APPENDIX A: 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 propanil, seven products have definitive LD50 values with associated confidence intervals. In the case of 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. Similarly, in the case of EPA Reg. Nos. 71085-09, 71085-16 and 71085-23, the product values can be attributed solely to the toxicity of propanil. When the LD50s and associated confidence intervals for these three products are adjusted for percent propanil (41.2, 80 and 60%, respectively), the adjusted LD50 and CI values

[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 products (EPA Reg. No. 71085-09: 1943 mg/kg, CI: 1126-3355 mg/kg; EPA Reg. No. 71085-16: 978 mg/kg, CI: 534-1792; and EPA Reg. No. 71085-23: 734 mg/kg, CI: 401-1344 mg/kg) fall within the confidence interval for propanil (868-1343 mg/kg). Likewise, the product LD50 values for EPA Reg. Nos. 71085-25, 71085-26 and 71085-29 can be attributed to the toxicity of propanil. The adjusted LD50 and CI values for these products are 463 mg/kg (CI: 391-567 mg/kg), 1345 mg/kg (CI: 753-2150 mg/kg) and 639 mg/kg (452-1624 mg/kg), respectively, and the values fall within the confidence interval for the propanil technical (868-1343 mg/kg).

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 propanil's potential effect on the CRLF when it is co-formulated with other active ingredients can based on the toxicity of propanil.

Pesticide Products Formulated with Propanil and Other Pesticide Active Ingredients

PROPANIL PRODUCTS [3, 4]

			PRODUCT		ADJUSTED FOR ACTIVE INGREDIENT	
PRODUCT/TRADE NAME	**EPA Reg.No.**	**% Propanil**	**LD 50 (mg/kg)**	**CI (mg/kg)**	**LD50 (mg/kg)**	**CI (mg/kg)**
SETRE PROWL HERBICIDE + PROPANIL	005905-00495	33.7	1110	913-1360	374	308-458
LONDAX PRO-PACK BNB	009779-00340	59.6	No Data	No Data	N/A	N/A
PRO-PACK 80EDF	009779-00343	79.2	No Data	No Data	N/A	N/A
DUET HERBICIDE	071085-00009	41.2	4717	2733-8143	1943	1126-3355
DUET DF RICE HERBICIDE	071085-00016	80	1223	668-2240	978	534-1792
DUET 60DF	071085-00023	60	1223	668-2240	734	401-1344
RICEMAX	071085-00025	41.7	1110	913-1360	463	381-567
RICEPRO	071085-00026	43	3129	1750-5000	1345	753-2150
RICEPYR	071085-00029	36.5	1750	1239-4450	639	452-1624

[3] From registrant submitted data to support registration. Compiled by Office of Pesticide Programs Registration and Health Effects Divisions.
[4] Propanil oral LD50= 1080 mg/kg
N/A= Not Applicable