Appendix A: Product Formulations Containing Multiple Active Ingredients for Mancozeb and Maneb

(1) Mancozeb

Mancozeb has twenty registered products that contain multiple active ingredients (Tables 1).

Table 1 Mancozeb products with multiple actives

Registration Number	*Product Name*	*Mancozeb %*	*Other Chemicals*	
			Chemical Name	*%*
00010000803	RIDOMIL GOLD MZ	64	Mefenoxam + Metalaxyl-M (see mefenoxam)	4+4
00010000944	MAXIM (R) MZ POTATO SEED PROTECTANT	9.6	Fludioxonil	0.5
00010001158	MAXIM MZ	5.7	Fludioxonil	0.5
00010001269	RIDOMIL GOLD MZ WG	64	Mefenoxam + Metalaxyl-M (see mefenoxam)	4+4
00024100383	ACROBAT MZ FUNGICIDE	60	Dimethomorph	9
00024100395	ACROBAT MZ WDG FUNGICIDE	60	Dimethomorph	9
00024100411	STATURE MZ FUNGICIDE	60	Dimethomorph	9
00026400958	TOPS MZ POTATO SEED-PIECE TREATMENT FUNGICIDE	6	Thiophanate-methyl	2.5
00026400972	MZ-CURZATE POTATO SEED-PIECE TREATMENT	6	Cymoxanil	1
00026400973	EVOLVE POTATO SEED PIECE TREATMENT FUNGICIDE	6	Cymoxanil	1
00026400977	TOPS-MZ-GAUCHO POTATO SEED-PIECE TREATMENT	6	Imidacloprid + Thiophanate-methyl	1.25+2.5
00026400978	GAUCHO-MZ POTATO SEED-PIECE TREATMENT	6	Imidacloprid + Thiophanate-methyl	1.25+2.5
00035200690	DUPONT MANKOCIDE FUNGICIDE	15	Copper hydroxide	46.1
00346800059	POTATO SEED TREATER A-STREP	8	Streptomycin sesquisulfate	0.02
00458100397	CUPROFIX MZ DISPERSS	30.4	Basic cupric sulfate	22.1
05818500031	DUOSAN WSB WETTABLE POWDER TURF AND ORNAMENTAL FUNGICIDE	64	Thiophanate-methyl	15.6
05818500032	DUOSAN BROAD SPECTRUM CONTACT TURF FUNGICIDE	64	Thiophanate-methyl	15.6
06271900418	RH-0611	60	Myclobutanil	2.25
06271900441	GAVEL 75 DF AGRICULTURAL FUNGICIDE	66.7	Zoxamide	8.3
07171100008	MONCOAT MZ	6	Flutolanil	1.5

The products LD_{50} before and after adjustments for the active ingredient are included in Table 2.

Table 2 LD_{50} for mancozeb formulated with other pesticide products [1] [2]

	PRODUCT		*ADJUSTED FOR ACTIVE INGREDIENT*	
PRODUCT/TRADE NAME	***LD 50 (mg/kg)***	***CI (mg/kg)***	***A.I Adjusted CI (mg/kg)***	***A.I Adjusted LD50 (mg/kg)***
Ridomil Gold MZ	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Maxim (R) MZ Potato Seed Protectant	>5050	NA Limit Dose	NA Limit Dose	NA Limit Dose
Maxim MZ	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Ridomil Gold MZ WG	No Data	No Data	No Data	No Data
Acrobat MZ Fungicide	2770	2273-3375	1662	1364-2025
Acrobat MZ WDG Fungicide	2770	2273-3375	1662	1364-2025
Stature MZ Fungicide	No Data	No Data	No Data	No Data
Tops MZ Potato Seed-Piece Treatment Fungicide	>5050	NA Limit Dose	NA Limit Dose	NA Limit Dose
MZ-Curzate Potato Seed-Piece Treatment	No Data	No Data	No Data	No Data
Evolve Potato Seed Piece Treatment Fungicide	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Tops-MZ-Gaucho Potato Seed-Piece Treatment	No Data	No Data	No Data	No Data
Gaucho-MZ Potato Seed-Piece Treatment	No Data	No Data	No Data	No Data
DuPont Mankocide Fungicide	No Data	No Data	No Data	No Data
Potato Seed Treater A-Strep	No Data	No Data	No Data	No Data
Cuprofix MZ Disperss	>2000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Duosan WSB Wettable Powder Turf and Ornamental Fungicide	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose
Duosan Broad Spectrum Contact Turf Fungicide	No Data	No Data	No Data	No Data
RH-0611	No Data	No Data	No Data	No Data
Gavel 75 DF Agricultural Fungicide	No Data	No Data	No Data	No Data
Moncoat MZ	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose

[1] From registrant submitted data to support registration; Compiled by Office of Pesticide Programs Health Effects Division.
[2] Mancozeb LD50: >5000 mg/kg; CI= N/A

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[3] [4].

Acute oral toxicity data (i.e., LD50 values) from mammalian studies for formulated products that contain mancozeb 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 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. 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. Of the 20 formulated products containing mancozeb, only two products (EPA Reg. No. 241-383 and 241-395) have definitive LD50 values and associated confidence intervals. Since there are no confidence intervals associated with mancozeb, it is not possible to undertake a quantitative or qualitative analysis for potential interactive effects. However, 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 mancozeb is the only reasonable approach that employs the available data to address the potential acute risks of the formulated products.

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

[4] 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).

(2) Maneb

Maneb has two registered products that contain multiple active ingredients (Tables 3).

Table 3 Maneb products with multiple actives

Registration Number	*Product Name*	*Maneb %*	*Other Chemicals*	
			Chemical Name	*%*
00055400140	DB-GREEN L	25.6	Lindane	8.6
00055400141	AGSCO DUSTRET "A"	8	Streptomycin sesquisulfate	0.01

The products LD_{50} are included in Table 2.

Table 4 LD_{50} for maneb formulated with other pesticide products [5] [6]

Product	*LD 50 (mg/kg)*	*CI (mg/kg)*	*LD50 (mg/kg)*	*CI (mg/kg)*
DB-GREEN L	ND	ND	ND	ND
AGSCO DUSTRET "A"	>5000	NA Limit Dose	NA Limit Dose	NA Limit Dose

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[7] [8].

There are no product LD50 values, with associated 95% Confidence Intervals (CIs) available for maneb.

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 the formulated products for maneb do not have LD50 data available it is not possible to undertake a quantitative or qualitative analysis for potential interactive effects. However, because the active ingredients are not expected to have similar mechanisms of action, metabolites, or toxicokinetic behavior, it is reasonable to conclude

[5] From registrant submitted data to support registration. Compiled by Office of Pesticide Programs Health Effects Division.

[6] Maneb: Male LD50: >500 mg/kg
Female LD50: >5000 mg/kg

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

[8] 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).

that an assumption of dose-addition would be inappropriate. Consequently, an assessment based on the toxicity of maneb is the only reasonable approach that employs the available data to address the potential acute risks of the formulated products.