Proposition 65 Maximum Allowable Daily Level (MADL) for Reproductive Toxicity for Quizalofop-Ethyl

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Office of Environmental Health Hazard Assessment
Reproductive and Cancer Hazard Assessment Section

Summary

The maximum allowable daily level (MADL) for quizalofop-ethyl exposure is **590 µg/day**. This value is applicable to oral, inhalation and dermal routes of exposure and was derived as described below, based on a 13 week feeding study in rats conducted by Nissan Chemical Industries, Ltd. (1982).

Background

This report describes the derivation of a maximum allowable daily level for quizalofop-ethyl (CAS # 76578-14-8), a chemical listed under Proposition 65 as known to the State to cause reproductive toxicity, effective December 13, 1999. Exposure at a level 1,000 times greater than the MADL is expected to have no observable effect. Procedures for the development of Proposition 65 MADLs are provided in regulation (Title 22, California Code of Regulations [22 CCR], Sections 12801 and 12803).

The Proposition 65 listing of quizalofop-ethyl was based on a finding by the Developmental and Reproductive Toxicant (DART) Identification Committee, the Proposition 65 state's qualified experts for reproductive toxicity, that the chemical had been clearly shown by scientifically valid testing according to generally accepted principles to cause male reproductive toxicity. As part of its deliberations, the Committee reviewed the document "Evidence on Developmental and Reproductive Toxicity of Quizalofop-Ethyl" (OEHHA, 1999), a comprehensive review of the scientific literature on the adverse reproductive effects of quizalofop-ethyl. This review serves as the primary reference for MADL development. As defined in regulations, MADLs are derived from No Observable Effect Levels (NOELs) or Lowest Observable Effect Levels (LOELs) (22 CCR Sections 12801 and 12803). The values discussed below are the highest exposure level at which no effect was observed, or the lowest exposure level at which an adverse effect was observed, under the specific conditions of the study in question.

Study Selection

Relevant studies were reviewed in the document "Evidence on Developmental and Reproductive Toxicity of Quizalofop-Ethyl" (OEHHA 1999), utilized by the DART

Identification Committee. An update of the literature search to find relevant studies published since the development of the OEHHA (1999) document identified no additional human or animal studies of interest for MADL development.

The NOEL is based on the most sensitive study deemed to be of sufficient quality (22 CCR Section 12803(a)(4)). The study meeting this criterion is the 13 week feeding study in rats conducted by Nissan Chemical Industries, Ltd. (1982). Male animals were exposed to quizalofop-ethyl in diet at concentrations of 0, 40, 128 or 1280 ppm. Clear evidence of testicular atrophy was seen at the highest dose tested, while no effects were observed at the intermediate or low doses. The NOEL is the highest dose level which results in no observable reproductive effect, expressed in milligrams of chemical per kilogram of bodyweight per day (22 CCR Section 12803(a)(1)). Thus, the dose resulting from consumption of diet containing 128 ppm quizalofop-ethyl is the NOEL. This dose was calculated by the study authors (Nissan, 1982) to be 8.4 mg/kg-day and is adopted as the NOEL for purposes of MADL development.

MADL Calculation

The NOEL is converted to a milligram per day dose level by multiplying by the assumed human body weight (22 CCR Section 12803(b)). For male reproductive toxicity, the assumed body weight is 70 kg. The NOEL is therefore calculated as follows:

NOEL = 8.4 mg/kg-day × 70 kg = 588 mg/day

The MADL is derived by dividing the NOEL by one thousand (1,000) to arrive at the maximum allowable dose level (22 CCR Section 12801(b)(1)). Thus, the adjusted NOEL was divided by 1,000 to obtain the MADL.

MADL = 588 mg/day ÷ 1000 = **590 µg/day** (rounded from 588 µg/day)

This MADL is based on oral exposure and is assumed to hold for inhalation and dermal routes in the absence of sufficient data for developing a separate MADL for inhalation and dermal exposure.

References

Nissan Chemical Industries, Ltd. (1982). NC-302: Potential Toxicity to Rats when Administered in the Diet for 13 Weeks followed by a 6 Week Recovery Period. (Conducted by Huntingdon Research Center, England).

Office of Environmental Health Hazard Assessment (OEHHA, 1999). Evidence on Developmental and Reproductive Toxicity of Quizalofop-Ethyl. Reproductive and Cancer Hazard Assessment Section, OEHHA, California Environmental Protection Agency, Sacramento CA 95812. [http://www.oehha.ca.gov /prop65/pdf/HIDQuiz.pdf].