



California Notice 2022-16

To: Pesticide Registrants and Other Stakeholders

Subject: JUSTIFICATION FOR WAIVING ACUTE DERMAL TOXICITY TESTS FOR ADJUVANT REGISTRATION IN CALIFORNIA AND GUIDANCE FOR SUBMITTING WAIVER REQUESTS

Introduction

The U.S. Environmental Protection Agency (U.S. EPA) published guidance for waiving acute dermal toxicity tests for pesticide formulations and technical grade active ingredients in 2016 and 2020, respectively. Both guidance documents indicated that acute oral toxicity studies could be used to predict acute dermal toxicity hazards for pesticide labeling, thus reducing the need for animal testing.

Since adjuvants are exempt from federal pesticide registration, the U.S. EPA guidance documents do not address waiving acute dermal toxicity studies for adjuvants. However, adjuvants are considered pesticides in California and must be registered by the Department of Pesticide Regulation (DPR). DPR requires registrants to submit acute toxicity data, including acute dermal toxicity studies, to register adjuvants in California. To support efforts to reduce animal testing, DPR conducted a retrospective analysis to determine if acute oral toxicity data could also be predictive of acute dermal toxicity for adjuvants.

Retrospective Analysis

DPR's retrospective analysis included 63 adjuvant products registered with DPR from 2010 to 2020. The adjuvant products contained principal functioning agents representing a variety of chemicals such as citric acid, glycerol, and esters.

The inclusion criteria for the analysis were:

- 1) Both *in vivo* acute oral and dermal LD₅₀ toxicity studies were conducted for an adjuvant.
- 2) Studies were performed following U.S. EPA health effects test guidelines.
- 3) DPR accepted the submitted studies for adjuvant registration in California.

The comparison of acute oral and dermal toxicity categories using the U.S. EPA classification system showed:

- 1) For 55 out of 63 adjuvants, the paired acute oral and dermal studies were in the same U.S. EPA acute toxicity category.
- 2) For four adjuvants, the acute oral study resulted in a lower (more protective) acute toxicity category than the acute dermal study.

- 3) For the other four adjuvants, the acute oral study resulted in a higher (less protective) acute toxicity category than the acute dermal study.

The agreement analysis of acute oral and dermal toxicity categories using Globally Harmonized System (GHS) classification systems, as adopted by the Occupational Safety and Health Administration (OSHA), indicated:

- 1) For 61 out of 63 adjuvants, the paired acute oral and dermal studies were in the same GHS/OSHA acute toxicity category.
- 2) For two adjuvants, the acute oral study resulted in a lower (more protective) acute toxicity category than the acute dermal study.

Results of Analysis

The results derived from the two parallel classification systems were consistent. The predictive capability of the acute oral toxicity category for the acute dermal hazard was 93.7% using the U.S. EPA classification system and 100% when using the GHS/OSHA classification systems. This analysis indicates that if no acute dermal toxicity study is available, an acute toxicity category can be assigned for acute dermal hazards based on the toxicity category for the acute oral hazards.

Acute Dermal Toxicity Study Waiver Guidance

DPR believes this retrospective analysis strongly supports the conclusion that waivers may be considered for acute dermal toxicity studies for adjuvant registration in California. To submit a formal acute dermal toxicity study waiver request as part of the registration application package, applicants should submit all relevant information to support the waiver, such as results of the acute oral toxicity LD₅₀ study and cite this notice.

Although DPR anticipates granting an acute dermal toxicity study waiver in most cases, DPR may request acute dermal toxicity studies on a case-by-case basis (e.g., unique chemical properties) if more comprehensive evaluation of acute dermal hazards is necessary for health-protective purposes.

If you have questions regarding the general registration process for adjuvants in California, please contact the Pesticide Registration Ombudsman, Mr. Aron Lindgren, by email at Registration.Ombudsman@cdpr.ca.gov or by telephone at 916-324-3563. If you have questions regarding this notice, please contact Dr. Shelley DuTeaux, Human Health Assessment Branch Chief, at Shelley.DuTeaux@cdpr.ca.gov or by telephone at 916-445-4268.

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