Appendix G – Multi-AI Products

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The Agency does not routinely include, in its risk assessments, an evaluation of mixtures of active ingredients, either those mixtures of multiple active ingredients in product formulations or those in the applicator's tank. In the case of the product formulations of active ingredients (that is, a registered product containing more than one active ingredient), each active ingredient is subject to an individual risk assessment for regulatory decision regarding the active ingredient on a particular use site. If effects data are available for a formulated product containing more than one active ingredient, they may be used qualitatively or quantitatively[1] [2].

Acute oral toxicity data (i.e., LD50 values) from mammalian studies for formulated products that contain prometon and one or more additional active ingredients are summarized below.

Currently, the Agency's guidance for assessing the potential risk of chemical mixtures is limited to human health applications (USEPA, 2000). However, the guidance includes principles for evaluating mixtures to assess potential interactive effects that are generally applicable. Consistent with EPA's Overview Document (USEPA 2004), the Agency's mixture guidance (USEPA 2000) discusses limitations in quantifying the risk of specified mixtures when there is differential degradation, transport and fate of chemical components following environmental release or application. The LD_{50} values are potentially useful only to the extent that a wild mammal would consume plants or animals immediately after these dietary items were directly sprayed by the product. Increasing time post application, the differential rates of degradation, transport, etc. for the active ingredients in the formulation only permit a qualitative discussion of potential acute risk (USEPA 2004).

As discussed in USEPA (2000) a quantitative component-based evaluation of mixture toxicity requires data of appropriate quality for each component of a mixture. In this mixture evaluation LD_{50}s, with associated 95% confidence intervals, are needed for the formulated product. The same quality of data is also required for each component of the mixture. Given that many of the formulated products do not have LD50 values of the required quality and since LD_{50} values are not available for all the components of these formulations a quantitative analysis of potential interactive effects is not possible.

[1] Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, Environmental Protection Agency (January 2004) (Overview Document).

[2] Memorandum to Office of Prevention, Pesticides and Toxic Substance, US EPA conveying an evaluation by the U.S. Fish and Wildlife Service and National Marine Fisheries Service of an approach to assessing the ecological risks of pesticide products (January 2004).

While a quantitative evaluation of the data is not possible with currently accepted scientific methods, as a screening tool, a qualitative analysis can be used to indicate if formulated products exhibit interactive effects (e.g., synergism or antagonism). In the case of prometon, a qualitative examination of the trends in LD50 values, with the associated confidence intervals, across the range of percent active ingredient, show no discernable trends in potency that would suggest synergistic (i.e., more than additive) or antagonistic (i.e., less than additive) interactions. In addition, when the product LD50s, and associated confidence intervals, are adjusted for the percent prometon (a conservative assumption that attributes all of the observed toxicity of the formulated product to prometon) in all cases where data are available the adjusted LD50 is below the LD50 used to evaluate the toxicity of prometon to mammals. Given the overall variability of the available acute toxicity data these differences are not considered biologically significant. Based on this qualitative evaluation of the best available data and the Agency's existing guidance it is reasonable to conclude that these formulations are reflecting an independent additive toxicity response and not an interactive effect. Given that the active and inert ingredients would not be expected to have similar mechanisms of action, metabolites or toxicokinetic behavior it is also reasonable to conclude that an assumption of dose-addition would be inappropriate. Consequently, an assessment of prometon's potential effect on the Barton Springs Salamander when it is co-formulated with other active ingredients can be based on the toxicity of prometon.

Pesticide Products Formulated with Prometon and Other Pesticide Active Ingredients

Prometon Products [3] [4]

PRODUCT/TRADE NAME	EPA Reg.No.	% Prometon	PRODUCT		ADJUSTED FOR ACTIVE INGREDIENT	
			LD50 (mg/kg)	CI (mg/kg)	LD50 (mg/kg)	CI (mg/kg)
Pratt NA Weed Killer	769-875	3.50%	No data		No data	
Pratt Triple X NA Weed Killer	769-898	10.50%	No data		No data	
Allpro Baracide 5PS	769-978	5.00%	3,396	3,063-3,766	170	153-188
Chemsico Herbicide Concentrate DP	9688-198	2.20%	>5,000	NA Limit dose	NA Limit dose	
Chemsico Herbicide RTU DP	9688-218	0.14%	>5,000	NA Limit dose	NA Limit dose	
Acme Vegetation Killer	33955-454	3.60%	2,280	1,921-2,706	82	69-97
Prometon 5PS	53883-97	5.00%	3,396	3,063-3,766	170	153-188
Pramitol 5PS	66222-23	5.00%	3,396	3,063-3,766	170	153-188
Pramitol 2L/Diuron 2L	66222-55	21.62%	6,168	Not determined	1,334	Not determined

[3] From registrant submitted data to support registration. Provided by Office of Pesticide Programs Health Effects Division.
[4] Prometon: LD50 (Female rats)= 1,518 mg/kg; CI= 1,107 to 2,080 mg/kg.