

**CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT**

**SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT OF 1986
(PROPOSITION 65)**

**Request For Relevant Information On Chemicals Being Considered For Listing By The
Authoritative Bodies Mechanism:
Clodinafop-Propargyl, Diclofop-Methyl, And Epoxiconazole**

November 13, 2009

The California Environmental Protection Agency's Office of Environmental Health Hazard Assessment (OEHHA) is requesting information as to whether the chemicals identified in the table below meet the criteria for listing under the Safe Drinking Water and Toxic Enforcement Act of 1986.¹ This action is being proposed under the authoritative bodies listing mechanism.²

Chemical	CAS No.	Endpoint	Reference	Chemical Use
<i>Clodinafop-propargyl</i>	105512-06-9	Cancer	U.S. EPA (1999)	Herbicide used on spring wheat
<i>Diclofop-methyl</i>	51338-27-3	Cancer	U.S. EPA (2000)	Herbicide used on wheat, barley and golf courses
<i>Epoxiconazole</i>	135319-73-2	Cancer	U.S. EPA (2001)	Triazole fungicide used on coffee and bananas outside the U.S.

Background on listing via the authoritative bodies mechanism: A chemical must be listed under the Proposition 65 regulations when two conditions are met:

- 1) An authoritative body formally identifies the chemical as causing cancer (Section 25306(d)³).
- 2) The evidence considered by the authoritative body meets the sufficiency criteria contained in the regulations (Section 25306(e)).

However, the chemical is not listed if scientifically valid data which were not considered by the authoritative body clearly establish that the sufficiency of evidence criteria were not met (Section 25306(f)).

The U.S. Environmental Protection Agency (U.S. EPA) is one of several institutions designated as authoritative for the identification of chemicals as causing cancer (Section 25306(m)).

¹ Commonly known as Proposition 65, the Safe Drinking Water and Toxic Enforcement Act of 1986 is codified in Health and Safety Code section 25249.5 *et seq.*

² See Health and Safety Code section 25249.8(b) and Title 27, Cal. Code of Regs., Section 25306.

³ All referenced sections are from Title 27 of the Cal. Code of Regulations.

OEHHA is the lead agency for Proposition 65 implementation. After an authoritative body has made a determination about a chemical, OEHHA evaluates whether listing under Proposition 65 is required using the criteria contained in the regulations.

OEHHA's determination: *clodinafop-propargyl*, *diclofop-methyl*, and *epoxiconazole* each appear to meet the criteria for listing as known to the State to cause cancer under Proposition 65, based on findings of the U.S. EPA (U.S. EPA, 1999; U.S. EPA, 2000; U.S. EPA, 2001).

Formal identification and sufficiency of evidence for clodinafop-propargyl: In 1999, the U.S. EPA published a report on clodinafop-propargyl entitled *Cancer Assessment Document – Evaluation of the Carcinogenic Potential of Clodinafop-Propargyl (CGA 184927)*. This report concludes that the chemical causes cancer, which appears to satisfy the formal identification and sufficiency of evidence criteria in the Proposition 65 regulations.

OEHHA is relying on the U.S. EPA's discussion of data and conclusions in the report that clodinafop-propargyl causes cancer. The U.S. EPA (1999) report found that in rats, “[i]n males there were significant increases in the pair-wise comparisons of the high-dose group (750 ppm or 26.28 mg/kg/day) with controls for prostate gland adenomas ($p < 0.05$) and combined adenomas/carcinomas ($p < 0.01$).” The U.S. EPA found that in mice, “males had a statistically significant ($p < 0.01$) increase in the pair-wise comparisons of the high dose group (250 ppm or 29.6 mg/kg/day) with the controls for hepatomas and combined hepatomas/carcinomas.”

The U.S. EPA report concludes clodinafop-propargyl is “**likely to be carcinogenic to humans**’ by the oral route based on the following weight-of-the-evidence considerations:

1. Increased incidences of prostate tumors in male rats, ovarian adenomas in female rats and liver tumors in male and female mice and blood vessel tumors in female mice.
2. The relevance of the observed tumors to human exposure cannot be discounted.
3. Structurally related compounds, haloxyfop-methyl and diclofop-methyl are hepatocarcinogens in mice. Both fluazifop-butyl and diclofop-methyl are non mutagens.” (emphasis in original)

Thus, the U.S. EPA (1999) has found that clodinafop-propargyl causes increased incidences of combined benign and malignant prostate tumors in male rats and combined benign and malignant liver tumors in male mice.

Formal identification and sufficiency of evidence for diclofop-methyl: In 2000, the U.S. EPA published a report on diclofop-methyl entitled *Cancer Assessment Document. Evaluation of the Carcinogenic Potential of Diclofop-Methyl (Second Review)*. This report concludes that the chemical causes cancer, which appears to satisfy the formal identification and sufficiency of evidence criteria in the Proposition 65 regulations.

OEHHA is relying on the U.S. EPA's discussion of data and conclusions in the report that diclofop-methyl causes cancer. The U.S. EPA (2000) report concludes that diclofop-methyl is “**likely to be carcinogenic to humans**’ by the oral route based on the following weight-of-the-evidence considerations:

1. Liver tumors were seen in both sexes of two species including both benign and malignant liver tumors in rats and mice. Increases in the incidence of thyroid follicular cell tumors in female rats and Leydig cell tumors in male rats were possibly treatment-related.
2. The relevance of the observed tumors to human exposure cannot be discounted.
3. Diclofop-methyl is not mutagenic in both in vivo and in vitro assays.
4. Structurally related diphenyl ethers cause liver tumors in rats and/or mice. Some of these compounds such as clodinafop-propargyl and lactofen, are also peroxisome proliferators.” (emphasis in original)

Thus, the U.S. EPA (2000) has found that diclofop-methyl causes increased incidences of combined malignant and benign liver tumors in male and female mice and rats.

Formal identification and sufficiency of evidence for epoxiconazole: In 2001, the U.S. EPA published a report on epoxiconazole entitled *Cancer Assessment Document. Evaluation of the Carcinogenic Potential of Epoxiconazole*. This report concludes that the chemical causes cancer, which appears to satisfy the formal identification and sufficiency of evidence criteria in the Proposition 65 regulations.

OEHHA is relying on the U.S. EPA’s discussion of data and conclusions in the report that epoxiconazole causes cancer. The U.S. EPA (2001) report found that in male rats there was an increased incidence of hepatocellular carcinomas and combined adenomas and carcinomas of the adrenal cortex in treated animals relative to controls. In female rats there was an increased incidence of combined adenomas and carcinomas of the adrenal cortex, and benign ovarian luteomas and granulosa cell tumors in treated animals relative to controls. In male and female mice there was an increased incidence of hepatocellular carcinomas and combined hepatocellular carcinomas and adenomas in treated animals relative to controls.

The U.S. EPA report concludes that epoxiconazole is “**likely to be carcinogenic to humans**’ by the oral route based on the following weight-of-the-evidence considerations:

1. There were increased incidences of liver tumors in male and female mice and rats. In addition, treatment-related increase [sic] were noted for adrenal tumors in male and female rats and ovarian tumors in female rats.
2. The relevance of the observed tumors to human exposure cannot be discounted.
3. The structurally related compounds are largely nonmutagens but are hepatocarcinogens.” (emphasis in original)

Thus, the U.S. EPA (2001) has found that epoxiconazole causes increased incidences of combined malignant and benign adrenal tumors in male and female rats, malignant liver tumors in male rats, and malignant and combined malignant and benign liver tumors in male and female mice.

Request for relevant information: OEHHA is committed to public participation in its implementation of Proposition 65. OEHHA wants to ensure that its regulatory decisions are based on a thorough consideration of all relevant information. OEHHA is requesting public comment concerning whether these chemicals meet the criteria set forth in the Proposition 65 regulations for authoritative bodies listings.

After reviewing all comments received, OEHHA will determine whether the identified chemicals meet the regulatory criteria for administrative listing and proceed with listing. For chemicals determined to meet the listing criteria, OEHHA will publish a Notice of Intent to List.

In order to be considered, **OEHHA must receive comments by 5:00 p.m. on Tuesday, January 12, 2010.** We encourage you to submit comments in electronic form, rather than in paper form. Comments transmitted by e-mail should be addressed to coshita@oehha.ca.gov. Comments submitted in paper form may be mailed, faxed, or delivered in person to the addresses below:

Mailing Address: Ms. Cynthia Oshita
Office of Environmental Health Hazard Assessment
P.O. Box 4010, MS-19B
Sacramento, California 95812-4010

Fax: (916) 323-8803

Street Address: 1001 I Street
Sacramento, California 95814

Optional public forum: Upon request, OEHHA will schedule a public forum to provide individuals an opportunity to present oral comments on the possible listing of these chemicals. At the forum, the public may discuss the scientific data and other relevant information related to whether any of these chemicals meet the criteria for listing in the regulations.

Requests for a public forum must be submitted in writing no later than December 11, 2009. The written request must be sent to OEHHA at the mailing address above. If a public forum is requested, a notice will be posted on the OEHHA web site at least ten days before the forum date. The notice will provide the date, time, location and subject matter to be heard. Notices will also be sent to those individuals requesting such notification.

If you have any questions, please contact Ms. Oshita at coshita@oehha.ca.gov or at (916) 445-6900.

References

U.S. Environmental Protection Agency (U.S. EPA, 1999). Cancer Assessment Document. Evaluation of the Carcinogenic Potential of Clodinafop-Propargyl (CGA 184927). Health Effects Division, Office of Pesticides Programs. December 7, 1999.

U.S. Environmental Protection Agency (U.S. EPA, 2000). Cancer Assessment Document. Evaluation of the Carcinogenic Potential of Diclofop-Methyl (Second Review). Health Effects Division, Office of Pesticide Programs. May 24, 2000.

U.S. Environmental Protection Agency (U.S. EPA, 2001). Cancer Assessment Document. Evaluation of the Carcinogenic Potential of Epoxiconazole. Health Effects Division, Office of Pesticide Programs. January 24, 2001.