Candidate for Proposition 65 Listing via the Authoritative Bodies Mechanism Found Not to Meet the Scientific Criteria (22 CCR 12306(g))

Office of Environmental Health Hazard Assessment
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The U.S. Environmental Protection Agency (U.S. EPA), an authoritative body for purposes of Proposition 65 (22 CCR Section 12306(l)), identifies chemicals as causing developmental or reproductive toxicity in implementing its Toxic Release Inventory (TRI) program (*i.e.*, Section 313 of the Emergency Planning and Community Right-to-Know Act of 1986 (EPCRA)). On this basis the U.S. EPA, in 1994, added a number of chemicals to the TRI list and published its findings in the *Federal Register* (**59:**1788-1859, 1994 and **59:**61432-61485, 1994). The Office of Environmental Health Hazard Assessment (OEHHA) has reviewed the bases for these TRI chemical additions in the context of the regulatory criteria governing Proposition 65 listing via the authoritative bodies mechanism (Title 22, California Code of Regulations, Section 12306 (22 CCR 12306)).

OEHHA determined for several TRI chemicals that the 22 CCR 12306 regulatory criteria were met and is in the process of placing these chemicals on the Proposition 65 list of chemicals known to cause reproductive toxicity. As described below, OEHHA has determined that scientific criteria for "as causing reproductive toxicity" given in regulation (22 CCR 12306(g)) were not satisfied for **fenbutatin oxide**, which was added by U.S. EPA in 1994 to the TRI list on the basis of developmental toxicity.

In accordance with 22 CCR 12306(i), fenbutatin oxide (CAS No. 013356-08-6) will be referred to the Developmental and Reproductive Toxicant Identification Committee of the OEHHA Science Advisory Board because this determination was made subsequent to the issuance of a notice of intent to list (*California Regulatory Notice Register (CRNR),* and January 29, 1999). Therefore, at a future meeting, the Committee will opine whether fenbutatin oxide has been "clearly shown through scientifically valid testing according to generally accepted principles" to cause reproductive toxicity.

Fenbutatin oxide (CAS No. 013356-08-6)

U.S. EPA (*Federal Register* 59(8):1813, 1994) based its finding of developmental toxicity on a rat developmental study, a rabbit developmental study, and a rat reproductive study. The rat developmental study (Shell Research, Ltd., 1980, *Report TLGR.80.145*) found a statistically significant increase in pre-implantation losses at the high dose. However, as treatment was begun on gestation day 6, the day on which implantation typically occurs, it is not clear that the finding was treatment-related. There was a greater mean increase in preimplantation loss at the low dose than the high dose. The rabbit developmental study (Shell Research, Ltd., 1981, *Report SBGR.81.055*) found increased post-implantation loss at the middle and high doses. Apparent developmental effects at the high dose could not be interpreted because of excessive maternal mortality. At the middle dose, maternal mortality was marginally above the level defined as "minimal" by U.S. EPA, and the increase in post-implantation loss was reported to be not statistically significant. The rat reproductive study (Hine Laboratories Inc. for Shell Chemical Co., 1973, *Report No. 33*) found reduced postnatal viability with fenbutatin oxide given in feed at the highest concentration used in the study. However, as treatment of the dams was continued postnatally, the relevant exposures may have occurred via nursing, or even from direct consumption of the dams' feed by pups. As currently interpreted, the Proposition 65 statute precludes listing on the basis of developmental effects resulting solely from postnatal exposures. Thus, the body of evidence related to prenatal exposures cited by U.S. EPA is not of sufficient quantity to satisfy the regulatory criteria for listing under the authoritative bodies provision (i.e., 22CCR 12306(g)).