Appendix A. Pesticide Products Formulated [1] with Bromacil and Other Pesticide 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[2], [3].

Acute toxicity data from fish and mammalian studies for formulated products that contain bromacil and one or more additional active ingredients are summarized in **Tables A1-A3**. Also included in these tables are toxicity data for the TGAI of bromacil, for comparison purposes.

Table A.1. Acute effects of bromacil formulations on rainbow trout.

Percent Bromacil	Other Active Ingredients	96-h LC_{50} for formulation (mg/L)	96-h LC_{50} based on bromacil (mg a.i./L)	Reference (MRID)
96.6	None (test substance was TGAI)	36	36	40951503
1.5	Sodium metaborate tetra hydrahydrate (66.5%); sodium chlorate (30.0%)	>180	>12,000	00024967
1.5	Sodium metaborate tetra hydrahydrate (66.5%); sodium chlorate (30.0%)	>180	>12,000	00024964

[1] From registrant submitted data to support registration. Compiled by Office of Pesticide Programs Health Effects Division.
[2] Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, Environmental Protection Agency (January 2004) (Overview Document).
[3] 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).

Table A.2. Acute effects of bromacil formulations on bluegill sunfish.

Percent Bromacil	Other Active Ingredients	96-h LC_{50} for formulation (mg/L)	96-h LC_{50} based on bromacil (mg a.i./L)	Reference (MRID)
95	None (test substance was TGAI)	127	127	40951502
80	NA	>100*	>80*	00024960
2.3	Mixed aromatic solvents (86.4); pentachlorophenol (2.84%); other chlorophenols (0.33%)	2.6	113	00024962
0.98	Aromatic petroleum distillate (94.94%); 2,4-dichlorophenoxyacetic acid, isooctyl ester (1.09%); pentachlorophenol (0.80%); other chlorophenols (0.09%)	3.95	395	00024961
0.61	Aliphatic hydrocarbons (96.1%); 2,4-dichlorophenoxyacetic acid isooctyl ester (1.09%); pentachlorophenol (0.8%); other chlorophenols (0.09%)	3.2	525	00024968
1.5	Sodium metaborate tetra hydrahydrate (66.5%); sodium chlorate (30.0%)	>100	>6,670	00024965
1.5%	Sodium metaborate tetra hydrahydrate (66.5%); sodium chlorate (30.0%)	>180	>12,000	00024969

*Based on 72-h exposure; NA = not available

Table A.3. Acute effects of bromacil formulations on mammals.

PRODUCT/TRADE NAME	EPA Reg.No.	% Bromacil	PRODUCT		ADJUSTED FOR ACTIVE INGREDIENT	
			LD_{50} (mg/kg)	CI (mg/kg)	LD_{50} (mg/kg)	CI (mg/kg)
Bromacil technical	NA	100%	812 (females) 1682 (males)	NA	812 (females) 1682 (males)	NA
Riverdale DiBro 2+2	228-227	2	>2000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Riverdale DiBro 4+2 Granular Weed Killer	228-386	2	No Data	No Data	No Data	No Data
DuPont Krovar I DF Herbicide	352-505	40	>2000	NA Limit Dose	NA Limit Dose	NA Limit Dose
NO. 1117 Hilco-X Weed Killer	402-98	0.61	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Double Kill	3862-92	0.98	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Knock-Out Non-Selective Weed Killer	3862-143	0.98	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Non-Selective Herbicide #1	10088-2	0.61	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Non-Selective Herbicide #2	10088-68	0.98	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Non-Selective Herbicide Aerosol	10088-114	0.98	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
2 Plus 2	10807-149	2	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Misty Repco Kill IV	10807-200	0.98	No Data	No Data	No Data	No Data
Misty Repco Kill VF	10807-201	0.61	No Data	No Data	No Data	No Data
Misty Repco Kill LF	10807-204	0.61	No Data	No Data	No Data	No Data
Misty Repco Kill III	10807-205	0.98	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Rainbow Professional Weed Killer	13283-09	2	No Data[4]	No Data[5]	No Data	No Data
Chapman Weed Free BCB-4P	19713-202	4	No Data	No Data	No Data	No Data
Bareground 21	33560-43	2	No Data	No Data	No Data	No Data
Ureabor	33560-47	1.5	3760	3390-4130	56	51-62

[4] The LD50 and confidence interval for bromacil was used for product registration, no product LD50 values available.

PRODUCT/TRADE NAME	EPA Reg.No.	% Bromacil	PRODUCT		ADJUSTED FOR ACTIVE INGREDIENT	
			LD $_{50}$ (mg/kg)	CI (mg/kg)	LD_{50} (mg/kg)	CI (mg/kg)
Weed Blast Residual Weed Control	34704-576	4	No Data[5]	No Data[5]	No Data	No Data
Weed Blast-4-G Weed Killer	34913-19	2	No Data[5]	No Data[5]	No Data	No Data
Weed Blast 8-G Weed Killer	34913-20	4	No Data[5]	No Data[5]	No Data	No Data
Bromo-D HERBICIDE	70506-84	40	>2000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Bromacil/Diuron 40/40	81927-3	40	No Data	No Data	No Data	No Data

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 mammalian 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.
In the case of bromacil, only one product (EPA Reg. No. 33560-47) has a definitive product LD_{50} value with associated confidence interval. However, there is no LD_{50} value with associated confidence interval available for one of the product components (sodium metaborate) and therefore it is not possible to undertake a quantitative or qualitative analysis for potential interactive effects

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 bromacil is the only reasonable approach that employs the available data to address the potential acute risks of the formulated products.