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].

Acute oral toxicity data (i.e., LD50 values) from mammalian studies for formulated products that contain diuron 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 mixture 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, an LD50 with associated 95% CI is 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 LD50 values are not available for all the components of these formulations, a quantitative analysis of potential interactive effects is not possible.

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[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 diuron, 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.

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

Pesticide Products Formulated with Diuron and Other Pesticide Active Ingredients

DIURON PRODUCTS[3,4]

PRODUCT/TRADE NAME	EPA Reg.No.	% Diuron	PRODUCT		ADJUSTED FOR ACTIVE INGREDIENT	
			LD 50 (mg/kg)	CI (mg/kg)	LD50 (mg/kg)	CI (mg/kg)
RIVERDALE DIBRO 2+2	000228-00227	2	>5000	N/A	N/A	N/A
RIVERDALE DIBRO 4+2 GRANULAR WEED KILLER	000228-00386	4	>5000	N/A	N/A	N/A
TOPSITE 2.5G HERBICIDE	000241-00344	2	>5000	N/A	N/A	N/A
SAHARA DG HERBICIDE	000241-00372	62.22	>5000	N/A	N/A	N/A
GINSTAR EC COTTON DEFOLIANT	000264-00634	6	>5000	N/A	N/A	N/A
GINSTAR(R) 4.5 SC COTTON DEFOLIANT	000264-00821	15.1	>2000	N/A	N/A	N/A
DUPONT KROVAR I DF HERBICIDE	000352-00505	40	2300 >2000	N/A	N/A	N/A
DUPONT K-4 HERBICIDE	000352-00618	46.8	2073	N/A	970	N/A
DUPONT VELPAR ALFAMAX MP HERBICIDE[5]	000352-00634	42.4	6100 1300	5083-7082 No Data	2586 551	2155-3003 N/A
LAYBY 74 HERBICIDE[6]	000352-00660	20	1919 3407	1446-2614 2419-4798	384 681	289-523 484-960
DUPONT VELPAR K-4 MAX HERBICIDE[5]	000352-00663	61.5	6100 1300	5083-7082 No Data	3752 800	3126-4355 N/A
DUPONT VELPAR ALFAMAX HERBICIDE[5]	000352-00665	42.4	6100 1300	5083-7082 No Data	2586 551	2155-3003 N/A

[3] From registrant submitted data to support registration. Compiled by Office of Pesticide Programs Registration and Health Effects Divisions.
[4] Diuron: Acute Oral LD50= Males: 4721 (CI: 2995-7441) mg/kg ; Females: >5000 mg/kg
[5] Blend of products 1812-662 and 352-581. The acute toxicity profiles for both products were cited for registration.
[6] Review concluded that data from either 66222-54 or 1812-245 could be used for registration.

PRODUCT/TRADE NAME	EPA Reg.No.	% Diuron	PRODUCT		ADJUSTED FOR ACTIVE INGREDIENT	
			LD 50 (mg/kg)	CI (mg/kg)	LD50 (mg/kg)	CI (mg/kg)
DUPONT VELPAR ALFAMAX GOLD[5]	000352-00666	55.4	6100 1300	5083-7082 No Data	3379 720	2816-3923 N/A
DUPONT KROVAR MUP	000352-00752	48.1	3248	No Data	1562	N/A
ROCIMA 63 INDUSTRIAL MICROBICIDE	000707-00303	20	>5000	N/A	N/A	N/A
POLYPHASE 663	005383-00109	15	>5000	N/A	N/A	N/A
MISTY 2 PLUS 2	010807-00149	2	>5000	N/A	N/A	N/A
RAINBOW WEED KILLER	013283-00009	2	3989	3281-4899	80	66-98
RAINBOW WEED KILLER 4037	013283-00018	6	No Data	N/A	N/A	N/A
RAINBOW WEED KILLER 4031	013283-00019	2	>5000	N/A	N/A	N/A
RAINBOW WEED KILLER 4049	013283-00021	3	>5050	N/A	N/A	N/A
DIUMATE	019713-00528	5.18	>2000	N/A	N/A	N/A
POND [FOUNTAIN] BLOCK	033034-00001	0.51	>5050	N/A	N/A	N/A
NO MORE ALGAE	033034-00002	0.67	>5050	N/A	N/A	N/A
NO MORE ALGAE LIQUID	033034-00003	0.67	>5050	N/A	N/A	N/A
BAREGROUND 21	033560-00043	2	3117	N/A	62	N/A
WEED AND GRASS KILLER	033560-00046	1.25	>4000 >5000	N/A	N/A	N/A
WEED BLAST RESIDUAL WEED CONTROL	034704-00576	4	No Data	N/A	N/A	N/A
GINMASTER COTTON DEFOLIANT	034704-00872	6	>5000	N/A	N/A	N/A
SPRAKIL SK-13 GRANULAR WEED KILLER	034913-00015	3	>5050	N/A	N/A	N/A
SPRAKIL SK-26 GRANULAR WEED KILLER	034913-00016	6	>5050	N/A	N/A	N/A
WEED BLAST 4-G WEED KILLER	034913-00019	2	3898	3281-4899	78	66-98
WEED BLAST 8-G WEED KILLER	034913-00020	4	No Data	N/A	N/A	N/A
SSI MAXIM TOPSITE 2.5G HERBICIDE	034913-00022	2	>5000	N/A	N/A	N/A
PRAMITOL 2L/DIURON 2L	066222-00055	21.62	6168	N/A	1333	N/A
REDI-PIK 1.5EC COTTON DEFOLIANT	066222-00137	6	No Data	N/A	N/A	N/A

PRODUCT/TRADE NAME	EPA Reg.No.	% Diuron	PRODUCT		ADJUSTED FOR ACTIVE INGREDIENT	
			LD 50 (mg/kg)	CI (mg/kg)	LD50 (mg/kg)	CI (mg/kg)
MOHAVE 70 EG BAREGROUND VEGETATION CONTROL	066222-00171	62.22	>2000	N/A	N/A	N/A
SWEEP	066222-00173	40	No Data	N/A	N/A	N/A
THIDIAZURON-DIURON EC	066330-00333	6	No Data	N/A	N/A	N/A
THIDIAZURON-DIURON SC	066330-00344	6	4138	1788-20000	248	107-1200
THIDIAZURON-DIURON 4.55C	066330-00364	18.04	No Data	N/A	N/A	N/A
ACTICIDE PM	067071-00002	19	>5000	N/A	N/A	N/A
ACTICIDE PM FLOWABLE	067071-00015	19	>5000	N/A	N/A	N/A
ACTICIDE SR-1216/6	067071-00017	19	>1310 & <2000	N/A	N/A	N/A
THOR GMBH ACTICIDE PAX	067071-00039	19	>1310 & <2000	N/A	N/A	N/A
ACTICIDE MKW1	067071-00053	15	No Data	N/A	N/A	N/A
BROMO-D HERBICIDE	070506-00084	40	>2000	N/A	N/A	N/A
IMAZURON E-PRO HERBICIDE	079676-00054	62.22	>5000	N/A	N/A	N/A
ETI 105 01 G	079676-00078	6	>5000	N/A	N/A	N/A
BROMACIL/DURON 40/40	081927-00003	40	No Data	N/A	N/A	N/A
ALLIGARE MOJAVE 70 EG BAREGROUND VEGETATION CONTROL	081927-00025	62.22	No Data	N/A	N/A	N/A