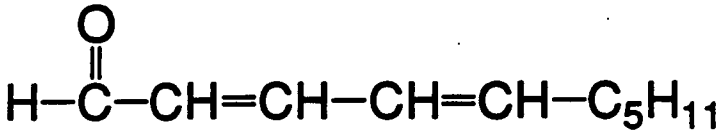
SUMMARY OF DATA FOR CHEMICAL SELECTION

CHEMICAL IDENTIFICATION:

CAS Registry Number:	25152-84-5
Chemical Abstr. Name:	2,4-Decadienal, (E,E)-(9CI)
Synonyms/Trade Names:	*trans,trans*-2,4-Decadienal; *trans,trans*-2,4-decadien-1-al; Deca-2,4-dienal; heptenyl acrolein; RIFM#77-102; 2,4-De
Other CAS Nos.:	25152-83-4 (trans, cis-2,4-De); 2363-88-4 (mixed isomers)

Structure, Molecular Formula, and Molecular Weight:



$C_{10}H_{16}O$ Mol. wt.: 152.24

Chemical and Physical Properties

Aldrich (1992) and/or Chapman & Hall (1992) unless otherwise specified.

Description:	Colorless to yellowish liquid with green grassy, green plant-like odor
Boiling Point:	58-61°C @ 0.05 mm; 114-116°C @ 10 mm
Specific Gravity:	0.857
Vapor Density:	>1
Flash Point:	214°F (101°C)

Technical Products and Impurities: 2,4-De is available from Aldrich Chemical Co. in 85% pure technical grade. No information on impurities was available.

Prepared for NCI by Technical Resources, Inc. under Contract No. NO1-CP-56019 (9/92; rev. 5/93)

BASIS OF NOMINATION OF THE CSWG

Dienaldehydes occur in a variety of foods and food components and are used as food additive/flavoring agents, for the most part in small concentrations. There is an overall lack of data generated from testing of dienals for either carcinogenicity or mutagenicity and a lack of evidence specifically relating exposures to cancer in humans. Therefore, testing of these two representative dienaldehydes would help mitigate the data gap. It is especially significant, in addition, that they are known to be lipid peroxidation products found in numerous meat, vegetable and fish oils. Polyunsaturated oils, according to Snyder *et al.* (1985), are especially susceptible to oxidation on aging during storage. These auto-oxidation products have been implicated in the development of off or tainted flavor. More importantly, several researchers have implied there could be a link between exposures to lipid peroxidation products in the diet and the development of human cancers. Lipid hydroperoxides have been shown to give rise to low intracellular levels of α,β-unsaturated aldehydes, including 2,4-Hx and 2,4-De, known to be reactive with DNA (Frankel *et al.*, 1987). Ingested lipid oxidation products and oxidized fats have been reported to cause increased excretion of mutagens, cellular injury to liver and kidneys, increased cell proliferation in the gastro-intestinal tract, and other non-specific tissue injury and irritation effects resulting from induced oxidative stress. Further investigation to gain greater insight into the possible role of consumed oxidized oils in gastro-intestinal carcinogenesis including the effects of oral intake of different doses of various biologically active compounds present in heated oils, effects of oxidative stress induced by chronic consumption of repeatedly heated oils, as well as interactions with other modulating dietary factors, including both macro- and micro-nutrients has been called for by Hageman *et al.* (1991).

Prepared for NCI by Technical Resources, Inc. under Contract No. NO1-CP-56019 (9/92; rev. 5/93)

SELECTION STATUS

ACTION BY CSWG: 9/18/92

Studies Recommended: Full evaluation (short term, preliminary screening, metabolism and distribution, as well as carcinogenicity) as a matched pair with 2,4-hexadienal.

Priority: High

Comments: Dr. Poirier wrote, "Although commercial production and exposure seem very limited, their formation in the oxidation of unsaturated fats both *in vivo* and in commercial products is extensive. While both compounds appear to be inactive in most standard mutagenicity prescreens, both show signs of mutagenic activity in the odd test...." 2,4-Decadienal forms a glutathione adduct when incubated *in vitro* with GSH transferase. The feeling was that both 2,4-decadienal and 2,4-hexadienal should be tested because they might behave quite differently.

EXPOSURE INFORMATION

Commercial Availability

Production and Producers: 2,4-De is produced by the condensation of hexaldehyde with crotonaldehyde (Opdyke, 1979). It is also produced as a flavor volatile component by the oxidation of linoleic acid (Chapman & Hall, 1992).

The FDA's Priority-based Assessment of Food Additives database (PAFA) contains the following data reported on food additive/flavoring agent manufacture and use of 2,4-De: market disappearance rate of 80 lb/yr for the survey year, 1987 (FDA, 1992). Up to 1,000 lb per year has been reported to be produced for use in fragrances, according to Opdyke (1979). It is a commercial product offered for sale in several companies' catalogs including Alfa Products, Aldrich Chemical Co., American Tokyo Kasei, Fluka Chemical, Janssen Chimca and Lancaster Synthesis. According to the Aldrich catalog, it is available from this company in research quantities only.

Use Pattern: 2,4-De is used as a synthetic flavoring and fragrance material (Opdyke, 1979; Chapman & Hall, 1992). It has also been evaluated as a corrosion inhibitor for steel in oil field operations (Growcock *et al.*, 1989).

Human Exposure: Low level human exposure to 2,4-De is virtually universal through the food chain, based on the scores of foods and food products that contain this compound either naturally or as a food additive/flavoring agent. Feron *et al.* (1991) reported that 2,4-De has been identified in 80 foods with the highest concentration (500 ppm) detected in the oil of tangerine peel. 2,4-De is present in oxidized, heated or cooked edible animal and vegetable fats and oils, including heated and off-flavor or rancid butter. 2,4-De development in canned goods, such as canned asparagus and canned meat products, has also been related to odor and spoilage.

Environmental Occurrence: 2,4-De is a secondary degradative product from 9-hydroperoxylinoleic acid by oxidative deterioration of the polyunsaturated fatty acid, linoleic acid. Katsuki *et al.* (1987) reported this compound to be one of 3 predominating of the 12 identified oxidation products of linoleic acid, along with pentane and hexanal. It has been identified in scores of food substances including fruit, vegetable and meat products, and processed foods - among them, mushrooms, salted and pickled prunes, and frozen strawberries.

2,4-De has been reported by numerous researchers to be one of the most important flavor components in vegetable oils and one which generally increases with storage and aging. Snyder *et al.* (1985) and others list 2,4-De as a component of canola, corn, cottonseed, olive, peanut, safflower, soybean and sunflower oils. It is often associated with non-hydrogenated, oxidized, heated or cooked vegetable oils and some meat-derived fats and oils as well, including warmed-over beef flavor volatiles, uncured pork, cooked beef, lamb and chicken, stored ground beef patties, and turkey breakfast sausage. The oxidation of unsaturated fatty acids yields carbonyl compounds which contribute significantly to the flavor of uncured but not cured meat according to Ramarthnam *et al.* (1991). They reported a concentration of 0.69 $\pm$ 0.16 mg/kg of 2,4-De in uncured pork but it was not detected in cured pork. 2,4-De is also a flavor volatile identified in heated or cooked butter oil and stored butter with an off or tainted flavor and in both peanut butter and, especially, rancid peanut butter.

2,4-De has been described by Tokarska *et al.* (1986) as one of the most important components of canola and other oils. These researchers studied storage stability of canola oil with and without the addition of antioxidants. They reported the following observations:

- 2,4-De was not found in fresh oil samples used as controls but reached > 17 ppm concentrations in 16 weeks of storage.

- Rapid, greater than 10 fold increases of 2,4-De were seen in oil stored for 16 weeks in clear glass bottles both without added antioxidant and with addition of BHT/BHA/citric acid even at maximum allowable concentration (in Canada) of 200 ppm.

- Addition of 200 ppm t-butylhydroquinone (TBHQ) as antioxidant effectively retarded 2,4-De formation (increases were only in the 1.7-3.5 ppm range) and retarded oxidative changes even at a 100 ppm level.

- Storage in amber bottles helped deter degradative changes during the first 12 weeks of storage after which the occurrence of off-flavor volatiles began to increase more markedly.

Raghavan *et al.* (1989) determined that levels of t,t-2,4-De in unhydrogenated soybean oil as well as aged processed soybean and corn oils correlated with flavor panel scores as indicators of flavor quality and recommended the use of headspace analysis of 2,4-De as an important tool for the food industry in determining flavor quality of these oils.

In addition, this compound has been identified in fish oils, including oxidized menhaden oil, and in mussels. It is in the essential oil of brown algae and *Patrina scarba* (a traditional Chinese drug), dried and stored Japanese piled tea, Indian black teas, roasted Colombian coffee beans, ginseng oil, and the essential oils of gentian and cinchona bark used in the production of liqueurs. It is an aroma volatile which has been associated with the off flavor of packaged, stored green tea; but analog, 2,4-heptadienal, was found to be more typical of green tea. 2,4-De has been identified in the flavor volatiles of tonka beans, which are regulated against use in foods.

Prepared for NCI by Technical Resources, Inc. under Contract No. NO1-CP-56019 (9/92; rev. 5/93)

Seeking greater understanding of the chemical nature of staling flavor of deep fried chicken or fish held for 3 days at 6°C, Josephson and Lindsay (1987) studied the further degradation of 2,4-alkadienals using 2,4-De in a water-mediated retro-aldol condensation reaction as a model system. 2,4-De degraded to 2-octenal and ethanal followed by degradation of the 2-octenal to hexanal and ethanal at a rate independent of oxygen but greatly accelerated by heat. There were two other significant compounds formed which were tentatively identified as either *cis* and *trans* 3-keto-4-decenals or *anti* and *syn* 2-carboxyaldehyde-5-pentyl-2,5-dihydrofurans. In another study of volatiles generated from reaction of 2,4-De with S-containing natural food materials, cysteine and glutathione, to simulate deep-frying interactions, 45 and 42 compounds were identified, respectively (Zhang and Ho, 1989).

Regulatory Status: 2,4-De is listed in EPA's TSCA inventory. No standards or guidelines have been set for occupational exposures to or environmental levels of 2,4-De. The American Conference of Governmental Industrial Hygienists (ACGIH) has not adopted a TLV/TWA for this compound.

According to Opdyke (1979) 2,4-De was given GRAS (generally recognized as safe) status after a review of flavoring ingredients and food additives by the Flavoring Extract Manufacturers' Association (FEMA) and was listed in 1974 by the Council of Europe as a flavoring substance that may be added to food.

Prepared for NCI by Technical Resources, Inc. under Contract No. NO1-CP-56019 (9/92; rev. 5/93)

EVIDENCE FOR POSSIBLE CARCINOGENIC ACTIVITY

Human Data: No information was found in the literature associating 2,4-De with a cancer risk in humans. Health hazard advisory information in the Aldrich Chemical Company's MSDS is as follows: harmful if inhaled or swallowed; may cause irritation (Aldrich, 1992).

A human 48 hour closed-patch irritation test with 5% 2,4-De in petrolatum produced no irritation. The same concentration in a maximization test for sensitization produced no sensitization reactions (Opdyke, 1979).

Lipid peroxides and secondary products of lipid peroxidation have been suggested to be causative agents for some diseases and biological damage. [See 2,4-hexadienal summary sheet for additional information.]

Animal Data: No information was found in the literature associating 2,4-De with a cancer risk in animals. The following acute toxicity information was reported in Opdyke (1979) and/or the RTECS database (NLM, 1992).

Acute Toxicity Data

Oral rat LD_{50}: >5 g/kg
Dermal rabbit LD_{50}: 1.25-2.5 g/kg

Irritation Data

Dermal rabbit: moderate to severe irritation.

Short Term Tests: O'Brien *et al.* (1989) reported that 2,4-De and related unsaturated aldehydes were genotoxic to Chinese hamster ovary (CHO) cells. The effectiveness of induction of micronuclei following mitosis was found to be in the order of acrolein > crotonaldehyde > 2,4-De. When the same aldehydes were incubated with microsomes and NADPH, their

effectiveness in supporting increased oxygen uptake and lipid peroxidation was in the order of 2,4-De > acrolein > crotonaldehyde.

Kaneko *et al.* (1987) studied linoleic acid and some of its aldehydic autoxidation products for toxicity to human diploid fibroblasts. Following 1 day exposures, 2,4-De was observed to be the most toxic and to show similar toxicity to both proliferating and arrested cells. 2,4-De was reported to be one of the most toxic of the autoxidation products of linoleic acid hydroperoxide studied for effect on human diploid fibroblasts. Also, 2,4-De, with an LC_{50} of 9 μM for cultured human endothelial cells, was highly cytotoxic (Kaneko *et al.*, 1988).

Frankel *et al.* (1987) reported that products of lipid free radical autoxidation and singlet oxidation interact with DNA.

Aikawa & Chikuni (1988) reported that 2,4-De from thermally oxidized linoleate greatly reduced the mutagenic effect of UV irradiation on *E. coli* (antimutagenesis),

In the NCI/DCE Short-Term Test Program, 2,4-De was negative in the *Salmonella* mutagenicity assay using tester strains TA98, TA100, TA1535, TA1537, AND TA1538 when tested at doses up to 10,000 μg/plate with or without metabolic activation. In the mouse lymphoma L5178Y TK+/- assay, 2,4-De was also negative when tested at doses ranging from 2.0 to 0.5 μg/ml without metabolic activation and at doses ranging from 500 to 2500 μg/ml with activation (NCI, 1992a).

Metabolism: Aldehydes are principally metabolized in the liver. Conjugation of glutathione (GSH) with 2,4-De resulting from lipid peroxidation, catalyzed by endogenous glutathione-S-transferase from lean pork muscle, was demonstrated by Williamson & Ball (1988). This research group subsequently reported conjugation of t,t-2,4-De with GSH, catalyzed by GSH-transferase from lamb muscle (Williamson, 1989). According to Brophy and Barrett (1990), this is a secondary mechanism for 2,4-alkadienal detoxification. A cytosolic

fraction prepared from a mouse fibroblast cell line also reduced secondary products of lipid peroxidation.

Other Biological Effects: α,β-Unsaturated aldehydes, including 2,4-De, react with thiobarbituric acid (TBA) forming a redish pigment which is the basis of human clinical lipid peroxidation analysis (Kosugi *et al.*, 1988). These researchers observed synergism between 2,4-alkadienals and other aldehydes and hydroperoxides as evidenced by the intensity of the red pigment formation. Hageman *et al.* (1991) reported that urinary concentrations of TBA-reactive substances were significantly increased in rats following consumption of heated polyunsaturated fatty-acid rich vegetable frying oils (PO) compared with levels in rats fed unheated PO. Furthermore, according to these authors, oxidative degradation products and metabolites of polyunsaturated fatty acids have been reported by several research groups to have caused enhanced cell proliferation in colonic tissue; and hydroperoxides of linoleic acid detected in heated POs but not in other oils, were thought to be the source of biologically active oxidation products which caused enhancement of cell proliferation in oesophagi of rats fed these oils.

2,4-De was demonstrated by Beppu *et al.* (1986) to extensively cross-link erythrocyte membrane proteins and phospholipids. The protein cross-linking ability of 2,4-De was comparable to that of 13-hydroperoxylinoleic acid (LOOH), malondialdehyde (MDA) and glutaraldehyde.

Structure/Activity Relationships: Citral (geranial, 3,7-dimethyl-2,6-octadienal) is a close analog of 2,4-De which lacks conjugation in the two C=C double bonds. This chemical was nominated by NCI from the aldehydes class study and has been selected for chronic bioassay by the NTP (NCI, 1992b). Genetic toxicology results are reported as follows: negative in an Ames *Salmonella* test system; positive for induction of sister chromatid exchanges in an *in vitro* cytogenic test system but negative for chromosomal aberrations (NTP, 1992).

Linoleic acid hydroperoxide autoxidation products showed enhanced toxicity to human diploid fibroblasts with an increase in the number of double bonds and with increasing chain length. 2,4-De was among the most toxic (Kaneko *et al.*, 1987).

According to the Aldehydes Class Study Report prepared for NCI by SRI in 1978, epoxides formed from compounds of the alkyl-substituted vinyl aldehyde structural type, including epoxy derivatives of acrolein and glycidaldehyde, may have carcinogenic potential as demonstrated by induction of local tumors in mice and rats following subcutaneous injections and in mice following topical applications. [See 2,4-hexadienal summary sheet for additional information.]

REFERENCES

Aikawa, K. and Chikuni, K. (1988) Antimutagenic effect of volatile decomposition products from thermally oxidized linoleate. Mutat. Res. 208(3-4):163-6

Aldrich (1992) Material Safety Data Sheet (MSDS), Aldrich Chemical Co., Inc., Milwaukee, WI

Beppu, M., Murakami, K., and Kikugawa, K. (1986) Fluorescent and cross-linked proteins of human erythrocyte ghosts formed by reaction with hydroperoxylinoleic acid, malonaldehyde, and monofunctional aldehydes. Chem. Pharm. Bull. 34(2):781-8

Brophy, P.M. and Barrett, J. (1990) Detoxification of secondary products of lipid perioxidation in the cytosol of a mouse fibroblast cell line. Biochem. Cell Biol. 68(11):1288-91

Chapman & Hall (1992) *Heilbron's Dictionary of Organic Compounds*, 5th Ed., main work, (File 360) Dialog Information Services, Palo Alto, CA.

FDA (1992) Center for Safety and Applied Nutrition, Priority-based assessment of food additives (PAFA) database, Washington, D.C. [telephone communication between Dorothy Cannon of TRI and Dan Benz of FDA, 3/92]

Feron, V.J., Til, H.P., de Vrijer, F., Woutersen, R.A., Cassee, F.R., and van Bladeren, P.J. (1991) Aldehydes: occurrence, carcinogenic potential, mechanism of action and risk assessment. Mutat. Res. 259(3-4):363-85

Frankel, E.N., Neff, W.E., Brooks, D.D., and Fujimoto, K. (1987) Fluorescence formation from the interaction of DNA with lipid oxidation degradation products. Biochem. Biophys. Acta. 919(3):239-244

Growcock, F.B., Frenier, W.W. and Andreozzi, P.A. (1989) Inhibition of steel corrosion in HCl by derivatives of cinnamaldehyde. Part II. Structure-activity correlations. Corrosion, 45(12):1007-1015

Hageman, G., Verhagen, H., Schutte, B., and Kleinjans, J. (1991) Biological effects of short-term feeding to rats of repeatedly used deep-frying fats in relation to fat mutagen content. Fd. Chem. Toxicol., 29(10):689-698

Josephson, D.B. and Lindsay, R.C. (1987) Retro-aldol related degradations of 2,4-decadienal in the development of staling flavors in fried foods. J. Food Sci., 52(5):1186-90, 1218.

Kaneko, T., Honda, S., Shun-Ichiro, N., and Matsuo, M. (1987) Lethal effects of a linoleic acid hydroperoxide and its autooxidation products unsaturated aliphatic aldehydes on human diploid fibroblasts. Chem.-Biol. Interact. 63(2):127-38

Prepared for NCI by Technical Resources, Inc. under Contract No. NO1-CP-56019 (9/92; rev. 5/93)

Kaneko, T., Kaji, K., and Matsuo, M. (1988) Cytotoxicities of a linoleic acid hydroperoxide and its related aliphatic aldehydes toward cultured human umbilical vein endothelial cells. Chem.-Biol. Interact. 67(3-4):295-304

Katsuki, Y., Matsumoto, S., and Tsuyuki, H. (1987) Air oxidation of unsaturated triglycerides and prevention of oxidation. II. Volatile decomposition products in the air oxidation of triolein and trilinolein. Shokuhin Eiseigaku Zasshi, 28(6):466-472 [STN abstract, CA109:5391g]

Kosugi, H., Kato, T, and Kikugawa, K. (1988) Formation of a red pigment by a two-step 2-thiobarbituric acid reaction of alka-2,4-dienals. Potential products of lipid oxidation. Lipids, 23(11):1024-31

Kosugi, H., Kojima, T. and Kikugawa, K. (1991) Characteristics of the thiobarbituric acid reactivity of oxidized fats and oils. J. Am. Oil Chem. Soc., 68(1):51-55

Marnett, L.J., Hurd, H.K., Hollstein, M.L., Levin, D.E., Esterbauer, H., and Ames, B.N. (1985) Naturally occurring carbonyl compounds are mutagens in Salmonella tester strain TA104. Mutat. Res., 148(1-2):25-34

NCI (1992a) NCI/DCE Shgort-term testing program in vitro results, 3/81-8/92. National Cancer Institute, Bethesda, MD

NCI (1992b) NCI tracking file. National Cancer Isntitute, Bethesda, MD

O'Brien, P.J., Kaul, H., McGirr, L., Drolet, D., and Silva, J.M. (1989) Molecular mechanisms for the involvement of the aldehydic metabolites of lipid peroxides in cytotoxicity and carcinogenesis. In: Kabara, J.J., Ed., *Pharmacological Effects of Lipids 3*, AOCS, Champaign, IL pp. 266-80

Opdyke, D.L. (1979) Monograph on fragrance raw material 2,4-Decadienal. Food Cosmet. Toxicol. 17(Suppl.):753

Raghavan, S.K., Reeder, S.K. and Khayat, A. (1989) Rapid analysis of vegetable oil flavor quality by dynamic headspace capillary gas chromatography. J. Am. Oil Chem. Soc., 66(7):942-947

Ramarathnan, N., Rubin, L.J., and Diosady, L.L. (1991) Studies on meat flavor. 1. Qualitative and quantitative differences in uncured and cured pork. J. Agric. Food Chem. 39(2):344-50

Snyder, J.M., Frankel, E.N., and Selke, E. (1985) Capillary gas chromatographic analyses of headspace volatiles from vegetable oils. J. Am. Oil Chem. Soc. 62(12):1675-9

Tokarska, B., Hawrysh, Z.J. and Clandinin, M.T. (1986) Study of the effect of antioxidants on storage stability of canola oil using gas liquid chromatography. Can. Inst. Food Sci. Technol.J., 19(3):130-133

Urbany, D. (1992) State cancer rate linked to lifestyles, Gazette Newspapers, Bethesda, MD, March 4, 1992, p.A-10

Williamson, G. (1989) Purification of glutathione-S-transferase from lamb muscle and its effect on lipid peroxidation. J. Sci. Food Agric. 48(3):347-60

Williamson, G. and Ball, S.K.M. (1988) Purification of glutathione-S-transferase from lean pork muscle and its reactivity with some lipid oxidation products. J. Sci. Food Agric. 44(4):363-74 [STN abstract. CA109(21):189016t]

Witz, G., Lawrie, N.J., Zaccaria, A., Ferran, Jr., H.E., and Goldstein, B.D. (1986) The reaction of 2-thiobarbituric acid with biologically active *alpha, beta*-unsaturated aldehydes. J. Free Rad. Biol. Med. 2:33-39

Zhang, Y. and Ho, C.-T. (1989) Volatile compounds formed from thermal interaction of 2,4-decadienal with cysteine and glutathione. J. Agric. Food Chem., 37(4):1016-1020

Prepared for NCI by Technical Resources, Inc. under Contract No. NO1-CP-56019 (9/92; rev. 5/93)

SEARCH RESOURCE LIST

DIALOG	NLM	STN INTL
BIOSIS (5)	CANCERLINE	CA/CAOLD
Chem. Ind. Notes (19)	CCRIS	CHEMLIST
Pollution Abstracts (41)	DART	MSDS-CCOHS
Food Ad Libra (79)	EMICBACK	REGISTRY
Coffeeline (164)	GENETOX	
F-D-C Reports (187)	RTECS	
K-O Online (302)	TOXLINE	
Heilbron (303)	TOXLINE65	
Chem. Bus. NewsBase (319)	TOXLIT	
Fine Chemical Database (360)	TOXLIT65	
	FDA	
	PAFA	

MANUAL SOURCES

Amdur, M.O., Klaassen, C.D. & Doull, J., eds. (1991) Casarett and Doull's Toxicology. The Basic Science of Poisons, 4th Ed., New York, Pergamon Press

American Conference of Governmental Industrial Hygienists (1990) 1990-1991 Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH, ACGIH

Budavari, S., ed. (1989) The Merck Index, 11th Ed., Rahway, NJ, Merck & Co., Inc. (available online as Merck Online)

Chemical Company Guides and Directories
Directory of World Chemical Producers

Clayton, G.D. & Clayton, F.E., eds. (1981) Patty's Industrial Hygiene and Toxicology, 3rd Rev. Ed., New York, John Wiley & Sons, Inc.

Considine, D.M., ed. (1974) Chemical and Process Technology Encyclopedia, New York, McGraw-Hill Book Company

Grayson, M., ed. (1978-1984) Kirk-Othmer Encyclopedia of Chemical Technology, 3rd Ed., New York, John Wiley & Sons, Inc. (available online as Kirk-Othmer Online)

IARC (1972-1990) IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vols. 1-49, Lyon, International Agency for Research on Cancer

Lide, D.R. (1991) CRC Handbook of Chemistry and Physics, 72nd Ed., CRC Press, Boca Raton, FL

National Toxicology Program (1990) Chemical Status Report, 6 November 1990 Report

National Toxicology Program (1990) NTP Results Report: Results and Status Information on All NTP Chemicals, 3 October 1990 Report

PHS-149 (1951-1988) Survey of Compounds Which Have Been Tested for Carcinogenic Activity, National Cancer Institute, U.S. Department of Health and Human Services

Sax, N.I. & Lewis, R.J., Sr. (1987) Hawley's Condensed Chemical Dictionary, 11th Ed., New York, Van Nostrand Reinhold Co.

Sax, N.I. (1981) Cancer Causing Chemicals

Sittig, M. (1985) Handbook of Toxic and Hazardous Chemicals and Carcinogens, 2nd Ed., Park Ridge, NJ, Noyes Publications

Verschueren, K. (1983) Handbook of Environmental Data on Organic Chemicals, 2nd Ed., New York, Van Nostrand Reinhold Co.