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MEMORANDUM

SUBJECT: **DISULFOTON:** Aggregate Risk Assessment (Revised)
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The Agency, as part of the disulfoton interim reregistration eligibility decision, is required by the Food Quality Protection Act to ensure "that there is reasonable certainty that no harm will result from *aggregate* exposure to pesticide chemical residue, including all anticipated dietary exposures and other exposures for which there is reliable information."

The following aggregate risk assessment integrates the assessments that HED has completed for disulfoton dietary and residential exposure, and has used the combined exposure estimates to evaluate the estimates of drinking water contamination modeled by the Environmental Fate and Effects Division (EFED). All routes of disulfoton exposure have been considered including oral (food and water consumption), dermal (applying granules to ornamental plants), and inhalation (also during application to ornamental plants). The possibility of children ingesting treated soil around ornamental plants has also been considered in this assessment. This aggregate risk assessment also considers the probable duration(s) of exposure to disulfoton and how these intervals of exposure may coincide. The intervals of exposure considered in the disulfoton aggregate risk assessment are acute (one-day), short-term (one-day to one-month), and chronic (one-year or more).

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Aggregate risk, and related drinking water levels of comparison (DWLOC) estimates have been made in accord with the HED interim guidance (*Updated "Interim Guidance for Incorporating Drinking Water Exposure into Aggregate Risk Assessments,"* 8/1/99).

Basis for Revision

The aggregate risk assessment section of the February 7, 2000 HED risk assessment chapter (D. Anderson memo, 02/07/00) did not include exposure from residential sources, as exposure from the residential pathway alone exceeded the Agency's level of concern. Since that time, HED has revised the residential risk estimates for disulfoton, based on new toxicity and exposure data, label changes, and revisions to the Residential Standard Operating Procedures. New toxicity and exposure data were submitted by the registrant to support the currently marketed residential product (Bayer Advanced Garden 2-in-1 Systemic Rose and Flower Care®). However, since other products marketed by registrants other than Bayer are currently available, this aggregate risk assessment will consider these products as well as the Bayer 1% a.i. product.

Dietary risk estimates and water contamination estimates for disulfoton have not been revised for this aggregate assessment.

Recent Data Submitted by Bayer

Toxicity Data: Based on the results of the newly submitted 3-day dermal toxicity study in rats (MRID 45239602), the HED Hazard Identification Assessment Review Committee (HIARC) amended the dose level used to estimate risk for short-term residential dermal exposure. The dose level for short-term dermal risk estimates has been revised from 0.4 mg/kg/day to 0.5 mg/kg/day (NOAEL) based on plasma and brain cholinesterase inhibition observed in female rats at 1.0 mg/kg/day (LOAEL). The Agency requires a margin of exposure (MOE) of 100 for short-term risk based on an uncertainty factor of 100 (10x for interspecies extrapolation and 10x for intraspecies variability). Following an evaluation of the disulfoton toxicity database, the FQPA Safety Factor Committee concluded (1/24/00) that the additional safety factor of 10x required by the FQPA should be reduced to 1x.

Exposure Data: The registrant also submitted a dermal and inhalation exposure study (MRID 45333401) for the residential application of Bayer Advanced Garden 2-in-1 Systemic Rose and Flower Care®. The Agency has found this study to be acceptable (on an *interim* basis pending clarification of several issues by the registrant), and has used the results of the study to estimate possible exposure during application. Note that aggregate risk estimates are based on residential dermal exposure *only,* since data indicate that inhalation exposure is negligible (all samples were either non-detectable or less than the level of quantitation).

Exposure/Risk Estimates for Food Uses

Disulfoton is currently used on a variety of food crops including asparagus, barley, soybeans, wheat, sorghum, potatoes, cotton, cabbage, lettuce, cole crops, beans, peppers, and peas. The greatest use, estimated by the Agency in lbs a.i. applied from 1987-98, is on cotton, wheat, potatoes, and peanuts. Dietary risk estimates for disulfoton are based on residue/usage estimates for the above crops and on the following dose levels:

aPAD: The disulfoton acute population adjusted dose (aPAD) is 0.0025 mg/kg based on a NOAEL of 0.25 mg/kg and an uncertainty factor of 100 (10x for interspecies extrapolation and 10x for intraspecies variability). No additional FQPA safety factor is required, based on a 1/24/00 decision by the FQPA Safety Factor Committee. Toxicological endpoints are signs of neurotoxicity, and plasma/erythrocyte cholinesterase inhibition in female rats.

cPAD: The disulfoton chronic population adjusted dose (cPAD) is 0.00013 mg/kg/day based on a NOAEL of 0.013 mg/kg/day and an uncertainty factor of 100 (10x for interspecies extrapolation and 10x for intraspecies variability). No additional FQPA safety factor is required, based on a 1/24/00 decision by the FQPA Safety Factor Committee. Toxicological endpoints are depressed plasma, erythrocyte and corneal cholinesterase levels in both sexes and depressed brain and retinal cholinesterase levels in females.

Dietary risk estimates were completed February 7, 2000 (W.O. Smith memo to D. Anderson) and have not been revised since that time. The dietary risk assessment used all available information including usage data (percent crop treated), PDP and FDA monitoring data, and processing data submitted by the registrant. The 2/7/2000 dietary risk assessment is considered a refined (tier 3) assessment that cannot be amended to any significant degree (unless new data is submitted).

In the acute (one-day) dietary exposure analysis the highest exposure estimate for any population subgroup is 0.000239 mg/kg (children 1-6 years old) and is taken from the 99.9th percentile of exposure since the assessment used a probabilistic (Monte Carlo) approach. The exposure estimate for children (1-6) is 10% of the disulfoton aPAD, or if expressed as a margin of exposure; MOE =1,044. The general U.S. population is estimated to be exposed at the level of 0.000176 mg/kg (7% of the aPAD).

In the chronic (one-year to lifetime) dietary exposure analysis the highest exposure estimate for any population subgroup is 0.000005 mg/kg/day (children 1-6 years old). The exposure estimate for children (1-6) is 4% of the disulfoton cPAD, or if expressed as a margin of exposure; MOE = 2,600. The general U.S. population is estimated to be exposed at the level of 0.000003 mg/kg/day (2% of the cPAD).

Exposure/Risk Estimates for Residential Use

Residential exposure scenarios (notably application by a belly grinder) with MOE values of less than 100 are not considered in the aggregate risk assessment. This also includes the use of disulfoton spikes that cannot be assessed for potential exposure due to a lack of data.

The disulfoton *short-term* aggregate risk assessment refers to three exposure scenarios from the 5/30/01 residential risk assessment: 1) an adult applying a granular product at the rate of 0.069 lb a.i./1,000 ft^2 to vegetables, 2) an adult applying Bayer Advanced Garden 2-in-1 Systemic Rose and Flower Care® to 25 shrubs at the label rate of 0.01 lb a.i./4 ft shrub, and 3) a small child (toddler) ingesting soil treated with disulfoton. Residential exposure scenarios are expected to occur within the short-term (1-30 day) interval.

The dermal exposure estimate for application to vegetables is 0.0034 mg/kg/day (MOE = 150) and represents the upper-end of exposure scenarios other than those with estimated MOEs of less than 100. The dermal exposure estimate for applying Bayer Advanced Garden 2-in-1 Systemic Rose and Flower Care® to 25 shrubs at 0.01 lb a.i./4 ft. shrub is 0.00033 mg/kg/day (MOE = 1,500).

The incidental oral exposure estimate for soil ingestion by a child following treatment is 0.00013 mg/kg/day (MOE = 230), based on the maximum application rate of 0.3 lb ai/1000 ft^2 to flowerbeds, and represents the upper-end of exposure scenarios other than those with estimated MOEs of less than 100. The incidental oral exposure estimate for soil ingestion by a child, based on the application of Bayer Advanced Garden 2-in-1 Systemic Rose and Flower Care® to flowerbeds at the maximum rate of 0.21 lb ai/1000 ft^2, is 0.0000917 mg/kg/day (MOE = 330).

Drinking Water Contamination Information

Data indicate that both parent disulfoton and its degradates may be found in groundwater and surface water. However, the Agency does not consider the available groundwater and surface water monitoring data for disulfoton adequate for the purposes of risk assessment. Instead, estimates of the potential contamination of groundwater and surface water by disulfoton are based on current Agency models, and are generally considered a screening tool rather than a predictor of residues in finished drinking water.

Groundwater estimated environmental concentrations (EECs) for disulfoton and its degradates were calculated using the Agency's SCI-GROW screening model. Using a scenario where disulfoton was applied to potatoes twice per season at the rate of 4 lb a.i./A, the maximum concentration of total residues was estimated to be 3.2 ug/L (this represents the high-end estimate for disulfoton agricultural use).

For surface water, the Agency has used a Tier II (PRZM-EXAMS) model with *index reservoir* and *percent cropped area* (PCA) factors to estimate levels of disulfoton and

sulfoxide/sulfone degradates in surface water at vulnerable (high run-off) sites. Surface water modeling scenarios chosen for disulfoton are representative of high run-off sites and are based on the highest use rates proposed by the registrant. The sites chosen are expected to represent the upper 10th percentile for run-off potential.

For this aggregate assessment, HED refers to the peak and annual average surface water run-off EEC estimates modeled by EFED for potatoes, spring wheat, and cotton. Peak (acute) EECs range from 5.3 ug/L in potatoes to 12.6 ug/L in cotton, and annual average (chronic) EECs range from 1.9 ug/L in cotton to 4.8 ug/L in potatoes. It should be noted that the disulfoton Quantitative Usage Analysis (S. Nako memo, 5/5/99) estimates that the major use of disulfoton is on cotton (with a weighted average of 420,000 lbs a.i./ year and an estimated maximum of 840,000 lbs a.i./year). Potatoes are also a major use of disulfoton (with a weighted average of 120,000 lbs a.i./ year and an estimated maximum of 195,000 lbs a.i./year).

Drinking Water Levels of Comparison

HED uses Drinking Water Levels of Comparison (DWLOC) values as surrogate measures of exposure. As part of aggregate risk assessment, HED compares the calculated DWLOC to the EEC(s) estimated for surface water and groundwater. If the DWLOC is greater than the estimated surface and groundwater concentration (i.e., if the DWLOC > EEC) a determination of safety can be made by the Agency for aggregate exposure to a particular pesticide. If the DWLOC values are not greater than the EEC values, the Agency may require additional data concerning water contamination.

The following equations were used to calculate the acute, chronic, and short-term DWLOC values required for disulfoton aggregate risk assessment:

Acute:

$$DWLOC_{acute}\ (\mu g/L) = \frac{[\text{allowable acute water exposure (mg/kg/day) x (kg body weight)}]}{[\text{consumption (L/day) x } 10^{-3}\ \text{mg/}\mu g]}$$

where "allowable" acute water exposure (mg/kg/day) = [aPAD - acute food (mg/kg/day)].

Chronic:

$$DWLOC_{chronic}\ (\mu g/L) = \frac{[\text{allowable chronic water exposure (mg/kg/day) x (kg body weight)}]}{[\text{consumption (L/day) x } 10^{-3}\ \text{mg/}\mu g]}$$

where allowable chronic water exposure (mg/kg/day) = [cPAD - (chronic food exposure (mg/kg/day) + chronic non-occupational exposure (mg/kg/day))].

Short-term:

A short-term DWLOC for residential applicators and a short-term DWLOC for soil ingestion were calculated using the reciprocal MOE approach. This approach was selected as the required MOEs are identical for all MOEs in the equation (i.e., MOE = 100).

$$\text{Aggregate MOE} = \frac{1}{\frac{1}{MOE_{FOOD}} + \frac{1}{MOE_{WATER}} + \frac{1}{MOE_{ORAL}} + \frac{1}{MOE_{DERMAL}} + \frac{1}{MOE_{INHALATION}}}$$

Where the aggregate MOE is equal to the required MOE of 100; the MOE_{FOOD} is based on the dietary exposure from average food residues (chronic dietary exposure) compared to the acute dietary NOAEL of 0.25 mg/kg/day; the MOE_{ORAL} is based on the calculated hand-to-mouth residential exposure compared to the intermediate-term oral NOAEL of 0.03 mg/kg/day (based on a special six-month oral study in the rat), the MOE_{DERMAL} is based on the calculated high-end dermal residential exposures compared to the short-term dermal NOAEL of 0.5 mg/kg/day; and the MOE_{WATER} is based on allowable short-term water exposure from average drinking residues compared to the acute dietary NOAEL of 0.25 mg/kg/day. The $MOE_{INHALATION}$ is not included in this calculation as exposure *via* the inhalation route of exposure is considered negligible (i.e., all residue was non-detectable, or below the level of quantitation).

After solving for the term MOE_{WATER}, allowable short-term water exposure can be calculated as follows, where the acute dietary NOAEL is 0.25 mg/kg/day.

$$MOE_{WATER} = \frac{\text{Short-term oral or acute dietary NOAEL}}{\text{Allowable Short-Term Water Exposure}}$$

Using the allowable short-term water exposure value, short-term DWLOC values are calculated as follows:

$$DWLOC_{short\text{-}term}\ (\mu g/L) = \frac{[\text{allowable short-term water exposure (mg/kg/day) x (kg body weight)}]}{[\text{consumption (L/day) x } 10^{-3}\ \text{mg/}\mu g]}$$

Acute Aggregate Risk

The acute aggregate risk assessment for disulfoton addresses exposure from food and drinking water *only*. Acute dietary risk estimates are well below the Agency's level of concern (≤100% of the aPAD) for the general U.S. population and all population subgroups. An acute DWLOC was calculated for disulfoton based on acute dietary food exposure and default body weight and water consumption figures.

As shown in Table 1 below, the disulfoton peak EEC for surface water (cotton) and the

EEC for ground water (potatoes) are below the Agency's estimated acute DWLOC for the U.S population and population subgroups.

Table 1: Acute Drinking Water Levels of Comparison

Acute Surface and Groundwater						
Population Subgroup[1]	**PRZM/EXAMS (µg/L)**	**SCI-GROW (µg/L)**	**aPAD (mg/kg/d)**	**Acute Food Exposure (mg/kg/d)**	**Allowable Acute Water Exposure (mg/kg/d)**	**$DWLOC_{acute}$ (µg/L)**
U.S. Population	12.6	3.2	0.0025	0.000176	0.00232	81
Children (1-6 years old)	12.6	3.2	0.0025	0.000239	0.00226	23
Females (13-50 years old)	12.6	3.2	0.0025	0.000084	0.00242	72
Seniors (55+ years old)	12.6	3.2	0.0025	0.000184	0.00232	81

[1]Population subgroups chosen were U.S. population (70 kg. body weight assumed, 2 liters water/day), the infant/child subgroup with the highest food exposure (10 kg. body weight assumed, 1 liter water/day), the female subgroup with the highest food exposure (60 kg. body weight assumed, 2 liters water/day), and the seniors 55+ subgroup (70 kg body weight assumed, 2 liters water/day) which has a higher dietary exposure than the U.S. population.

Chronic Aggregate Risk

The chronic aggregate risk for disulfoton addresses exposure from food and drinking water *only*. Chronic residential exposures to disulfoton are not expected and therefore are not included in this aggregate assessment. Chronic dietary risk estimates are below the Agency's level of concern (≤100% of the cPAD) for the general U.S. population and all population subgroups. A chronic DWLOC was calculated for disulfoton based on chronic dietary food exposure and default body weight and water consumption figures.

As shown in Table 2 below, the disulfoton annual average EEC for surface water run-off from potato usage is higher than the DWLOC calculated for the general U.S., females and children. The disulfoton annual average EEC for surface water run-off from cotton usage is higher than the DWLOC calculated for children, but less than the DWLOC calculated for the general U.S. or adult females.

Table 2: Chronic Drinking Water Levels of Comparison

Chronic Surface and Groundwater						
Population Subgroup[1]	**PRZM/EXAMS (µg/L)**	**SCI-GROW (µg/L)**	**cPAD (mg/kg/d)**	**Chronic Food Exposure (mg/kg/d)**	**Allowable Chronic Water Exposure (mg/kg/d)**	**$DWLOC_{chronic}$ (µg/L)**
U.S. Population	1.9 - 4.8	3.2	0.00013	0.000003	0.000127	4.5
Children (1-6 years old)	1.9 - 4.8	3.2	0.00013	0.000005	0.000125	1.3
Females (13-50 years old)	1.9 - 4.8	3.2	0.00013	0.000003	0.000127	3.8

[1]Population subgroups chosen were U.S. population (70 kg. body weight assumed, 2 liters water/day), the infant/child subgroup with the highest food exposure (10 kg. body weight assumed, 1 liter water/day), and the female subgroup with the highest food exposure (60 kg. body weight assumed, 2 liters water/day).

Short-term Aggregate Risk

The short-term aggregate risk for disulfoton addresses exposure from food uses, residential use, and drinking water contamination. Residential use is assessed for dermal exposure to adult handlers and oral exposure to children through incidental soil ingestion. Inhalation exposure is not part of the short-term aggregate assessment as data indicate negligible exposure. Short-term DWLOC estimates are calculated for disulfoton based on chronic dietary (food) exposure estimates and default body weight and water consumption values.

Short-term DWLOC estimates are presented in Tables 3A and 3B below. Table 3A presents the DWLOC estimates based on short-term dermal and incidental oral exposure to the non-Bayer supported homeowner products. Table 3B presents the DWLOC estimates based on short-term dermal and incidental oral exposure to the Bayer Advanced Garden 2-in-1 Systemic Rose and Flower Care®.

Table 3a: Short-term Drinking Water Levels of Comparison for the Non-Bayer Supported Products

Population Subgroup[1]	PRZM/ EXAMS (µg/L)	SCI-GROW (µg/L)	High-end Dermal Exposure[2] (mg/kg/d)	High-end Inhalation Exposure (mg/kg/d)	Hand-to-mouth Oral Exposure (mg/kg/d)[3]	Chronic Food Exposure (mg/kg/d)	Allowable Short-Term Water Exposure (mg/kg/d)	$DWLOC_{short-term}$ (µg/L)
U.S. Population	1.9 - 4.8	3.2	0.0034	negligible	n/a	0.000003	0.000797	28
Children (1-6 years old)	1.9 - 4.8	3.2	n/a	negligible	0.00013	0.000005	0.00141	14
Females (13-50 years old)	1.9 - 4.8	3.2	0.0034	negligible	n/a	0.000003	0.000797	24

[1]Population subgroups chosen were U.S. population (70 kg. body weight assumed, 2 liters water/day), the infant/child subgroup with the highest food exposure (10 kg. body weight assumed, 1 liter water/day), and the female subgroup with the highest food exposure (60 kg. body weight assumed, 2 liters water/day).
[2]High-end dermal exposure value of 0.0034 mg/kg/d is based on the "loading/applying granulars using a spoon, measuring scoop, shaker can, or by hand" to vegetable gardens scenario.
[3]Hand-to-mouth oral exposure value of 0.00013 mg/kg/d is based on incidental soil ingestion for flowerbeds.

Table 3b: Short-term Drinking Water Levels of Comparison for the Bayer-Supported 1% Granular Formulation

Population Subgroup[1]	PRZM/ EXAMS (µg/L)	SCI-GROW (µg/L)	High-end Dermal Exposure[2] (mg/kg/d)	High-end Inhalation Exposure (mg/kg/d)	Hand-to-mouth Oral Exposure[3] (mg/kg/d)	Chronic Food Exposure (mg/kg/d)	Allowable Short-Term Water Exposure (mg/kg/d)	$DWLOC_{short-term}$ (µg/L)
U.S. Population	1.9 - 4.8	3.2	0.00033	negligible	n/a	0.000003	0.002332	82
Children (1-6 years old)	1.9 - 4.8	3.2	n/a	negligible	0.0000917	0.000005	0.00173	17
Females (13-50 years old)	1.9 - 4.8	3.2	0.00033	negligible	n/a	0.000003	0.002332	70

[1]Population subgroups chosen were U.S. population (70 kg. body weight assumed, 2 liters water/day), the infant/child subgroup with the highest food exposure (10 kg. body weight assumed, 1 liter water/day), and the female subgroup with the highest food exposure (60 kg. body weight assumed, 2 liters water/day).
[2]High-end dermal exposure value of 0.00033 mg/kg/d is based on the "loading/applying Bayer Advanced Garden 2-in-1 Systemic Rose and Flower Care® Disulfoton 1% granulars using a measuring cup/lid" to shrubs scenario.
[3]Hand-to-mouth oral exposure value of 0.0000917 mg/kg/d is based on incidental soil ingestion for flowerbeds.

Conclusion

The Agency's aggregate risk assessment for disulfoton is based on exposure estimates for food and residential uses and provides a screening level assessment of modeled estimates for drinking water contamination . Dietary risk estimates are based on a refined assessment that incorporates percent crop treated data, monitoring data, and processing data. It is unlikely that this dietary assessment can be refined to any significant degree. Residential risk estimates are based, in part, on a registrant-submitted homeowner garden study that was conducted specifically for the Bayer 1% granular formulation. It is unlikely also that the residential assessment (for the 1% granular product) can be refined to any significant degree. However, the drinking water assessment is based on limited monitoring data and modeled estimates, and is not considered a refined estimate that represents actual disulfoton contamination in finished tapwater.

The EEC estimates for disulfoton residues in surface and groundwater are below the Agency's estimated *acute* and *short-term* DWLOC values for all population subgroups. Therefore, based on all available information, the Agency concludes with reasonable certainty that residues of disulfoton in drinking water, when considered along with exposures from food and residential uses, will not result in an aggregate acute or short-term exposure above the Agency's level of concern. However, it should be noted that the short-term DWLOC values are based on dermal exposure values from exposure scenarios that have individual MOEs **greater than** 100 only. Exposure scenarios with MOEs **less than** 100 were not included in the short-term aggregate assessment. These scenarios include the following:

(1) loading/applying granulars with a belly grinder for flower and vegetable gardens (pre-planting) using an application rate of 0.3 lb ai/1000 ft^2 (flower gardens, MOE = 1.1) and 0.069 lb ai/1000 ft^2 (vegetable gardens, MOE = 4.6)

(3) loading/applying granulars, using a spoon, measuring scoop, shaker can or by hand, to flower gardens and ornamental shrubs/small trees using an application rate of 0.3 lb ai/1000 ft^2 (flower gardens, MOE = 34) and 0.01 lb ai/ four foot shrub (shrubs/small trees, MOE = 41).

Since there are no expected long-term residential exposures to disulfoton, the chronic aggregate assessment is based on food and drinking water only. The modeled EEC estimates for disulfoton residues in surface and groundwater are, in general, above the estimated *chronic* DWLOC values. At this time, the Agency cannot conclude with reasonable certainty that no harm will result from chronic aggregate exposure to disulfoton, as required by the Food Quality Protection Act.