

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

## PACKAGE 31b

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

The chemical listed in the table below meets the criteria for listing as known to the State to cause cancer under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Health and Safety Code Section 25249.5 *et seq.*), more commonly known as Proposition 65, via the authoritative bodies mechanism. The regulatory requirements for listing by this mechanism are set forth in Title 27, California Code of Regulations, section 25306<sup>1</sup>. The regulations include the criteria for evaluating the documentation and scientific findings by the authoritative body that the Office of Environmental Health Hazard Assessment (OEHHA) uses to determine whether listing under Proposition 65 is required.

The U.S. Environmental Protection Agency (U.S. EPA) is one of five institutions that have been identified as an authoritative body for identification of chemicals as causing cancer for the purposes of Proposition 65 (Section 25306(1)). OEHHA has found that oryzalin appears to be “formally identified” by U.S. EPA as causing cancer as defined in Section 25306(d). Oryzalin is the subject of a report published by U.S. EPA that concludes that the chemical causes cancer. Also, the document specifically and accurately identifies oryzalin, and meets one or more of the criteria outlined in Section 25306(d)(2).

OEHHA also finds that the criteria given in regulation for “as causing cancer” in Section 25306(e) have been satisfied for oryzalin. In making this evaluation, OEHHA relied upon the discussion of data by the U.S. EPA in making its finding that oryzalin 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 (Section 25306(e)). The full citation for the U.S. EPA document is given in this report.

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<sup>1</sup> Formally Title 22, California Code of Regulations, section 12306. All further references are to Title 27 of the California Code of Regulations unless otherwise indicated.

**Chemical Meeting the Criteria for Listing as  
Known to the State to Cause Cancer**

<b>Chemical</b>	<b>CAS No.</b>	<b>Chemical Use</b>	<b>U.S. EPA Classification</b>	<b>Reference</b>
Oryzalin	19044-88-3	Herbicide used on almonds, grapes, fruit trees, pistachios, pomegranates; in gardening and landscape maintenance; and in rights-of-way.	Likely to be carcinogenic to humans	U.S. EPA (2003)

Oryzalin (CAS No. 19044-88-3)

**Increased incidence of combined malignant and benign tumors in male and female rats.**

The U.S. EPA (2003) has classified oryzalin as “Likely to be carcinogenic to humans.” This classification was based on increased incidences of skin fibroma and fibrosarcoma in male rats, thyroid follicular cell tumors in male and female rats, combined malignant and benign skin tumors in female rats, and mammary gland fibroadenomas in female rats. The studies evaluated by U.S. EPA are summarized below.

Male and female F344 rats (60 animals/group/sex) were exposed to oryzalin via diet for two years. The U.S. EPA (2003) considered the highest dose in these studies to be excessively toxic. The mid-dose was considered adequate for carcinogenicity assessment, and tumors supporting the cancer classification were considered to be treatment-related at the mid-dose (U.S. EPA, 2003).

In male rats, incidences of skin fibroma (3/54, 3/59, 9/54 [p<0.05], and 11/50 [p<0.01] for control, low-, mid-, and high-dose groups, respectively) and combined fibroma and fibrosarcoma (4/55, 5/59, 13/57 [p<0.05] and 13/55 [p<0.01]) were statistically significant at the two highest dose groups and occurred with positive trends [p<0.01]. Thyroid follicular cell tumors (adenoma: 1/55, 6/59, 5/57 and 4/55; carcinoma: 0/48, 0/43, 0/36 and 3/36; and combined adenoma or carcinoma, 1/55, 6/59, 5/57 [p<0.05] and 6/55 [p<0.05]) were also increased. U.S. EPA (2003) considered thyroid tumors to be related to oryzalin treatment at all three doses.

In female rats, the incidence of combined benign and malignant skin tumors (3/56, 7/59, 16/56 [p<0.01] and 13/53 [p<0.01] for control, low-, mid-, and high-dose groups, respectively) was significantly increased at the two highest dose groups and occurred with a positive trend [p<0.01]. The skin tumors observed were: papillomas (0/47, 1/44, 0/44 and 1/36), sebaceous gland adenomas (2/56, 4/59, 12/56 [p<0.01] and 5/53), squamous cell carcinomas (0/47, 0/44, 1/41 and 0/36), basal cell adenomas (0/44, 1/41, 0/37 and 1/31), and keratoacanthoma (1/55, 1/58, 3/55 and 8/53 [p<0.01]). U.S. EPA (2003) also concluded that mammary gland fibroadenomas and thyroid follicular cell tumors in female rats were related to oryzalin exposure. The increased incidence of mammary gland fibroadenoma (10/58, 20/60, 37/60 [p<0.01], and 29/57 [p<0.01]) was

significantly greater than that in control animals and occurred with a positive trend [p<0.01]. The increase in thyroid follicular cell tumors (adenoma: 1/55, 1/58, 3/54, and 8/50 and combined thyroid follicular cell adenoma or carcinoma: 1/55, 1/58, 3/54, and 9/50 [p<0.05]; positive trend [p<0.01]) was statistically significant at the high dose only, but U.S. EPA (2003) concluded that the increases in thyroid follicular cell tumors at the two highest doses were treatment-related.

Male and female B6C3F<sub>1</sub> mice were exposed, in two separate replicate studies, to oryzalin via diet for two years (40 animals/group/sex/replicate). No treatment-related tumors were found.

### **Reference**

U.S. Environmental Protection Agency (U.S. EPA, 2003). *Cancer Assessment Document. Third Evaluation of the Carcinogenic Potential of Oryzalin*. Cancer Assessment Review Committee. Health Effects Division. Office of Pesticide Programs. June 25, 2003.