Bayer CropScience

REGULATORY TOXICOLOGY
POSITION PAPER

Subject :
Cyfluthrin and Beta-cyfluthrin

CONTENTS :

Expert Statement on the Acute Oral Toxicity and Relevant LD50 Values for Classification and Labelling

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BACKGROUND AND PURPOSE

Cyfluthrin (CAS 68359-37-5) and beta-cyfluthrin (an enriched mix of the biologically-active isomers of cyfluthrin) are pyrethroid insecticides. The acute toxicity of cyfluthrin and beta-cyfluthrin technical is low-to-high via the oral route of exposure, depending on the vehicle used.

For cyfluthrin and beta-cyfluthrin technical, the range of LD50 values by acute oral exposure depend on the type of dose preparation, which is problematic for classification and labelling. The purpose of this document is to provide a rigorous scientific assessment to support the choice of specific LD50 values by oral exposure, based on their relevance to circumstances of human exposure.

ACUTE ORAL TOXICITY STUDIES

Published and proprietary studies have shown the acute oral (gavage) toxic potency of pyrethroid insecticides varies with the choice of vehicle used to solubilize the dose for administration. For cyfluthrin technical, acute oral LD50 values in fasted adult male Wistar rats are 16.2, 254, 396, 590 or 500-1000 mg/kg bw when administered by gavage in Cremophor EL/distilled water, acetone/oil, DMSO, PEG 400 or N-methyl pyrrolidon, respectively ([redacted] 1982). In a GLP study conducted in accordance with OECD TG 401, acute oral LD50 values in fasted male and female Wistar rats administered cyfluthrin by gavage in acetone / peanut oil solution were 155 and 160 mg/kg bw, respectively ([redacted] 1987). A similarly-broad range of values was reported for beta-cyfluthrin technical using a variety of vehicles, with LD50 values of 11, 77, 211 and 380 mg/kg bw when administered by gavage in Cremophor EL/distilled water, acetone/peanut oil, xylene (suspension) and PEG 400, respectively ([redacted] 1986 and 1987).

Table 1. Acute oral LD50 values (mg/kg bw) in adult Wistar rats for technical-grade cyfluthrin and beta-cyfluthrin

	Cremophor EL / Distilled	Acetone / Peanut Oil[1]	DMSO or Xylene	PEG 400	N-methyl pyrrolidon
Cyfluthrin	**16.2**	**254 (155/160 mg/kg bw in guideline study)**	**396**	**590**	**500-1000**
Beta-cyfluthrin	**11**	**77**	**211**	**380**	**NA**

[1]*LD50 values reported by Heimann (1982) in males and Heimann (1987) in males/females*

The LD50 values reported for cyfluthrin and beta-cyfluthrin administered in Cremophor EL are particularly low, which is consistent with Cremophor being a non-ionic solubilizer and emulsifier that was commercialized and is used to enhance the absorption of drugs, thereby rendering them more effective (BASF, 1997). Moreover, in its review of the available data the U.S. EPA concluded that Cremophor significantly enhances the toxicity of cyfluthrin and beta-cyfluthrin, relative to all other vehicles (EPA 2002), and the EPA cites LD50 values in acetone/peanut oil, rather than in Cremophor.

U.S. EPA and OECD guidance for the choice of vehicle indicates the vehicle should neither reduce nor enhance the toxicity of the test substance. Furthermore, OECD TG 401, 420 and 423 indicate "With respect to the formulation of the dosing preparation, the use of an aqueous solution / suspension / emulsion in oil (e.g. corn oil) and then possibly solution in other vehicles". Therefore, the exaggerated toxic potency expressed in studies that used the emulsifying agent Cremophor EL indicates the resulting LD50 values are not appropriate for classification or labelling. Likewise, the relatively high LD50 values reported for cyfluthrin and beta-cyfluthrin administered in an aqueous or organic suspension may underestimate acute toxicity for classification or labelling.

Therefore, studies that employ corn oil or peanut oil as the vehicle to formulate a pyrethroid into a solution are best suited for reference. Based on guideline studies with cyfluthrin and beta-cyfluthrin in acetone/peanut oil, the LD50 values are 155 and 77 mg/kg bw, respectively.

According to the WHO Hazard Classification system as outlined in Table 2 below, the appropriate classification for both cyfluthrin and beta-cyfluthrin, based on acute oral LD50 values in the rat of 155 and 77 mg/kg bw, respectively, is :

WHO Classification II – Moderately hazardous

Table 2. WHO Hazard Classification for Pesticides

WHO Class		LD50 for the rat (mg/kg body weight)	
		Oral	Dermal
Ia	Extremely hazardous	< 5	< 50
Ib	Highly hazardous	5-50	50-200
II	Moderately	50-2000	200-2000
III	Slightly harardous	Over 2000	Over 2000
U	Unlikely to present acute hazard	5000 or higher	

CONCLUSIONS

The LD50 values that are used for classification and labelling should be derived from experimental conditions that most closely model anticipated conditions of human exposure. For cyfluthrin and beta-cyfluthrin, the acute LD50 values by oral route of exposure are 155 and 77 mg/kg bw, respectively.

According to the WHO Hazard Classification system as outlined, the appropriate classification for both cyfluthrin and beta-cyfluthrin, based on acute oral LD50 values in the rat of 155 and 77 mg/kg bw, respectively, is :

WHO Classification II – Moderately hazardous

REFERENCES

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