



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

JUL 8 1994

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: New Chemical/First Permanent Food Use: Acute and Chronic Dietary Exposure Analyses for the Proposed Use of Tebuconazole on Peanuts (PP#9F3724/9F3818).

FROM: Teung F. Chin, Biologist  
Dietary Risk Evaluation Section  
Science Analysis Branch/ HED

*Teung F. Chin*

TO: Steve Robbins/Denise Greenway, Acting PM 21  
Fungicide-Herbicide Branch  
Registration Division (7505C)

THROUGH: Jim Kariya, <sup>Manager</sup> Head  
DRES/SAB  
Health Effects Division

*W. Robbins*

Action Requested

The Fungicide-Herbicide Branch has requested a Dietary Risk Evaluation System (DRES) analysis be performed for the new chemical tebuconazole at the listed proposed conditional tolerances for the following commodities: 0.1 ppm peanuts; peanut hulls 4.0 ppm (Expiration date: 7/96) (6/15/94 CBRS memo G.F. Otakie to S. Robbins).

Discussion

1. Toxicological Information:

For chronic exposure, the Dietary Risk Evaluation System (DRES) used a Reference Dose (RfD) of 0.01 mg/kg body weight/day, based on a lower no observed effect level (NOEL) of 1 mg/kg bwt/day in dogs and an uncertainty factor of 100 (7/11/91 memo G. Z. Ghali to S. Lewis and 8/6/93 memo A. Protzel to B. Chambliss/S. Lewis). The Carcinogenicity Peer Review Committee concluded that Tebuconazole is a Class C - possible human carcinogen and recommended that, for the purpose of risk characterization, the Reference Dose (RfD) approach should be used for quantification of human risk (9/15/93 memo A. Protzel to B. Chambliss/S. Lewis).



Recycled/Recyclable  
Printed with Soy/Canola Ink on paper that  
contains at least 50% recycled fiber

For developmental toxicity,, tebuconazole tested positive in mice, rats, and rabbits at levels less than those inducing maternal toxicity. NOEL = 10 mg/kg/day was utilized for this DRES analysis was based on NMRI/ORIG Kissleg pregnant mice (9/14/92 Memo G.J. Burin to S. Lewis).

The exposure being calculated in this analysis are from tebuconazole residues alone. In March 1, 1994, the HED/Metabolism Committee concluded on non-inclusion of triazolylalanine residues with the tolerance expression of the parent compound (4/1/94 memo A. Protzel to The Metabolism Committee).

2. Residue Information: Food uses evaluated in this analysis, in terms of DRES vocabulary, were peanuts (0.1 ppm) (6/15/94 G.F. Otakie memo to S. Robbins/D. Greenway) and peanut oil (0.1 ppm). Although the proposed tolerance is for peanuts (whole), the DRES system also considers peanut oil when peanuts (whole) are considered. Since CBTS concluded that tebuconazole does not concentrate in peanut oil, a residue value of 0.1 ppm was used, the same as for peanuts. Peanut hulls were not assessed although the petition includes peanut hulls (4.0 ppm) because humans do not consume peanut hulls. Also, CBTS concluded that any hulls consumed by animals as a feed stuff would not result in secondary residues in meat, milk, poultry and eggs. The CBTS memo also concluded that tebuconazole does not concentrate in peanut meal. While residues do concentrate in peanut soapstock, EPA no longer considers peanut soapstock as an animal feed item. Furthermore, the label included a restriction against feeding peanut hay/vines to livestock temporary tolerances. Since tebuconazole is a new chemical, there are no § 185 food additive tolerances or § 186 tolerances. For the same reason, there were no tolerances in the Tolerance Index System (TIS) listing or the CFR. The proposed tolerance level of 0.1 ppm for peanuts (raw, cooked, baked) and 0.1 ppm for peanuts - oil were used as the residue values for both the acute and chronic exposure analyses.

3. Percent Crop Treated - No percent crop treated information was utilized for both the DRES acute and chronic exposure analyses. None would be available since this is a new chemical/new use pattern. It was assumed that 100 percent of the peanut crop is treated with tebuconazole.

4. Anticipated Residues (AR) - No anticipated residue (AR) information was utilized for both the DRES acute and chronic exposure analyses. The use of available processing data was considered unnecessary since the calculated risks were so extremely low even at tolerance levels.

## Results

1. Chronic Exposure: The DRES chronic exposure analysis used tolerance level residues and assumed 100 percent crop treated to estimate the Theoretical Maximum Residue Contribution (TMRC) for

the overall U.S. population and 22 population subgroups. Because tebuconazole is a new chemical, there are no anticipated residues and percent crop treated information, and therefore no estimated Anticipated Residue Contribution (ARC). The ARC is considered the more refined estimate of exposure over the TMRC. A summary of the TMRCs and their representations as percentages of the RfD is in Table 1A. It should be noted again that the residue of interest in this analysis is tebuconazole.

Comments - Chronic Dietary Risk: The TMRC from the proposed new uses of tebuconazole for the general population of the 48 States is 0.000007 mg/kg/bwt/day, which represents 0.07% of the RfD. There were no pending or published tolerances at the time of the calculations. The TMRCs for the most highly exposed subgroups, children (1-6 years old) and children (7-12 years old) are 0.000024 mg/kg bwt/day (0.24% of the RfD), and 0.000017 mg/kg bwt/day (0.17% of the RfD), respectively. All other groups were between 0.02 - 0.24 % of the RfD. Since calculated intake never exceeded the RfD, minimal to no risk for all subpopulations is expected from a chronic dietary intake of tebuconazole at this time.

2. Acute Exposure: 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 tebuconazole in the commodity (peanut) supply. Since the toxicological endpoint to which exposure is being compared in this analysis is developmental toxicity, the females (13+ years) is the subpopulation of particular interest.

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 ( $NOEL / exposure = MOE$ ). For chemicals whose acute NOELs are derived from animal studies, the Agency is generally not concerned unless the MOE is below 100.

Comments - Acute Dietary Risk

Table 1B contains the distribution of acute exposures used for this analysis.  $MOE_{100} = 0.1$  mg/kg bwt/day (Calculations on Page 6 of Table 1B). Calculations (also on page 6, Table 1B) show that for the high-end of the subpopulation of concern, females (13+ yrs),  $MOE = 83,000$ ; therefore females (13+ yrs) have a negligible acute risk for developmental toxicity.

Attachments

cc: DRES, FHB, CCB, Tox II, CBTS I, Caswell # 463P

TABLE 1A: Chronic Dietary Exposure Analysis - Tebuconazole on Peanuts, Whole and Oil

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

DATE: 06/30/94

PAGE: 1

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES		DATA GAPS/COMMENTS	STATUS		
			PADI OPP RfD= 0.010000 EPA RfD= 0.000000	UF -->100				
Tebuconazole (Follicur) Caskell #463P CAS No. 107534-96-3 A.I. CODE: 128997 CFR No.	1yr feeding- dog NOEL= 1.0000 mg/kg 40.00 ppm LEL= 5.0000 mg/kg 200.00 ppm ONCO: Negative- 1 species	Lenticular & corneal opacity and hepatic toxicity. No evidence of oncogenicity in rat; MTD not reached in mouse study.			Chronic Feed/Onco- mouse Devel Peer Review 6/92. Devel toxicity NOEL=10 mg/kg/day (mouse oral); dermal studies were inconclusive.	RfD/PR reviewed 03/05/91 RfD/PR reviewed 06/08/93		
POPULATION SUBGROUP			TOTAL TMRC (MG/KG BODY WEIGHT/DAY)	NEW TMRC AS PERCENT OF RFD	NEW TMRC AS PERCENT OF RFD	EFFECT OF ANTICIPATED RESIDUES	ARC	%RFD
U.S. POPULATION - 48 STATES			0.000000	0.000007	0.074810	0.074810		
U.S. POPULATION - SPRING SEASON			0.000000	0.000008	0.076690	0.076690		
U.S. POPULATION - SUMMER SEASON			0.000000	0.000008	0.082260	0.082260		
U.S. POPULATION - FALL SEASON			0.000000	0.000007	0.071940	0.071940		
U.S. POPULATION - WINTER SEASON			0.000000	0.000007	0.068340	0.068340		
NORTHEAST REGION			0.000000	0.000008	0.080860	0.080860		
NORTH CENTRAL REGION			0.000000	0.000008	0.079930	0.079930		
SOUTHERN REGION			0.000000	0.000006	0.058700	0.058700		
WESTERN REGION			0.000000	0.000009	0.087090	0.087090		
HISPANICS			0.000000	0.000004	0.037550	0.037550		
NON-HISPANIC WHITES			0.000000	0.000008	0.083010	0.083010		
NON-HISPANIC BLACKS			0.000000	0.000004	0.040850	0.040850		
NON-HISPANIC OTHERS			0.000000	0.000006	0.061740	0.061740		
NURSING INFANTS (< 1 YEAR OLD)			0.000000	0.000002	0.018000	0.018000		
NON-NURSING INFANTS (< 1 YEAR OLD)			0.000000	0.000003	0.029280	0.029280		
FEMALES (13+ YEARS, PREGNANT)			0.000000	0.000006	0.056190	0.056190		
FEMALES 13+ YEARS, NURSING			0.000000	0.000008	0.079340	0.079340		
CHILDREN (1-6 YEARS OLD)			0.000000	0.000024	0.235250	0.235250		
CHILDREN (7-12 YEARS OLD)			0.000000	0.000017	0.170500	0.170500		
MALES (13-19 YEARS OLD)			0.000000	0.000008	0.081290	0.081290		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)			0.000000	0.000006	0.055260	0.055260		
MALES (20 YEARS AND OLDER)			0.000000	0.000005	0.045450	0.045450		
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)			0.000000	0.000003	0.032000	0.032000		

\*Current TMRC does not include new or pending tolerances.  
\*\*New TMRC includes new, pending, and published tolerances.





MENU CATEGORY 18: VEGETABLE OILS

270070A PEANUTS-OIL  
18 PROCESSED OIL

MENU CATEGORY 19: DRY BEANS, PEANUTS (W/O OILS)

15006AA PEANUTS-WHOLE

10 RAW-FRESH OR NFS  
21 COOKED-FRESH

22 COOKED-FRESH-BAKED

DETAILED ACUTE ANALYSIS INCLUDING AR/S: ALL STATISTICS BASED ON USERS' DAILY CONSUMPTION  
\*\*\*\*\*  
NAME: DUMMYCIDE STUDY RDV NOEL SF STUDY TYPE SPECIES EFF. LEV. CORE GRADE DOC. NO.\*  
\*CASWELL NO: 900 CFR NO: CFR A 00000.1000 000100 Chronic Rat Enzymatic 08:45 Friday, July 1, 1994 5  
\*CAS NO: SHAUGHNESSY NO: 900999 B 00000.0500 001000 Terata Rabbit Systemic Minimum  
\*STATUS CODES: C  
\*RDV INFO: The LD value used in this analysis is .0001 Mg/Kg of BODY WEIGHT/DAY  
\*FILE INFO: No Tolerance Data Are Used--Without User Modifications.  
\*\*\*\*\*

FOOD CODE	FOOD AND FOOD FORM DESCRIPTION	NUMBER OF CONSUMER	DAYS AS PERCENT OF	POTENTIAL PERSON DAYS	TOLEANCE DATA	AR DATA	DAILY MAXIMUM ANTICIPATED RESIDUE	DAILY ANTICIPATED RESIDUE
		0.29			0.1000		0.061999	
		16.28			0.1000		0.132228	
		2.93			0.1000		0.045557	

LISTING OF RELEVANT FOODS & FOOD FORMS, ORDERED BY MENU CATEGORY. MENU PATTEM = 1-F  
CHEMICAL IS ASSUMED TO BE FAT SOLUBLE  
POPULATION = FEMALE<13+ YRS>

MENU CATEGORY 18: VEGETABLE OILS

270070A PEANUTS-OIL  
18 PROCESSED OIL

MENU CATEGORY 19: DRY BEANS, PEANUTS (W/O OILS)

15006AA PEANUTS-WHOLE

10 RAW-FRESH OR NFS  
21 COOKED-FRESH

22 COOKED-FRESH-BAKED

DETAILED ACUTE ANALYSIS INCLUDING AR/S: ALL STATISTICS BASED ON USERS' DAILY CONSUMPTION  
\*\*\*\*\*  
NAME: DUMMYCIDE STUDY RDV NOEL SF STUDY TYPE SPECIES EFF. LEV. CORE GRADE DOC. NO.\*  
\*CASWELL NO: 900 CFR NO: CFR A 00000.1000 000100 Chronic Rat Enzymatic 08:45 Friday, July 1, 1994 6  
\*CAS NO: SHAUGHNESSY NO: 900999 B 00000.0500 001000 Terata Rabbit Systemic Minimum  
\*STATUS CODES: C  
\*RDV INFO: The LD value used in this analysis is .0001 Mg/Kg of BODY WEIGHT/DAY  
\*FILE INFO: No Tolerance Data Are Used--Without User Modifications.  
\*\*\*\*\*

FOOD CODE	FOOD AND FOOD FORM DESCRIPTION	NUMBER OF CONSUMER	DAYS AS PERCENT OF	POTENTIAL PERSON DAYS	TOLEANCE DATA	AR DATA	DAILY MAXIMUM ANTICIPATED RESIDUE	DAILY ANTICIPATED RESIDUE
		0.43			0.1000		0.022262	
		7.03			0.1000		0.043058	
		1.26			0.1000		0.014094	

AR DATA: User Modifications  
\*\*\*\*\*  
\*RDV INFO: The LD value used in this analysis is .0001 Mg/Kg of BODY WEIGHT/DAY  
\*FILE INFO: No Tolerance Data Are Used--Without User Modifications.  
\*\*\*\*\*

\*\*\*\*\*  
 LISTING OF RELEVANT FOODS & FOOD FORMS, ORDERED BY MENU CATEGORY. MENU PATTERN = I-F  
 CHEMICAL IS ASSUMED TO BE FAT SOLUBLE  
 POPULATION = MALES(13+ YRS)

FOOD CODE	FOOD AND FOOD FORM DESCRIPTION	NUMBER OF CONSUMER DAYS AS PERCENT OF POTENTIAL PERSON DAYS	TOLERANCE DATA VALUE	AR DATA VALUE (PPM) REF.	DAILY MAXIMUM RESIDUE (EXCL. AR)	DAILY ANTICIPATED RESIDUE (INCL. AR)
270070A	PEANUTS-OIL		98.44	0.1000		0.000486
18	PROCESSED OIL					

MENU CATEGORY 18: VEGETABLE OILS

FOOD CODE	FOOD AND FOOD FORM DESCRIPTION	NUMBER OF CONSUMER DAYS AS PERCENT OF POTENTIAL PERSON DAYS	TOLERANCE DATA VALUE	AR DATA VALUE (PPM) REF.	DAILY MAXIMUM RESIDUE (EXCL. AR)	DAILY ANTICIPATED RESIDUE (INCL. AR)
15006AA	PEANUTS-WHOLE					
10	RAW-FRESH OR NFS		0.52	0.1000		0.021764
21	COOKED-NFS		9.20	0.1000		0.049246
22	COOKED-FRESH-BAKED		1.50	0.1000		0.016681

15006AA PEANUTS-WHOLE  
 10 RAW-FRESH OR NFS  
 21 COOKED-NFS  
 22 COOKED-FRESH-BAKED

TOLERANCE SOURCES: P=PUBLISHED, A=APPROVED, N=NEW ACTION, U=USER-SUPPLIED  
 DETAILED ACUTE ANALYSIS INCLUDING AR'S. ALL STATISTICS BASED ON USER'S DAILY CONSUMPTION  
 \*\*\*\*\*  
 \*NAME: DUMNYCID  
 \*CASWELL NO: 900  
 \*CAS NO: 900999 B 00000.0500  
 \*STATUS CODES: C  
 \*RDV INFO: The LD value used in this analysis is .0001  
 \*FILE INFO: No Tolerance Data Are Used--Without User Modifications.  
 \*\*\*\*\*  
 -U.S. POP.--48 STATES

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	0.00	0.00
96.79	0.000008	7.91

ESTIMATED % OF POPULATION USER-DAYS WITH RESIDUE CONTRIBUTION EXCEEDING X TIMES THE RDV, FOR X=

ESTIMATED % OF POPULATION	0	1	2	3	4	5	10	15	20
0	.2	.4	.6	.8	1.2	1.4	1.6	1.8	2

ESTIMATES BASED ON TOLERANCES:

PERSON DAYS THAT ARE USER-DAYS	MG/KG BODY WEIGHT/DAY	AS PERCENT OF RDV
0	0.00	0.00
100	0.000000	0.00



# Infants (21 year)

0 ANTICIPATED RESIDUES: 27.86 0.000009 9.02  
 ESTIMATED % OF POPULATION USER-DAYS WITH RESIDUE CONTRIBUTION EXCEEDING X TIMES THE RDV, FOR X=

0 ANTICIPATED RESIDUES: 0 .2 .4 .6 .8 1 1.2 1.4 1.6 1.8 2 3 4 5 10 15 20  
 CHILDREN(1-6 YRS)  
 TOLERANCES: 100 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0  
 ANTICIPATED RESIDUES: 100 5 4 4 4 3 3 3 3 2 1 1 0 0 0 0 0 0  
 ESTIMATED % OF POTENTIAL MEAN DAILY RESIDUE CONTRIBUTION PER USER-DAY

0 ESTIMATES BASED ON PERSON DAYS THAT ARE USER-DAYS MG/KG BODY WEIGHT/DAY AS PERCENT OF RDV  
 TOLERANCES: 0.00 0.000000 0.00  
 ANTICIPATED RESIDUES: 97.70 0.000024 24.44  
 ESTIMATED % OF POPULATION USER-DAYS WITH RESIDUE CONTRIBUTION EXCEEDING X TIMES THE RDV, FOR X=

0 TOLERANCES: 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0  
 ANTICIPATED RESIDUES: 100 18 16 14 11 9 7 6 5 4 3 1 0 0 0 0 0 0  
 ESTIMATED % OF POPULATION USER-DAYS WITH RESIDUE CONTRIBUTION EXCEEDING X TIMES THE RDV, FOR X=

0 \*NAME: DUMMYCID  
 \*CASWELL NO: 900 CFR NO: CFR A 00000.1000  
 \*CAS NO: SHAUGHNESSY NO: 900999 B 00000.0500  
 \*STATUS CODES: C  
 \*RDV INFO: The LD value used in this analysis is .0001 MG/Kg of BODY WEIGHT/DAY  
 \*FILE INFO: No Tolerance Data Are Used--Without User Modifications.  
 \*AR DATA: User Modifications

0 -FEMALES(13+ YRS)  
 ESTIMATED % OF POTENTIAL MEAN DAILY RESIDUE CONTRIBUTION PER USER-DAY  
 ESTIMATES BASED ON PERSON DAYS THAT ARE USER-DAYS MG/KG BODY WEIGHT/DAY AS PERCENT OF RDV  
 TOLERANCES: 0.00 0.000000 0.00  
 ANTICIPATED RESIDUES: 96.98 0.000004 3.87  
 ESTIMATED % OF POPULATION USER-DAYS WITH RESIDUE CONTRIBUTION EXCEEDING X TIMES THE RDV, FOR X=

0 TOLERANCES: 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0  
 ANTICIPATED RESIDUES: 100 6 3 2 1 1 0 0 0 0 0 0 0 0 0 0 0 0  
 ESTIMATED % OF POTENTIAL MEAN DAILY RESIDUE CONTRIBUTION PER USER-DAY  
 ESTIMATES BASED ON PERSON DAYS THAT ARE USER-DAYS MG/KG BODY WEIGHT/DAY AS PERCENT OF RDV  
 TOLERANCES: 0.00 0.000000 0.00  
 ANTICIPATED RESIDUES: 98.54 0.000005 5.45  
 ESTIMATED % OF POPULATION USER-DAYS WITH RESIDUE CONTRIBUTION EXCEEDING X TIMES THE RDV, FOR X=

0 TOLERANCES: 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0  
 ANTICIPATED RESIDUES: 100 7 5 3 2 2 1 1 0 0 0 0 0 0 0 0 0 0  
 ESTIMATED % OF POPULATION USER-DAYS WITH RESIDUE CONTRIBUTION EXCEEDING X TIMES THE RDV, FOR X=

MOES for High-End Consumers of sub-population

General Population  $3 \times 0.0001 = 0.0003$   $MOE = \frac{10}{0.0003} = 33,333 \approx 33,000$

Infants (<1yr)  $4 \times 0.0001 = 0.0004$   $MOE = \frac{10}{0.0004} = 25,000$

Kids (1-6yrs)  $4 \times 0.0001 = 0.0004$   $MOE = \frac{10}{0.0004} = 25,000$

♀ (13+ yrs)  $1.2 \times 0.0001 = 0.00012$   $MOE = \frac{10}{0.00012} = 83,333 \approx 83,000$

♂ (13+ yrs)  $1.4 \times 0.0001 = 0.00014$   $MOE = \frac{10}{0.00014} = 71,428 \approx 71,000$

NOEL = 10 mg/kg bw<sup>d</sup>/day

$R_{DV} = 0.0001$

$MOE_{100} = \frac{10}{100} = 0.1 \text{ mg/kg bw}^d/\text{day}$

CHEMICAL INFORMATION FOR CASWELL NUMBER 463P

DATE: 06/24/94

PAGE: 1

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES		DATA GAPS/COMMENTS	STATUS
			PADI	UF		
Tebuconazole (Folicur) Caswell #463P CAS No. 107534-96-3 A.I. CODE: 128997 CFR No.	1yr feeding- dog NOEL= 40.00 mg/kg LEL= 5.0000 mg/kg 200.00 ppm ONCO: Negative- 1 species	Lenticular & corneal opacity and hepatic toxicity. No evidence of oncogenicity in rat; MTD not reached in mouse study.	OPP Rfd= 0.0100000 EPA Rfd= 0.0000000	-->100	Chronic Feed/Onco- mouse Devel Peer Review 6/92. Devel toxicity NOEL=10 mg/kg/day (mouse oral); dermal studies were inconclusive.	RfD/PR reviewed 03/05/91 RfD/PR reviewed 04/08/93

FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM)	
			NEW	PENDING PUBLISHED
15006AA	PEANUTS-WHOLE	9F3724	0.100000	
270070A	PEANUTS-OIL	9F3724	0.100000	