CHEMICAL MEETING THE CRITERIA FOR LISTING AS CAUSING CANCER VIA THE AUTHORITATIVE BODIES MECHANISM

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Reproductive and Cancer Hazard Assessment Section
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency

The chemical listed in the table below meets the criteria for listing under Proposition 65 via the authoritative bodies listing mechanism. The regulatory guidance for listing by this mechanism is set forth in Title 22, California Code of Regulations (CCR), Section 12306. For example, the regulations include provisions covering the criteria for evaluating the documentation and scientific findings by the authoritative body to determine whether listing under Proposition 65 is required.

The National Toxicology Program (NTP) is one of five institutions which has been identified as an authoritative body for the purposes of Proposition 65 (22 CCR 12306(l)). NTP has identified the chemical in the table below as causing cancer. The Office of Environmental Health Hazard Assessment (OEHHA) has found that this chemical has been "formally identified" as causing cancer according to the regulations covering this issue (22 CCR 12306(d)): The chemical below is the subject of a report published by the authoritative body which concludes that the chemical causes cancer. Also, the document specifically and accurately identifies the chemical and meets one or more of the criteria outlined in 22 CCR 12306(d)(2).

OEHHA also finds that the criteria given in regulation for "as causing cancer" (22 CCR 12306(e)) have been satisfied for the chemical in the table below. In making this evaluation, OEHHA relied upon the discussion of data by the authoritative body in making its findings that the specified chemical causes cancer. A brief discussion of the relevant carcinogenesis studies providing evidence for the finding is presented below. The statement in bold reflects data and conclusions that satisfy the criteria for the sufficiency of evidence for carcinogenicity (22 CCR 12306(e)). The full citation for the authoritative body document is given in this report.

Chemical Meeting the Criteria for Listing as Causing Cancer

Chemical	CAS No.	Chemical Use	Reference
Methyleugenol	93-15-2	Flavoring agent in jellies, baked goods, nonalcoholic beverages, chewing gum, candy, pudding, relish and ice cream; fragrance in perfumes, creams, lotions, detergents and soaps.	NTP (2000)

Methyleugenol (CAS No. 93-15-2)

Increased incidence of malignant and combined malignant and benign tumors in mice and rats of both sexes with tumors at multiple sites in male and female rats and male mice.

NTP (2000) has concluded that there is clear evidence of the carcinogenic activity of methyleugenol in male and female F344/N rats and in male and female B6C3F_1 mice.

NTP (2000) treated F344/N rats and B6C3F_1 mice with methyleugenol by gavage five days per week for two years. In rats, statistically significant increases in tumors at multiple sites were observed in treated animals of both sexes. The incidence of hepatocellular carcinoma was 2/50, 3/50, 14/50, 25/50, and 36/50 for vehicle control, low-, mid-, mid-high and high-dose male rats, respectively and 0/50, 0/50, 4/49, 8/49, and 22/50 for female rats. The combined incidence of hepatocellular adenoma or carcinoma was 7/50, 14/50, 28/50, 43/50, and 45/50 in male rats and 1/50, 8/50, 14/49, 34/49, and 43/50 in female rats. The combined incidence of hepatocholangioma and hepatocholangiocarcinoma was 0/50, 0/50, 1/50, 2/50, and 13/50 in male rats and 0/50, 0/50, 0/49, 3/49, and 17/50 in female rats. The incidence of tumors of the glandular stomach was also greater in treated rats of both sexes than in vehicle controls. In male rats, the incidence of malignant mesothelioma was 1/50, 3/50, 5/50, 12/50, and 5/50, which was significantly greater in the two highest dose groups compared to the vehicle control group. There were also statistically significant increases in the incidences of mammary gland fibroadenoma at the mid-dose levels (5/50, 5/50, 15/50, 13/50, 6/50) and in renal tubule adenoma at the three highest dose levels (extended and standard evaluation combined: 4/50, 6/50, 17/50, 13/50, 20/50) in male rats.

In mice of both sexes statistically significant increases in liver tumors were observed in treated animals. The combined incidence of hepatocellular carcinoma and hepatoblastoma was 10/49, 20/50, 20/50, and 11/50 in male mice and 7/50, 38/50, 48/49, and 49/50 in female mice. The combined incidence of hepatocellular adenoma, carcinoma or hepatoblastoma was 31/49, 47/50, 46/50, and 41/50 in male mice and 25/50, 50/50, 49/49, and 49/50 in female mice. In

addition, two malignant endocrine tumors of the glandular stomach were observed in two high-dose male mice. Because these neoplasms had not been previously observed in NTP gavage studies and because they were also observed in rats, these neoplasms were considered to be related to methyleugenol administration.

REFERENCES

National Toxicology Program (NTP, 2000). *Toxicology and Carcinogenesis Studies of Methyleugenol (CAS No. 93-15-2) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies).* NTP Technical Report Series No. 491 NIH Publication No. 00-3950. U.S. Department of Health and Human Services, NTP, Research Triangle Park, NC.