA, but not AA, caused a dose-dependent decrease in sperm production and a reduction of testicular weight at 500 and 125 mglkglday. [L:ahdetie J; Mutat Res; 202 (1): 171-8 (1988)] **PEER REVIEWED**

NON-HUMAN TOXICITY VALUES

LC50 Rat inhalation 3680 ppm/4 hr [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). V39 122 (1986)] **PEER REVIEWED**

NON-HUMAN TOXICITY VALUES

LC50 Mouse inhalation 5150 ppm/4 hr [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). V39 122 (1986)) **PEER REVIEWED"

NON-HUMAN TOXICITY VALUES

LC50 Guinea pig inhalation 21800 ppm/4 hr [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). V39 122 (1986)] "PEER REVIEWED"

NON-HUMAN TOXICITY VALUES

LC50 Rabbit inhalation 8800 ppm/4 hr [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). V39 122 (1986)] "PEER REVIEWED"

NON-HUMAN TOXICITY VALUES

L D50 Rat oral 2.92 g/kg [Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989. , p. 1572] **PEER REVIEWED**

IARC SUMMARY AND EVALUATION
No data are available in humans. Inadequate evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 3: The agent is not classifiable as to its carcinogenicity to humans. [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). S7 73 (1987)] "PEER REVIEWED"*
POPULATIONS AT SPECIAL RISK
Applicants or employees found during examinations to have medical conditions that could be directly or indirectly aggravated by exposure to vinyl acetate, eg, chronic irritation of the respiratory tract, chronic inflammatory conditions of the skin, or chronic eye irritation, shall be counseled on the increased risk of impairment of their health from working with the compound. [NIOSH; Criteria Document: Vinyl Acetate p.2 (1978) DHEW Pub. NIOSH 78-205] **PEER REVIEWED"'

MECHANISM OF ACTION
/It has been suggested that/ vinyl acetate disturbs glutathione metabolism, . . . by acting as a substrate for glutathione transferase. [NIOSH; Criteria Document: Vinyl Acetate p.26 (1978) DHEW Pub, NIOSH 78-205] **PEER REVIEWED**

N,N-Dimethylformamide

NAME OF SUBSTANCE N,N-DIMETHYLFORMAMIDE
CAS REGISTRY NUMBER 68-l 2-2

o CLINICAL EFFECTS :

SUMMARY

o DMF is mildly irritating to the eyes, has CNS effects such as vertigo, and sleep disorders, may produce vomiting and abdominal pain (even on inhalation) and is a known hepatotoxin. Renal, hematologic, cardiovascular, and dermatologic effects have also been noted.

HEENT

o Conjunctivitis has been noted after exposure. Effects have been mild when tested in animals.

CARDIOVASCULAR

o Hypertension has been noted in animals.

NEUROLOGIC .

o Sleep disorders, dizziness, and various function CNS effects have been noted, Poisoned animals showed agitation and hind leg paralysis.

GASTROINTESTINAL

o Anorexia, vomiting, and abdominal pain have been seen, even after inhalation.

HEPATIC

o DMF is a hepatotoxin in both animals and man.

GENITOURINARY

o Kidney damage has been shown in animals.

METABOLISM

o Hypercholesterolemia may occur with exposure.

HEMATOLOGIC

o Anemia, leukopenia, and hypothrombopenia may occur in humans and have been reported in animals,

DERMATOLOGIC

o Contact dermatitis, as well as dermatitis due to skin defatting may occur.

PREGNANCY/BREAST MILK

o Data would indicate an increase rate of abortions and miscarriages rather than teratogenesis.

CARCINOGENICITY

o There is some evidence that DMF may promote testicular cancer.

HUMAN TOXICITY EXCERPTS

... /FROM 9 INVESTIGATIONS IN POLYACRYLONITRILE FACTORY/ SOME PATIENTS COMPLAINED OF NERVOUSNESS & DIFFICULTY IN SLEEPING. OTHERS COMPLAINED OF FACIAL CONGESTION. [Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968. , p. 115] **PEER REVIEWED"

HUMAN TOXICITY EXCERPTS

... FOLLOWING EXPOSURES . . . SYMPTOMS SUCH AS STOMACH PAIN, NAUSEA, VOMITING & EPIGASTRIC CRAMPS HAVE BEEN REPORTED. BECAUSE OF ABILITY OF

DMF TO READILY PENETRATE INTACT SKIN, IT HAS BEEN DIFFICULT TO RELATE EXPOSURES WITHOUT SKIN CONTACT TO CONCN OF DMF IN AIR IN THESE CASES OF ILLNESS. [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 1986. , p. 209] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

Testicular cancer is the most common malignancy among white men aged 15-44. Age-adjusted mortality in the United States has not varied in the past 40 years but the incidence in white males has almost doubled. Three men working as swabbers on the spray lines in the feather finishing process, after latency periods of 8, 13, and 14 years, developed testicular cancers with common histological features. Dimethylformamide (DMF) may have been responsible. [Levin SM et al; Lancet II (8568): 1154 (1987)] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

N,N-DIMETHYLFORMAMIDE IS CONSIDERED TO BE MODERATELY HAZARDOUS BY INHALATION . . . AND IS A DEFINITE HAZARD BY SKIN ABSORPTION. [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , p. 1834] **PEER REVIEWED**

HUMAN TOXICITY EXCERPTS

Points of attack Liver, kidneys, skin, cardiovascular system. [Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, 1985. 2nd ed. Park Ridge, NJ: Noyes Data Corporation, 7985. , p. 365] "'PEER REVIEWED'"

NON-HUMAN TOXICITY EXCERPTS

___ DOGS /EXPOSED TO CONCENTRATIONS > 20 PPM/ EXHIBITED POLYCYTHEMIA AND CARDIOVASCULAR EFFECTS: DECREASED PULSE RATE, DECLINE IN SYSTOLIC PRESSURE, AND DEGENERATIVE CHANGES IN HEART MUSCLE. [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984. II-201] **PEER REVIEWED'*

NON-HUMAN TOXICITY EXCERPTS

... RATS EXPOSED TO 91 PPM DIMETHYLFORMAMIDE (DMF) 6 HR/DAY FOR 10 DAYS SHOWED SLIGHTLY ENLARGED LIVERS . . . . A NUMBER OF ANIMALS /WERE EXPOSED/ 5.5 HR/DAY TO 23 PPM, FOLLOWED BY 1/2 HOUR TO 426 PPM. AFTER 58 SUCH EXPOSURES TOXIC EFFECTS, PARTICULARLY ON LIVER, WERE NOTED. [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 1986. , p. 209] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

... REPEATED EXPOSURES TO 100 PPM WERE INJURIOUS TO CATS . . . LIVER DAMAGE WAS THE MOST PROMINENT FEATURE OF INTOXICATION. [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 1986. , p. 209] "'PEER REVIEWED'"

NON-HUMAN TOXICITY EXCERPTS

THERE IS EXPERIMENTAL EVIDENCE OF LIVER AND KIDNEY DAMAGE IN RABBITS AND CATS AND TO A LESSER EXTENT IN RATS WHEN THE CMPD IS GIVEN BY INJECTION OR INHALATION (RATS TOLERATED 420 PPM DAILY FOR LONG PERIODS, WHILE CATS WERE AFFECTED BY 100 PPM). [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II:

Toxicology. 2nd ed. New York: Interscience Publishers, 1963. , p. 1834] **PEER REVIEWED**
NONHUMAN TOXICITY EXCERPTS
IN MICE EXPOSED TO 1120 MG/KG ('1.2 ML/KG) IP, HIND LEG PARALYSIS AND DEPRESSION WERE PRECEDED BY NERVOUSNESS. [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984. II-201] "PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
TESTED BY DROP APPLICATION TO RABBIT EYES, A 25% SOLN IN WATER HAD NO EFFECT; 50% SOLN WAS SLIGHTLY IRRITATING; 75-100% PRODUCED A MORE SEVERE REACTION, BUT NO DETAILS OF REACTION WERE REPORTED. A DROP OF PURE DIMETHYLFORMAMIDE APPLIED TO RABBIT EYES . . . CAUSED ONLY EDEMA OF CORNEAL EPITHELIUM & EYES RETURNED TO NORMAL . . . . [Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. , p. 348] **PEER REVIEWED"'
NON-HUMAN TOXICITY EXCERPTS
ELEVATION OF BLOOD SUGAR OCCURRED IN RATS AFTER ORAL & IP ADMIN OF DIMETHYLFORMAMIDE. MINIMUM EFFECTIVE DOSES WERE 0.5 MUKG IP & 2 ML/KG ORALLY. [GRANT AM; TOXICOL LETT (AMST) 3 (5): 259-64 (1979)] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
DMF & DIMETHYL SULFOXIDE INHIBITED MOUSE LIVER ALCOHOL DEHYDROGENASE IN VITRO. INHIBITION IS UNCOMPETITIVE WITH DMF & DIMETHYL SULFOXIDE. EACH CHEM PROLONGED SIGNIFICANTLY THE ETHANOL-INDUCED LOSS OF RIGHTING REFLEX. [SHARKAWI M; TOXICOL LETT (AMST) 4 (6): 493-8 (1979)] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS
HUMAN COLON CARCINOMA CELLS TREATED IN VITRO WITH DMF COMPLETELY LOST CLONOGENICITY, WHEREAS UNTR'EATED CELLS HAD CLONING EFFICIENCIES OF APPROX 77%. AFTER REMOVAL OF DMF FROM CULTURE MEDIUM, ORIGINAL CELL CULTURE CHARACTERISTICS REAPPEARED. [DEXTER DL ET AL; CANCER RES 39 (3): 1020-5 (1979)] **PEER REVIEWED"
NON-HUMAN TOXICITY EXCERPTS
HISTOCHEMICAL REACTIONS IN WHITE RAT LIVER, KIDNEY & LUNG IN THE COURSE OF ACUTE DIMETHYLFORMAMIDE TOXICITY ARE DESCRIBED. [WOLANSKI I; ANN UNIV MARIAE CURIE-SKLODOWSKA SECT D MED: 33: 261-6 (1980)] **PEER REVIEWED**
NONHUMAN TOXICITY EXCERPTS
LESIONS WERE INDUCED IN RATS EXPOSED TO INHALATION OF DIMETHYL FORMAMIDE (DMF). THE MOST SERIOUS CHANGES APPEARED TO OCCUR IN THE LIVER. HEPATOCYTES SHOWED MITOTIC TYPE PATTERNS AND ACCUMULATIONS OF LIVER CELLS IN THE REGENERATIVE PHASE. DIFFUSE SINUSOIDAL CONGESTION AND LYMPHOCYTE ACCUMULATIONS WERE OBSERVED. THE KIDNEYS SHOWED SOME CONGESTION, EDEMA AND SPORADIC HEMORRHAGIC FOCI. THERE WERE BLOOD EFFUSIONS IN THE LUNGS AND FOCI OF EDEMA WITH CONGESTION AND SEPTAL THICKENING. CHANGES IN THE MYOCARDIUM ARE ALSO DESCRIBED. DMF HAS PRONOUNCED VASCULOTROPIC PROPERTIES, CAUSING SEVERE VASCULAR CHANGES, WITH MORPHOLOGIC DISRUPTION OF VESSEL WALLS. [CRUZ GS ET AL; BOLL SOC ITAL BIOL SPER 54 (18): 1710-6 (1978)] **PEER REVIEWED**
NON-HUMAN TOXICITY EXCERPTS

ALBINO RATS WERE GIVEN SINGLE IP INJECTIONS OF 0.6, 0.9 & 1.2 MUKG DIMETHYL FORMAMIDE (DMF). AT 0.6 ML/KG SOME HISTOLOGICAL LESIONS OF LIVER OCCURRED (MAX AT 48 HR). AT 0.9 & 1.2 ML/KG SEVERE CENTRAL PHLEBITIS WITH CENTRILOBULAR NECROSIS OF CEL.LS ASSOC WITH HEAVY INFLAMMATORY INFILTRATE OCCURRED. [MATHEW T ETAL; LAB INVEST 42 (2): 257-62 (1980)] **PEER REVIEWED*'

NONHUMAN TOXICITY EXCERPTS

DMF IN AQUEOUS SOLN ADMIN BY STOMACH TUBE TO RABBITS FROM 6TH-18TH DAY PAST INSEMINATION SHOWED EMBRYOTOXIC & WEAKLY TERATOGENIC EFFECTS AT CONCN NOT TOXIC TO MOTHER. RABBIT WAS MORE SENSITIVE TO DMF THAN OTHER SPECIES, WITH FETAL ANOMALIES INDUCED AT DOSES MATERNALLY ACCEPTABLE. [MERKLE J ET AL; ARZNEIM-FORSCH 30 (9): 1557-62 (1980)] **PEER REVIEWED'*

NON-HUMAN TOXICITY EXCERPTS

RATS WERE EXPOSED TO A FOG OF DIMETHYLFORMAMIDE (DMF) FOR 0.5 HR/DAY FOR DAYS & SACRIFICED. EDEMA IN MYOCARDIAL SECTIONS WAS SEEN. THE MOST SALIENT FINDING SHOWED VACUOLAR FORMATIONS, FREQUENTLY DISPLACED AT INTIMAL LEVEL IN WALLS OF INTRAPARENCHYMAL ARTERIAL VESSELS. [CRUZ GS ET AL; BOLL ITAL BIOL SPER 54 (18): 1717-22 (1978)] '*PEER REVIEWED*'

NON-HUMAN TOXICITY EXCERPTS

N,N-Dimethylformamide was tested for mutagenicity in the Salmonella/ microsome preincubation assay using the standarcl protocol approved by the National Toxicology Program. N,N-Dimethylformamide was tested usiing a wide range of doses in as many as 5 Salmonella typhimurium strains (TA1535, TA1537, TA97, TA98, and TA100) in the presence and absence of rat or hamster liver S-9. N,N-dimethylformamide was negative in these tests and the highest ineffective dose in any Samonella tuphimurium strain was 10 mg/plate. [Mortelmans K et al; Environ Mutagen 8: l-l 19 (1986)] **PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS

ACUTE TOXICITY OF FORMAMIDES TO RATS AND MICE WAS IN INCR ORDER; FORMAMIDE, N-METHYLFORMAMIDE, N,N-DIMETHYLFORMAMIDE, N-ETHYLFORMAMIDE, AND N,N-DIETHYLFORMAMIDE. MICE WERE MORE SUSCEPTIBLE THAN RATS. THE COMPOUNDS INDUCED TESTICULAR LESIONS. REPEATED SMALL DOSES OF DMF STIMULATED GROWTH, WHEREAS 'THE OTHER DERIVATIVES WERE GROWTH INHIBITORY. [PHAM HUU CHANH ET AL; THERAPIE 26 (3): 409-24 (1971)] **PEER REVIEWED"

NON-HUMAN TOXICITY EXCERPTS

DMF was applied as a liquid to the skin of pregnant rabbits during the period of fetal organogenesis. Slight teratogenic effects were demonstrated with DMF. The skin approximate lethal dose for DMF was lower for pregnant rabbits than for pregnant rats. [Stula EF et al; Toxicol Appl Pharmacol 41 (I): 1977 35-56] "PEER REVIEWED**

NON-HUMAN TOXICITY VALUES

LD50 MOUSE IP 1120 MG/KG (1.2 ML/KG) [Gosselin, R.E., R.P. Smith, H.C. Hodge. Clinical Toxicology of Commercial Products. 5th ed. Baltimore: Williams and Wilkins, 1984. II-201] "PEER REVIEWED"

NON-HUMAN TOXICITY VALUES

LD50 Mouse oral 6.8 ml/kg [The Merck Index, 10th ed. Rahway, New Jersey: Merck Co., Inc., 1983. , p. 473] "PEER REVIEWED*'

I-Dodecene

NAME OF SUBSTANCE **1-DODECENE**
CAS REGISTRY NUMBER **112-41-4**

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The following Overview, • ** HYDROCARBONS ● **,
is relevant for this HSDB record chemical.

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o CLINICAL EFFECTS :

SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

o ACUTE EFFECTS: INGESTION

1. SIMPLE PETROLEUM DISTILLATES

a. low viscosity, highly volatile hydrocarbons (e.g., kerosene, gasoline, liquid furniture polish) are chiefly **aspiration** hazards. Pulmonary damage, transient CNS depression or excitement and secondary effects of hypoxia, infection, pneumatocele formation, and chronic lung dysfunction can occur. Cardiac complications are rare.

b. These hydrocarbons are poorly absorbed from the gastrointestinal tract and do not cause appreciable systemic toxicity by this route unless aspiration has occurred.

2 CHLORINATED AND AROMATIC HYDROCARBONS

a. Many chlorinated, aromatic and other substituted hydrocarbons can produce systemic toxicity following ingestion. CNS, respiratory depression, arrhythmias, gastrointestinal disturbances and other effects may occur depending on the agent and amount ingested.

o ACUTE EFFECTS: INHALATION

1. Cardiac **arrhythmias** and CNS depression are major concerns of acute exposure. Straight chain hydrocarbons with few carbon **atoms** (e.g., methane, ethane, propane gases) can cause asphyxiation if exposure occurs in poorly ventilated spaces.

2 INHALATIONAL ABUSE **("sniffing")** of some hydrocarbons can result in sudden death, encephalopathy, residual neurological impairment, nephrotoxicity, hepatotoxicity, acid-base disturbances and rhabdomyolysis.

o INJECTION

1. Injection of kerosene, naphtha, turpentine, gasoline, or hydrocarbon insecticides has resulted in febrile reactions, local tissue inflammation and systemic effects, including pulmonary edema, pneumonia and mild CNS depression. Injection of pressurized hydrocarbons has caused severe tissue damage.

o DERMAYEYE

1. Mild to moderate eye initation and reversible ocular injury may occur after contact with most hydrocarbons. Acute but prolonged exposure to some hydrocarbons can result in dermal bums and occasionally, systemic effects. Frostbite can result from contact with some liquefied gases (e.g. propane, methane, ethane).

o CHRONIC EFFECTS

1. Long term or repeated exposure to certain aromatic and chlorinated hydrocarbons can result in hematologic (e.g., benzene), hepatotoxic (e.g., chlorinated hydrocarbons), renal (e.g., **chorinated** hydrocarbons), neuropsychiatric (e.g., toluene), neurological (e.g., n-hexane) and carcinogenic (e.g. benzene, vinyl chloride) effects.

2. Some effects have occurred primarily in chronic solvent abusers or glue sniffers. Example: neuropsychiatric, renal and hepatic effects of toluene

3. Chronic or repeated exposure can result in skin irritation due to defatting of the skin. Greases, coal pitch and cutting oils can produce acne and folliculitis. Aromatic hydrocarbon exposure can result in chloracne.

o TYPES OF HYDROCARBONS

1. LOW VISCOSITY, UNSUBSTITUTED: Hydrocarbons with low viscosity (less than 100 S.U.S.), low surface tension, and high volatility are most likely to cause aspiration pneumonitis. Vapor inhalation can cause CNS depression or excitation and other effects. Examples: kerosene, mineral seal oil, gasoline, petroleum naphtha

2. HIGH VISCOSITY, UNSUBSTITUTED ALIPHATIC: Hydrocarbons with high viscosity and low volatility are less likely to be aspirated after ingestion and are generally poorly absorbed from the gastrointestinal tract. Petroleum jelly may cause a mild laxative effect. Oil mist inhalation may cause lipoid pneumonia. Examples: motor oil, petroleum jelly

3. TERPENES: In addition to aspiration, these tend to produce a mild CNS depression after ingestion. Examples: turpentine oil, pine oil. Pine oil cleaners may contain approximately 10% isopropyl alcohol and other additives which may contribute to the observed toxic effects.

4. AROMATICS: These have a high potential for CNS depression, a mild tendency to cause cardiac irritation, and little risk of aspiration. Adverse effects can result from vapor inhalation, ingestion or skin exposure. Examples: benzene, xylene. Many polyaromatic hydrocarbons are potential carcinogens.

5. HALOGENATED- CHLORINATED: These can produce CNS effects, arrhythmias, renal and hepatic effects. Aspiration is a small risk. Adverse effects can result from vapor inhalation, ingestion or skin exposure. Examples: chloroform, carbon tetrachloride, trichloroethylene

6. Brominated hydrocarbons, fluorinated hydrocarbons, alcohols, esters, ethers, chlorinated hydrocarbon pesticides, and other hydrocarbons are covered in other managements.

CARDIOVASCULAR

025.1 ACUTE EXPOSURE

o Arrhythmias may occur following inhalation.

RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

o Coughing, choking, tachypnea, dyspnea, cyanosis, rales, hemoptysis, pulmonary edema, pneumatoceles, lipoid pneumonia, or respiratory arrest may develop following ingestion and aspiration

o Respiratory arrest can occur secondary to CNS depression following vapor inhalation. Intravenous injection of turpentine immediately resulted in pulmonary edema and hypoxia in 1 case,

NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

o Mild central nervous system depression or excitation may occur after ingestion or vapor inhalation. CNS effects can occur secondary to hydrocarbon pneumonitis and hypoxia, or from additives and contaminants (aniline, heavy metals, camphor, or pesticides). Some hydrocarbons are simple asphyxiants which can produce CNS effects secondary to hypoxia.

GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

o Nausea, vomiting, diarrhea, and abdominal pain may occur following ingestion.

HEPATIC

0.2.9.1 ACUTE EXPOSURE

o Elevated transaminases may occasionally occur following ingestion or vapor inhalation of some hydrocarbons. Carbon tetrachloride is a potent hepatotoxin which can produce potentially fatal hepatorenal damage following ingestion, inhalation or dermal exposure.

GENITOURI NARY

0.2.10.1 ACUTE EXPOSURE

o Renal effects (acute renal tubular necrosis, proteinuria, or hematuria) occur infrequently following acute exposure to petroleum distillates and other unsubstituted hydrocarbons.

o Some studies have reported an increased risk of glomerulonephritis following long term inhalation and/or dermal exposure to various hydrocarbons. Acute renal failure and other renal effects have been reported in some chronic glue, solvent, or paint sniffers. Exposures in addition to hydrocarbons can not be ruled out in many of these reports.

o Many halogenated hydrocarbons are nephrotoxic. Examples of potentially nephrotoxic halogenated hydrocarbons include chloroform, carbon tetrachloride, ethylene dichloride, tetrachloroethane, 1,1 ,I-trichloroethane, trichloroethylene (infrequently reported) and tetrachloroethylene (weakly nephrotoxic).

HEMATOLOGIC

0.2.13.1 ACUTE EXPOSURE

o Disseminated intravascular coagulation, hemolytic anemia and pancytopenia have occasionally been reported following vapor inhalation, aspiration, or ingestion of hydrocarbons. Benzene is a bone marrow toxin. Chronic benzene exposure has been associated with acute leukemia.

o Contaminants or additives can cause hematologic abnormalities. Examples include, aniline and nitrobenzene (methemoglobinemia).

MUSCULOSKELETAL

0.2.15.1 ACUTE EXPOSURE

o Rhabdomyolysis has occasionally been reported in chronic glue or paint sniffers and in a case of prolonged inhalational exposure to mineral spirits. Muscle necrosis, compartment syndrome and/or sterile abscess have been reported following hydrocarbon injection.

CARCINOGENICITY

0.2.21.1 IARC CATEGORY

o A partial list of hydrocarbons or related work processes classified by the IARC (1987) in Group 1, Carcinogenic to Humans, includes:

1. benzene; benzidine; bis(chloromethyl) ether and technical-grade chloromethyl methyl ether; boot & shoe repair; coal gasification; coal tar; coal tar pitches; coke production; mineral oils, untreated and mildly treated; rubber industry; shale oils; soots; vinyl choride

o A partial list of hydrocarbons classified by the IARC (1987) in Group 2A, Probably Carcinogenic to Humans, includes:

1. benz[a]anthracene; benzidine-based dyes; benzo[a]pyrene; creosotes; formaldehyde; polychlorinated biphenyls; styrene oxide; vinyl bromide

o A partial list of hydrocarbons or processes classified by the IARC (1987) in Group 2B, Possibly Carcinogenic to Humans, includes:

1. para-aminoazobenzene; ortho-aminoazobenzene; bitumens, extracts of steam- refined and air-refined; I ,3-butadiene; carbon-black extracts; carbon tetrachloride; alpha-chlorinated toluenes; chloroform; dibenzo[a,e]pyrene; dibenzo[a,h]pyrene; dibenzo[a,l]pyrene;

dichlommethane (methylene chloride); hexachlorobenzene; polybrominated biphenyls; polycyclic aromatic hydrocarbons (various listed); styrene; 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD); tetrachloroethylene; ortho-toluidine

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o RANGE OF TOXICITY :

o Less than 1 mL of some hydrocarbons directly aspirated into the lungs in animals has produced severe pneumonitis.

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o REFERENCE :

[Rumack BH: POISINDEX(R) Information System. Micromedex Inc., Englewood, CO, 1995; CCIS CD-ROM Volume 87, edition exp Feb, 1996. Hall AH & Rumack BH (Eds): TOMES(R) Information System. Micromedex, Inc., Englewood, CO, 1995; CCIS CD-ROM Volume 87, edition exp Feb, 1996.]

"PEER REVIEWED'*

HUMAN TOXICITY EXCERPTS

... IRRITANT AND /CNS DEPRESSANT/ . . . IN HIGH CONCENTRATIONS. [Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 1 lth ed. New York: Van Nostrand Reinhold Co., 1987. , p. 439] "PEER REVIEWED-

2-Methylpropene

NAME OFSUBSTANCE **ISOBUTYLENE**
CAS REGISTRY NUMBER 115-11-7

HUMAN **TOXICITY** EXCERPTS
BUTYLENE ISOMERS ARE SIMILAR IN PHARMACOLOGICAL ACTIVITY AS ASPHYXIANTS **&** WEAK ANESTHETICS. **...ABOUT** 4.5 TIMES AS TOXIC AS ETHYLENE. /BUTYLENE **ISOMERS/** [Patty, F. (ed.). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New **York:** Interscience Publishers, 1963. , **p. 1204]** "PEER REVIEWED**

Allyl Benzene

NAME OF SUBSTANCE ALLYL BENZENE
CAS REGISTRY NUMBER 300-57-2

No specific toxicological information found.