PRODUCT FORMULATIONS CONTAINING MULTIPLE ACTIVE INGREDIENTS

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].

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 LD50 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, LD50s 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.

In the case of pendimethalin, only three products (EPA Reg. Nos. 241-331, 241-376 and 5905-495) have definitive product LD50 values with associated confidence intervals. Although there are no 95% confidence intervals associated with the pendimethalin technical, an evaluation of the three products listed above show that for EPA Reg. Nos. 241-331 and 241-376, the product LD50 values can be attributed solely to the toxicity of pendimethalin. When these product LD50s (3506 and 2500 mg/kg, respectively) and associated confidence intervals (892-1223 and 504-800 mg/kg, respectively) are adjusted

[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).

for the percent pendimethalin (30.24% and 25.4%, respectively), the adjusted LD50 values for EPA Reg. No. 241-331 (1060 mg/kg, CI: 892-1223) and EPA Reg. No. 241-376 (635 mg/kg, CI: 504-800) are not toxicologically distinct from the LD50 of pendimethalin (1050 mg/kg). Similarly, for EPA Reg. No. 5905-495, the toxicity can be attributed to propanil. When the LD50 for this product (1110 mg/kg) and its confidence interval (913-1360 mg/kg) are adjusted for the percent propanil (33.7%), the adjusted LD50 value of 374 mg/kg (CI: 308-458 mg/kg) is within a factor of two of the confidence interval for propanil (1080 mg/kg; CI: 868-1343 mg/kg) and the difference is not considered to be toxicologically significant.

Because the active ingredients are not expected to have similar mechanisms of action, metabolites, or toxicokinetic behavior, it is reasonable to conclude that an assumption of dose-addition would be inappropriate. Consequently, an assessment based on the toxicity of pendimethalin is the only reasonable approach that employs the available data to address the potential acute risks of the formulated products.

Pesticide Products Formulated with Pendimethalin and Other Pesticide Active Ingredients

PENDIMETHALIN PRODUCTS [3] [4]

			PRODUCT		ADJUSTED FOR ACTIVE INGREDIENT	
PRODUCT/TRADE NAME	**EPA Reg.No.**	**% Pendimethalin**	**LD 50 (mg/kg)**	**CI (mg/kg)**	**LD50 (mg/kg)**	**CI (mg/kg)**
SQUADRON HERBICIDE	000241-00327	21.96	>5000	NA	NA	NA
PURSUIT PLUS EC HERBICIDE	000241-00331	30.24	3506	2949-4045	1060	892-1223
STEEL HERBICIDE	000241-00376	25.4	2500	1984-3150	635	504-800
ORNAMENTAL HERBICIDE II	000538-00172	1.0	>5000	NA	NA	NA
FERTILIZER WITH WEED CONTROL	000538-00251	0.25	>5000	NA	NA	NA
FERTILIZER PLUS PREEMERGENT WEED CONTROL II	000538-00257	1.25	>5000	NA	NA	NA
TURF BUILDER PRE/POST 2	000538-00299	0.81	No Data	No Data	NA	NA
SETRE PROWL HERBICIDE + PROPANIL	005905-00495	11.25	1110	913-1360	125	103-153
BAS 756 00 H HERBICIDE	007969-00254	33.0	>2000	NA	NA	NA

[3] From registrant submitted data to support registration. Compiled by Office of Pesticide Programs Registration and Health Effects Divisions.
[4] Pendimethalin LD50= males: 1250 mg/kg; females: 1050 mg/kg

			PRODUCT		ADJUSTED FOR ACTIVE INGREDIENT	
PRODUCT/TRADE NAME	**EPA Reg.No.**	**% Pendimethalin**	**LD 50 (mg/kg)**	**CI (mg/kg)**	**LD50 (mg/kg)**	**CI (mg/kg)**
FREEHAND 1.75G HERBICIDE	007969-00273	1.0	>2000	NA	NA	NA
ANDERSONS GOLF PRODUCTS KANSEL + FERTILIZER	009198-00230	0.62	>5000	NA	NA	NA
REVOKE PRE-EMERGENT HERBICIDE	058185-00034	1.25	No Data	No Data	NA	NA