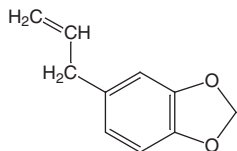


## Safrole

### CAS No. 94-59-7

Reasonably anticipated to be a human carcinogen  
First Listed in the *Second Annual Report on Carcinogens* (1981)



### Carcinogenicity

Safrole is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1976). When given by gavage followed by dietary administration, safrole increased the incidences of liver cell tumors in mice of both sexes. When administered in the diet, safrole increased the incidences of liver hepatocellular carcinomas and cholangiocarcinomas in rats of both sexes, and hepatocellular carcinomas in male mice. When administered to infant mice by subcutaneous injection, safrole induced lung adenomas and adenocarcinomas in mice of both sexes and hepatomas in male mice (IARC 1976).

No adequate human studies of the relationship between exposure to safrole and human cancer have been reported (IARC 1976).

### Properties

Safrole is a colorless to slightly yellow liquid with an odor of sassafras. Its molecular weight is 162.2, its melting point is 11.2°C, and it boils at 234.5°C at 760 mm Hg. It is insoluble in water and glycerol, slightly soluble in propylene glycol, and very soluble in ethanol, ether, and chloroform (IARC 1976, HSDB 2001).

### Use

Safrole, a naturally occurring substance, has been used as a flavoring agent in drugs, beverages, and foods, and in the manufacture of heliotropin and piperonyl butoxide. Safrole has also been used in soap and perfumes. Oil of sassafras, which contains safrole, was formerly used to flavor some soft drinks, such as root beer. However, as of 1960, this use was no longer permitted in the United States (IARC 1976, HSDB 2001).

### Production

Safrole is produced by distillation of oils rich in safrole. Chem Sources (2001) identified seven current U.S. suppliers of safrole. U.S. production was 258,000 lb and 278,000 lb in 1969 and 1970, respectively, but was only 12,000 lb in 1977 (IARC 1976, HSDB 2001). The 1979 TSCA Inventory identified four companies producing 2.8 million lb of dihydrosafrole, three companies producing 55,000 lb of isosafrole, and four companies importing 1,000 lb (TSCA 1979). Approximately 36,000 lb of safrole were imported from Brazil in 1980 (HSDB 2001). No current import or export data were found.

### Exposure

Minimal exposure to safrole may occur through the use of edible spices, including nutmeg and mace, which contain low levels of naturally occurring safrole (IARC 1976, HSDB 2001). Potential occupational exposure to workers handling safrole may occur through dermal contact. Health professionals, such as pharmacists, physicians, and nurses may possibly be exposed during formulation, preparation, administration, or clean-up of drugs containing safrole or sassafras. The National Occupational Exposure Survey (1981-1983) estimated that 6,475 workers were potentially exposed to safrole in the United States (HSDB 2001). In 1981, OSHA estimated that 30 workers were

possibly exposed to safrole. The Toxic Chemical Release Inventory listed four industrial facilities that released a total of 9,526 lb of safrole in 1999; however, 97% of the total released was from one facility (TRI99 2001).

### Regulations

#### EPA

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable Quantity (RQ) = 100 lb

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed substance subject to reporting requirements

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste codes in which listing is based wholly or partly on substance - U203

Listed as a Hazardous Constituent of Waste

#### FDA

Safrole is prohibited from direct addition to food or use as human food

#### REFERENCES

- ChemSources. 2001. Chemical Sources International, Inc. <http://www.chemsources.com>.  
 HSDB. 2001. Hazardous Substances Data Base. National Library of Medicine. <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>.  
 IARC. 1976. Some Naturally Occurring Substances. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 10. Lyon, France: International Agency for Research on Cancer. 353 pp.  
 TRI99. 2001. Toxic Chemical Release Inventory 1999. Data contained in the Toxic Chemical Release Inventory (TRI). National Library of Medicine. <http://www.epa.gov/triexplorer/>.  
 TSCA. 1979. Toxic Substances Control Act, Chemical Substances Inventory.