The California Environmental Protection Agency’s Office of Environmental Health Hazard Assessment (OEHHA) intends to list the chemicals isopyrazam and 3,3’,4,4’-tetrachloroazobenzene as known to the State to cause cancer under the Safe Drinking Water and Toxic Enforcement Act of 1986.¹ This action is being proposed under the authoritative bodies listing mechanism.²

### Chemicals Meeting Criteria for Listing as Known to Cause Cancer

<table>
<thead>
<tr>
<th>Chemical (CAS No.)</th>
<th>Reference</th>
<th>Occurrence and Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>3,3’,4,4’-Tetrachloroazobenzene (14047-09-7)</td>
<td>NTP (2010b)</td>
<td>Contaminant of 3,4-dichloroaniline and the related herbicides linuron, diuron, and propanil, and a degradation product of 3,4-dichloroaniline and chloroanilide herbicides.</td>
</tr>
</tbody>
</table>

OEHHA requested information relevant to the possible listing of isopyrazam and 3,3’,4,4’-tetrachloroazobenzene in a notice published in the California Regulatory Notice Register on February 10, 2012 (Register 2012, Vol. No. 6-Z). OEHHA received comments for isopyrazam, but not for 3,3’,4,4’-tetrachloroazobenzene.

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

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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.
1) An authoritative body formally identifies the chemical as causing cancer (Section 25306(d))

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) and the National Toxicology Program (NTP) are two of several institutions designated as authoritative for the identification of chemicals as causing cancer (Section 25306(m)).

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:** Isopyrazam and 3,3',4,4'-tetrachloroazobenzene meet the criteria for listing as known to the State to cause cancer under Proposition 65, based on findings of U.S. EPA and NTP, respectively (U.S. EPA, 2011; NTP, 2010).


OEHHA is relying on U.S. EPA’s discussion of data and conclusions in the report that isopyrazam causes cancer. The U.S. EPA report concludes that isopyrazam is “likely to be carcinogenic to humans.” Evidence described in the report includes studies showing that isopyrazam increased the incidences of thyroid follicular cell carcinomas and combined adenomas and carcinomas in male Wistar rats, and uterine endometrial adenocarcinomas in female Wistar rats.

Thus, U.S. EPA (2011) has found that isopyrazam causes increased incidences of malignant and combined malignant and benign thyroid tumors in male rats and malignant tumors of the uterus in female rats.

**Formal identification and sufficiency of evidence for 3,3',4,4'-tetrachloroazobenzene:** In 2010, NTP published a report on 3,3',4,4'-tetrachloroazobenzene (TCAB) entitled *Toxicology and Carcinogenesis Studies of 3,3',4,4'-Tetrachloroazobenzene (TCAB) (CAS No. 14047-09-7) in Harlan Sprague-Dawley Rats and B6C3F1 Mice (Gavage Studies)*, that concludes that the chemical causes cancer (NTP, 2010). This

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3 All referenced sections are from Title 27 of the Cal. Code of Regulations.
report satisfies the formal identification and sufficiency of evidence criteria in the Proposition 65 regulations.

OEHHA is relying on NTP's discussion of data and conclusions in the report that 3,3',4,4'-tetrachloroazobenzene causes cancer. The NTP (2010) report concludes:

"Under the conditions of these 2-year gavage studies, there was clear evidence of carcinogenic activity of TCAB in male Harlan Sprague-Dawley rats based on increased incidences of cystic keratinizing epithelioma of the lung, cholangiocarcinoma of the liver, and gingival squamous cell carcinoma of the oral mucosa. The increased incidences of follicular cell adenoma of the thyroid gland were also considered to be related to TCAB administration. The marginally increased incidence of malignant schwannoma may have been related to TCAB administration. There was clear evidence of carcinogenic activity of TCAB in female Harlan Sprague-Dawley rats based on increased incidences of cystic keratinizing epithelioma of the lung and gingival squamous cell carcinoma of the oral mucosa. The increased incidences of cholangiocarcinoma of the liver and squamous cell papilloma or squamous cell carcinoma (combined) of the forestomach were also considered to be related to TCAB administration. The marginally increased incidences of adenoma of the adrenal cortex may have been related to TCAB administration. There was clear evidence of carcinogenic activity of TCAB in male B6C3F1 mice based on increased incidences of carcinoma of the urethra and alveolar/bronchiolar neoplasms of the lung. The increased incidences of squamous cell carcinoma of the forestomach were also considered to be related to TCAB administration. The marginally increased incidence of carcinoma of the ureter may have been related to TCAB administration. There was clear evidence of carcinogenic activity of TCAB in female B6C3F1 mice based on increased incidences of fibrosarcoma and fibrosarcoma or malignant schwannoma (combined) of the skin. The increased incidences of carcinoma of the urethra, alveolar/bronchiolar neoplasms and cystic keratinizing epithelioma of the lung, and squamous cell carcinoma of the forestomach were also considered to be related to TCAB administration. The marginally increased incidences of malignant lymphoma may have been related to TCAB administration."

Thus, NTP (2010) has found that 3,3',4,4'-tetrachloroazobenzene causes increased incidences of malignant tumors at multiple sites in male rats, rare malignant tumors of the oral cavity in female rats, malignant tumors at multiple sites in male mice, and malignant tumors at multiple sites in female mice.
Request for comments: 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 comments as to whether these chemicals meet the criteria set forth in the Proposition 65 regulations for authoritative bodies listings. In order to be considered, OEHHA must receive comments by 5:00 p.m. on Monday, June 25, 2012. We encourage you to submit comments via e-mail, rather than in paper form. Comments transmitted by e-mail should be addressed to P65Public.Comments@oehha.ca.gov with “NOIL” and the name of the chemical in the subject line. Hard copy comments 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

Comments received during the public comment period will be posted on the OEHHA web site after the close of the comment period.

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

References
