



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

APR 30 1996

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OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Dietary Exposure Analysis for Sulprofos in Support of
the Reregistration Eligibility Decision.

FROM: Brian Steinwand *BS*
Dietary Risk Evaluation Section
Science Analysis Branch/HED (7509C)

Through: Elizabeth Doyle, Section Head *E.A. Doyle*
Dietary Risk Evaluation Section
SAB/Health Effects Division *WJ Brown*

TO: Mike Metzger, Chief
Risk Characterization Analysis Branch
Health Effects Division (7509C)

Action Requested

Provide a dietary exposure analysis to estimate the chronic and acute dietary exposure and risk from sulprofos for uses which are being supported through reregistration.

Discussion

Toxicological Endpoint:

The Reference Dose (RfD) used in the analysis is 0.003 mg/kg bwt/day, based on a NOEL of 0.25 mg/kg bwt/day from a two year dog feeding study with an uncertainty factor of 100 that demonstrated plasma, RBC, and brain cholinesterase inhibition (See IRIS). Sulprofos is negative for carcinogenicity in both rats and mice.

The endpoint for acute dietary risk assessment is the Neurotoxicity NOEL (3.0 mg/kg/day) from the rat neurotoxicity toxicity study (See Tox Endpoint Selection Document, 4/16/96).

Residue Information

Tolerances for sulprofos are published in 40 CFR §180.374, 185.3000 and 186.3000. Tolerances had been established in/on cotton, soybean and livestock commodities. The available data support the established tolerances in/on cottonseed and livestock commodities. CBRS recommends that the tolerances for cottonseed oil and soybean RACs and processed commodities be revoked as registered uses of sulprofos on soybeans are no longer supported by the registrant, while the residues of sulprofos do not concentrate in cottonseed oil. However, CBRS recommends that the soybean tolerances not be revoked until the required soybean rotational crop trials are submitted and accepted. There are no other suggested revocations or reassessed tolerances (See memo, C. Eiden, 11/1/95). Even with these crops included in the chronic risk analysis, the %RfD was not exceeded in any subgroup. Tolerance level residues and 100 percent crop treated assumptions were made for all commodities. No anticipated residue (AR) information was used in this analysis. The existing food/feed additive tolerance should be revoked as the registrant is no longer supporting any registered uses of sulprofos on soybeans; adequate livestock feeding studies are available to support the currently established tolerances on meat, milk, poultry and eggs (See memo, C. Eiden, 11/1/95).

Results

A summary of the residue information included in this analysis is attached as Table 1. A DRES chronic exposure analysis was performed using tolerance level residues and 100 percent crop treated information to estimate the Theoretical Maximum Residue Contribution (TMRC) for the general population and 22 subgroups. Summaries of the TMRCs and their representations as percentages of the Reference Dose (RfD) are included as Table 2 and 3. The results of the acute dietary analysis are included in Table 4.

Existing tolerances (See Table 3) result in a TMRC which represents 20.2% of the RfD for the U.S. general population, 41.1% for children 1-6 and 30.2% for children 7-12.

The analysis for sulprofos is a worst case estimate of dietary exposure with all residues at tolerance level and 100 percent of the commodities assumed to be treated with sulprofos. Based on the risk estimates calculated in this analysis, it appears that chronic dietary risk from the uses recommended through reregistration, is not of concern.

However, it should be noted that if granted, the pending tolerances for sulprofos on tomatoes and corn (pop, sweet, grain) will result in risk levels above the Agency's level of concern for the subgroups (Non-Nursing Infants < 1 year old, 127.6 %), Children (1-6 years old, 195.7 %), and Children (7-12 years old, 152%) (See Table 2).

Acute Exposure:

The acute analysis (See Table 4) entailed all published uses of sulprofos and includes those commodities which CBRS recommends to be revoked. Even with these commodities included in the acute analysis, it appears that acute dietary risk from the uses recommended through reregistration, is not of concern.

The DRES detailed acute analysis estimates the distribution of single-day exposures for the overall U.S. population and certain subgroups. The analysis evaluates individual food consumption as reported by respondents in the USDA 1977-78 Nationwide Food Consumption Survey (NFCS) and accumulates exposure to the chemical for each commodity. Each analysis assumes uniform distribution of sulprofos in the commodity supply.

The Margin of Exposure (MOE) is a measure of how close the high end exposure comes to the NOEL (the highest dose at which no effects were observed in the laboratory test), and is calculated as the ratio of the NOEL to the exposure ($\text{NOEL/exposure} = \text{MOE}$). Generally, acute dietary margins of exposure greater than 100 tend to cause no dietary concern when the data are compared to an endpoint from an animal study. The lowest MOE value of 600 (See Table 4) is above the acceptable level and demonstrates no acute dietary concern.

Attachments

cc: DRES; Caswell 453AA; CBRS II (C. Eiden)

TABLE 1

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DATE: 04/23/96

CHEMICAL INFORMATION FOR CASWELL NUMBER 453AA

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Sulprofos (Merpafo/Bolstar) Caswell #453AA CAS No. 35400-43-2 A.I. CODE: 111501 CFR No. 180.374 185.3000	2yr feeding- dog NOEL= 0.2500 mg/kg 10.00 ppm LEL= 2.5000 mg/kg 100.00 ppm ONCO: E (Rfd/PR Committee)	Plasma, RBC, brain CHE inhibition. No evidence of carcinogenicity in rats or mice.	ADI UF -->100 OPP Rfd= 0.003000 EPA Rfd= 0.000000	No data gaps.	HED reviewed 03/14/86 EPA deferred 11/25/86 Rfd/PR reviewed 01/25/96
FOOD CODE	FOOD NAME	PETITION NUMBER	NEW	PENDING	PUBLISHED
11005AA	TOMATOES-WHOLE	0F2296	1.000000		
11005JA	TOMATOES-JUICE	0F2296	4.000000		H
11005RA	TOMATOES-PUREE	0F2296	4.000000		H
11005TA	TOMATOES-PASTE	0F2296	4.000000		H
11005UA	TOMATOES-CATSUP	0F2296	4.000000		H
15004AA	CORN, POP	0F2296	0.300000		
15005AA	CORN, SWEET	0F2296	2.000000		0.500000
15029AA	SOYBEANS-SPROUTED SEEDS	2F2715			
24002HA	CORN, GRAIN-BRAN	0F2296	0.300000		
24002SA	CORN SUGAR	0F2296	0.300000		
270020A	CORN, GRAIN-OIL	0F2296	6.000000		
270030A	COTTONSEED-OIL	2F2715			
27003WA	COTTONSEED-MEAL	2F2715			
270100A	SOYBEANS-OIL	2F2715			
28023AA	SOYBEANS-UNSPECIFIED	2F2715			
28023AB	SOYBEANS-MATURE, SEEDS DRY	2F2715			
28023WA	SOYBEANS-FLOUR, FULL FAT	2F2715			
28023WB	SOYBEANS-FLOUR, LOW FAT	2F2715			
28023WC	SOYBEANS-FLOUR, DEFATTED	2F2715			
50000DB	MILK-NON-FAT SOLIDS	2F2715			
50000FA	MILK-FAT SOLIDS	2F2715			
50000SA	MILK SUGAR (LACTOSE)	2F2715			
53001BA	BEEF-MEAT BYPRODUCTS	2F2715			
53001BB	BEEF(ORGAN MEATS)-OTHER	2F2715			
53001DA	BEEF-DRIED	2F2715			
53001FA	BEEF(BONELESS)-FAT (BEEF TALLOW)	2F2715			
53001KA	BEEF(ORGAN MEATS)-KIDNEY	2F2715			
53001LA	BEEF(ORGAN MEATS)-LIVER	2F2715			
53001MA	BEEF(BONELESS)-LEAN (W/O REMOVEABLE FAT)	2F2715			
53002BA	GOAT-MEAT BYPRODUCTS	2F2715			
53002BB	GOAT(ORGAN MEATS)-OTHER	2F2715			
53002FA	GOAT(BONELESS)-FAT	2F2715			
53002KA	GOAT(ORGAN MEATS)-KIDNEY	2F2715			
53002LA	GOAT(ORGAN MEATS)-LIVER	2F2715			
53002MA	GOAT(BONELESS)-LEAN (W/O REMOVEABLE FAT)	2F2715			
53003AA	HORSE	2F2715			
53004AA	RABBIT	2F2715			
53005BA	SHEEP-MEAT BYPRODUCTS	2F2715			
53005BB	SHEEP(ORGAN MEATS)-OTHER	2F2715			
53005FA	SHEEP(BONELESS)-FAT	2F2715			

CHEMICAL INFORMATION FOR CASWELL NUMBER 453AA

DATE: 04/23/96

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CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES		DATA GAPS/COMMENTS	STATUS
			AD1	UF -->100		
Sulprofos (Merpatos/Bolstar)	2yr feeding- dog	Plasma, RBC, brain Che inhibition.	OPP Rfd= 0.003000		No data gaps.	HED reviewed 03/14/86 EPA deferred 11/25/86 Rfd/PR reviewed 01/25/96
Caswell #453AA	NOEL= 0.2500 mg/kg					
CAS No. 35400-43-2	10.00 ppm					
A.I. CODE: 111501	LEL= 2.5000 mg/kg					
CFR No. 180.374	100.00 ppm	No evidence of carcinogenicity in rats or mice.				
185.3000	ONCO: E (Rfd/PR Committee)					

FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM)	
			NEW	PENDING PUBLISHED
53005KA	SHEEP(ORGAN MEATS)-KIDNEY	2F2715		0.100000
53005LA	SHEEP(ORGAN MEATS)-LIVER	2F2715		0.100000
53005MA	SHEEP(BONELESS)-LEAN (W/O REMOVEABLE FAT	2F2715		0.100000
53006BA	PORK-MEAT BYPRODUCTS	2F2715		0.100000
53006BB	PORK(ORGAN MEATS)-OTHER	2F2715		0.100000
53006FA	PORK(BONELESS)-FAT (INCLUDING LARD)	2F2715		0.100000
53006KA	PORK(ORGAN MEATS)-KIDNEY	2F2715		0.100000
53006LA	PORK(ORGAN MEATS)-LIVER	2F2715		0.100000
53006MA	PORK(BONELESS)-LEAN (W/O REMOVEABLE FAT)	2F2715		0.100000
55008BA	TURKEY-BYPRODUCTS	2F2715		0.010000
55008LA	TURKEY-GIBLETS (LIVER)	2F2715		0.010000
55008MA	TURKEY-FLESH(W/O SKIN, W/O BONES)	2F2715		0.010000
55008MB	TURKEY-FLESH(+SKIN, W/O BONES)	2F2715		0.010000
55008MC	TURKEY-UNSPECIFIED	2F2715		0.010000
55013BA	POULTRY, OTHER-BYPRODUCTS	2F2715		0.010000
55013LA	POULTRY, OTHER-GIBLETS(LIVER)	2F2715		0.010000
55013MA	POULTRY, OTHER-FLESH (+SKIN, W/O BONES)	2F2715		0.010000
55014AA	EGGS-WHOLE	1F2561		0.001000
55014AB	EGGS-WHITE ONLY	1F2561		0.001000
55014AC	EGGS-YOLK ONLY	1F2561		0.001000
55015BA	CHICKEN-BYPRODUCTS	2F2715		0.010000
55015LA	CHICKEN-GIBLETS(LIVER)	2F2715		0.010000
55015MA	CHICKEN-FLESH(W/O SKIN, W/O BONES)	2F2715		0.010000
55015MB	CHICKEN-FLESH(+SKIN, W/O BONES)	2F2715		0.010000

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TABLE 2

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

DATE: 04/23/96

PAGE: 1

CHEMICAL INFORMATION		STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Sulprofos (Merpafo/Bolstar) Caswell #453AA CAS No. 35400-43-2 A.I. CODE: 111501 CFR No. 180.374 185.3000	2yr feeding- dog NOEL= 0.2500 mg/kg 10.00 ppm LEL= 2.5000 mg/kg 100.00 ppm ONCO: E (Rfd/PR Committee)		Plasma, RBC, brain Che inhibition. No evidence of carcinog- enicity in rats or mice.	ADI UF -->100 OPP Rfd= 0.003000 EPA Rfd= 0.000000	No data gaps.	HED reviewed 03/14/86 EPA deferred 11/25/86 Rfd/PR reviewed 01/25/96
TOTAL TMRC (MG/KG BODY WEIGHT/DAY)						
CURRENT TMRC*			NEW TMRC**		DIFFERENCE AS PERCENT OF RFD	%RFD
POPULATION SUBGROUP						
U.S. POPULATION - 48 STATES						
U.S. POPULATION - SPRING SEASON			0.000607	0.002983	99.424033	79.182767
U.S. POPULATION - SUMMER SEASON			0.000594	0.002843	94.781367	74.970300
U.S. POPULATION - FALL SEASON			0.000609	0.003074	102.452067	82.158867
U.S. POPULATION - WINTER SEASON			0.000620	0.003022	100.726233	80.046367
			0.000605	0.002993	99.765400	79.583333
NORTHEAST REGION						
NORTH CENTRAL REGION			0.000592	0.002946	98.215967	78.489033
SOUTHERN REGION			0.000622	0.003133	104.425200	83.701133
WESTERN REGION			0.000587	0.002783	92.756733	73.196367
			0.000642	0.003159	105.307633	83.896367
HISPANICS						
NON-HISPANIC WHITES			0.000686	0.003354	111.813167	88.955733
NON-HISPANIC BLACKS			0.000607	0.003057	101.903367	81.672400
NON-HISPANIC OTHERS			0.000570	0.002362	78.727100	59.715000
			0.000623	0.002676	89.189267	68.419700
NURSING INFANTS (< 1 YEAR OLD)						
NON-NURSING INFANTS (< 1 YEAR OLD)			0.000461	0.001125	37.512833	22.153433
FEMALES (13+ YEARS, PREGNANT)			0.001726	0.003830	127.663767	70.123067
FEMALES 13+ YEARS, NURSING			0.000427	0.002371	79.019267	64.785067
CHILDREN (1-6 YEARS OLD)			0.000510	0.002565	85.514700	68.523333
CHILDREN (7-12 YEARS OLD)			0.001233	0.005872	195.747867	154.651433
MALES (13-19 YEARS OLD)			0.000907	0.004560	152.012700	121.772200
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)			0.000659	0.003216	107.200200	85.218000
MALES (20 YEARS AND OLDER)			0.000535	0.002658	88.597633	70.779400
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)			0.000492	0.002423	80.750167	64.351267
			0.000420	0.002217	73.906567	59.915633

*Current TMRC does not include new or pending tolerances.

**New TMRC includes new, pending, and published tolerances.

TABLE 3

TOLERANCE ASSESSMENT SUMMARY FOR Sulprofos (Merpafos/Bolstar) DATE: 04/23/96
CASWELL #453AA

ANALYSIS FOR POPULATION SUB-GROUP: U.S. POPULATION - 48 STATES

EXISTING TOLERANCES (PUBLISHED ONLY)		
RESULT IN A TMRC OF:	0.000608	MG/KG/DAY
THE EXISTING TMRC IS EQUIVALENT TO:	20.241	% OF THE ADI.
PROPOSED NEW TOLERANCES (CURRENT PETITION ONLY)		
RESULT IN A TMRC OF:	0.002376	MG/KG/DAY
THESE NEW TOLERANCES WILL OCCUPY:	79.183	% OF THE ADI.
IF THE NEW TOLERANCES (CURRENT PETITION ONLY)		
ARE APPROVED THE RESULTANT TMRC WILL BE:	0.002983	MG/KG/DAY
THE NEW TMRC WILL OCCUPY	99.424	% OF THE ADI.

NO OTHER PENDING TOLERANCES ARE IN THE FILE

ANALYSIS FOR POPULATION SUB-GROUP: CHILDREN (1-6 YEARS OLD)

EXISTING TOLERANCES (PUBLISHED ONLY)		
RESULT IN A TMRC OF:	0.001233	MG/KG/DAY
THE EXISTING TMRC IS EQUIVALENT TO:	41.096	% OF THE ADI.
PROPOSED NEW TOLERANCES (CURRENT PETITION ONLY)		
RESULT IN A TMRC OF:	0.004640	MG/KG/DAY
THESE NEW TOLERANCES WILL OCCUPY:	154.651	% OF THE ADI.
IF THE NEW TOLERANCES (CURRENT PETITION ONLY)		
ARE APPROVED THE RESULTANT TMRC WILL BE:	0.005873	MG/KG/DAY
THE NEW TMRC WILL OCCUPY	195.748	% OF THE ADI.

NO OTHER PENDING TOLERANCES ARE IN THE FILE

ANALYSIS FOR POPULATION SUB-GROUP: CHILDREN (7-12 YEARS OLD)

EXISTING TOLERANCES (PUBLISHED ONLY)		
RESULT IN A TMRC OF:	0.000908	MG/KG/DAY
THE EXISTING TMRC IS EQUIVALENT TO:	30.241	% OF THE ADI.
PROPOSED NEW TOLERANCES (CURRENT PETITION ONLY)		
RESULT IN A TMRC OF:	0.003654	MG/KG/DAY
THESE NEW TOLERANCES WILL OCCUPY:	121.772	% OF THE ADI.
IF THE NEW TOLERANCES (CURRENT PETITION ONLY)		
ARE APPROVED THE RESULTANT TMRC WILL BE:	0.004561	MG/KG/DAY
THE NEW TMRC WILL OCCUPY	152.013	% OF THE ADI.

NO OTHER PENDING TOLERANCES ARE IN THE FILE

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DETAILED ACUTE ANALYSIS INCLUDING AR S: ALL STATISTICS BASED ON USERS DAILY CONSUMPTION
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*NAME: MERPAFOS (BOLSTAR)
*CASWELL NO: 453AA CFR NO: CFR180.374 A 00000.0250 000010.000 000010 Chronic SF STUDY TYPE SPECIES EFF. LEV. CORE GRADE DOC. NO.*
*CAS NO: 35400-43-2 SHAUGHNESSY NO: 111501 B 000006.000 000006.000 Rat Enzymatic Minimum 0000001331*
*STATUS CODES: C 000400.000 Chron-onco Mouse Systemic Minimum 0000001331*
*RDV INFO: The LD value used in this analysis is 0.001 MG/KG of BODY WEIGHT/DAY
*FILE INFO: No Tolerance Data Are Used--Without User Modifications.
*****
AR DATA: No User Modifications
*****
*****
08:22 Wednesday, April 24, 1996 27
*****

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[illegible]

ESTIMATED % OF POTENTIAL		MEAN DAILY RESIDUE CONTRIBUTION PER USER-DAY															
PERSON DAYS THAT ARE USER-DAYS		MG/KG BODY WEIGHT/DAY		AS PERCENT OF RDV													
0.00		0.000000		0.00													
92.17		0.001582		158.21													
ESTIMATED % OF POPULATION USER-DAYS WITH RESIDUE CONTRIBUTION EXCEEDING X TIMES THE RDV, FOR X=																	
0	.2	.4	.6	.8	1	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20	
TOLERANCES:																	
ANTICIPATED RESIDUES:		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ANTICIPATED RESIDUES:		100	96	93	89	83	73	62	51	42	34	27	7	2	0	0	0

ESTIMATED % OF POTENTIAL		MEAN DAILY RESIDUE CONTRIBUTION PER USER-DAY														
PERSON DAYS THAT ARE USER-DAYS		MG/KG BODY WEIGHT/DAY		AS PERCENT OF RDV												
0.00		0.000000		0.00												
99.90		0.001234		123.40												
ESTIMATED % OF POPULATION USER-DAYS WITH RESIDUE CONTRIBUTION EXCEEDING X TIMES THE RDV, FOR X=																
0	.2	.4	.6	.8	1	1.2	1.4	1.6	1.8	2	3	4	5	10	15	20
TOLERANCES:																
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ANTICIPATED RESIDUES:																
100	99	95	87	73	58	44	32	23	16	11	2	1	0	0	0	0

Infants (1 year)

Exposure = $RDV \times X$
= 0.001×5
High End Exposure = 0.005

MOE = Noel + Exposure
= $3.0 \text{ mg/kg/day} + 0.005 \text{ mg/kg/day}$
MOE = 600

Children (1-6 years)

Exposure = $RDV \times X$
= 0.001×5
High End Exposure = 0.005

MOE = Noel + Exposure
= $3.0 \text{ mg/kg/day} + 0.005 \text{ mg/kg/day}$
MOE = 600

Females (13+ Years)

Exposure = $RDV \times X$
= 0.001×1.6
High End Exposure = 0.0016

MOE = Noel + Exposure
= $3.0 \text{ mg/kg/day} + 0.0016 \text{ mg/kg/day}$
MOE = 1875

Males (13+ Years)

Exposure = $RDV \times X$
= 0.001×1.8
High End Exposure = 0.0018

MOE = Noel + Exposure
= $3.0 \text{ mg/kg/day} + 0.0018 \text{ mg/kg/day}$
MOE = 1666