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

MAY 20 1992

MAY 20 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

Subject: De Minimis Risk Assessmenmt for Temporary Tolerance and Experimental Use Permit for Tebuconazole on Peanuts.

From: Alberto Protzel, Ph.D. Alberto Protzel 5/20/92
Review Section III
Toxicology Branch II
Health Effects Division (H7509C)

To: Susan T. Lewis/Julie Fairfax, PM 21
Fungicide-Herbicide Branch
Registration Division (H7505C)

Thru: James N. Rowe, Ph.D., Head James N. Rowe 5/20/92
Review Section III
Toxicology Branch II
Health Effects Division (H7509C)

and

Marcia van Gemert, Ph.D., Chief
Toxicology Branch II
Health Effects Division (H7509C)

Action Requested

Toxicology Branch II (Section III) was requested to review a Miles submission, dated 4/10/92, entitled "Dietary Exposure and Risk Assessment for the Use of Tebuconazole in Peanuts" and determine whether this information allows for the granting of the EUP and temporary tolerance on peanuts. [FOLICUR 3.6 F (3125-EUP-ENN), Tolerance Petitions (9G3817 and 2H562800). DP Barcode D177018, Case 194452, Submission S416118].

Background

The Registrant initially tested tebuconazole for oncogenicity in NMRI mice in the diet at levels 0, 20, 60, or 180 ppm for 21 months (MRID 407009-41, 1/25/88). In the review of this 1988 initial study ("First study", J.N Rowe, DER dated 12/24/88), the reviewer concluded that:

- Based on the findings reported in the study it appeared that the high-dose treatment (180 ppm) was not high enough to approximate the maximum tolerated dose (MTD) and the study was classified as CORE Supplementary
- There was a slight (non statistically significant) apparent elevation in male benign, but not malignant liver tumors; the combined incidences of these tumors were within the historical control range.

To satisfy the MTD requirement, the Registrant conducted an additional study with NMRI mice (MRID 421750-01, 12/12/91) administered HWG 1608 in the diet at 0, 500 or 1500 ppm for up to 91 weeks. Based on the findings reported in this study, the reviewer ("Second study", A. Protzel, DER dated 2/20/92) concluded that:

- The MTD was reached at 500 ppm.
- The separate and combined incidences of hepatocellular adenomas and hepatocellular carcinomas in males were statistically significant at the high dose and were considered to be treatment-related.
- The incidence of hepatocellular carcinomas in females was statistically significant at the high dose and was considered to be treatment-related.
- There was a dose-related increase in the incidence of histiocytic sarcomas in both sexes, without pairwise statistical significance vs. controls.
- Further evaluation of the histiocytic sarcomas was deferred pending submission of historical control data and the study was classified CORE supplementary.

Contemporary with the Agency's review of the Miles oncogenicity study, a Miles application for EUP on Peanuts [FOLICUR 3.6 F (3125-EUP-ENN), Tolerance Petitions (9G3817 and 2H562800] was being processed. Concern over the significant incidence of hepatocellular neoplasmas observed in the second study in high-dose mice prompted Toxicology Branch II, Section III, to recommend a delay in granting the EUP pending a determination of the carcinogenic risk posed by the granting of the subject EUP and temporary tolerance in peanuts. In a meeting dated 3/26/92, it was suggested to the Miles representative that a favorable <u>de minimis</u> risk (i.e. an upper bound carcinogenic risk $\leq 10^{-6}$) may allow the subject EUP to be issued for 1992.

The results of such a calculations are summarized below.

A. <u>Results of Registrant's Calculations</u>

a. <u>Q_1^* Calculation</u>

To analyze the tumor data, the results of the first and second studies were pooled (Table 1) by the Registrant based on the following rationale:

- Same strain of mouse (Bor:NMRI(SPF-Han))
- Same supplier.
- Same duration (21 months).
- Same testing facility (BAYER AG, Toxicology Division, FRG).
- Studies were conducted within four years of one another (1984 and 1988).
- Similarities in non-neoplastic liver effects.
- Body-weight depression.

Table 1. Pooled[a] mouse liver tumor data (From Miles, 1992, p. 6)

Dose (ppm)	Adenomas	Carcinomas	Combined (Total)
Males			
0	5/97	1/97	6/97
20	2/49	0/49	2/49
60	4/50	0/50	4/50
180	6/49	1/49	6/49
500	2/48	0/48	2/48
1500	17/48	10/48	27/48***
Females			
0	1/96	1/96	2/96
20	0/49	0/49	0/49
60	0/50	0/50	0/50
180	0/50	1/50	1/50
500	0/45	0/45	0/45
1500	2/46	12/46	14/46***

[a] Data from the first study (0, 20, 60, and 180 ppm) and the second study (0, 500, 1500 ppm were pooled)
*** $p \leq 0.001$, Fisher's Exact Test.

Based on the data of Table 1 and the TOX-Risk V2.Q (Clement Assoc. Inc) software package, the registrant obtained the values for Q_1^* shown in Table 2. The value of Q_1^* equal to 1.5×10^{-2} $(mg/kg\ BW/day)^{-1}$ (the highest), corresponding to combined adenomas carcinomas in males (linearized multistage model), was used for the risk calculations corresponding to a worst case scenario.

Table 2. Q_1^* values obtained using the data in Table 1 (From Miles, 1992, p. 10).

Tumor type	Q_1^* $(mg/kg\ BW/day)^{-1}$	Goodness of Fit (p)
Males		
Adenomas	1.7×10^{-2}	0.39
Carcinomas	6.1×10^{-3}	0.63
Combined Total	1.5×10^{-2}	0.45
Females		
Adenomas	3.2×10^{-3}	0.73
Carcinomas	6.4×10^{-3}	0.65
Combined Total	5.3×10^{-3}	0.55

b. Exposure Assessment and Risk Calculations

Two separate dietary exposure analyses, under two different scenarios, were conducted by the Registrant:

- Analysis 1: The feeding restriction on the label will prevent peanut byproducts from being fed and there will be no secondary residues in meat, milk, poultry or eggs.

- Analysis 2: Processing byproducts are not covered by the feeding restriction and may be included in livestock diets.

These dietary exposure estimates were based on the nationwide survey of food intake conducted by the U.S. Department of Agriculture's Human Nutrition Information Service. The U.S. EPA is currently using data that were collected during 1977-78 in DRES analyses. The Registrant used the results of the most recent survey, completed in 1987-88. This more recent survey has been criticized on grounds that include a low response rate.

The results of the dietary exposure analysis under the first assumption (Feeding restriction, raw and processed commodities only) are shown in Table 3. The highest exposure (Non-hispanic other than black or white) corresponds to 0.000021 mg/kg BW/day. This exposure corresponds to a life time carcinogenic risk of 3.1×10^{-7} for the worst-case Q_1^* of $1.5 \times ^{-2}$ $(mg/kg\ BW/day)^{-1}$. This highest life time carcinogenic risk of 3.10×10^{-7} shown in Table 3, and therefore all others in the table, are smaller than the 1×10^{-6} de minimis carcinogenic risk acceptable to the EPA.

The results of the dietary exposure analysis under the second assumption (No feeding restriction) are shown in Table 4. The results, except for round-off, are essentially identical to those shown in Table 3. The highest life-time carcinogenic risk of 3.16×10^{-7} (non-hispanic other than black or white) for the worst-case Q_1^* of $1.5 \times ^{-2}$ $(mg/kg\ BW/day)^{-1}$ is also smaller than the 1×10^{-6} de minimis carcinogenic risk acceptable to the EPA.

Table 3. Registrant's dietary exposure analysis and lifetime carcinogenic risk determination based on an assumed feeding restriction. (Table obtained from Miles, 1992, Appendix 2, Table 2)

MILES
EXPOSURE 1-87 ANALYSIS FOR TEBUCONAZOLE (NFCS87/88 DATA)
RESIDUE FILE NAME: TEBUC1 ADJUSTMENT FACTOR #2 NOT USED
DATE 04-06-1992 DATE RESIDUE FILE LAST UPDATED: 04-06-1992/12:44:05/1

COMMENT 1: TOLERANCES. DOES NOT INCLUDE MMPE. Q*=0.015

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE MG/KG BODY WT/DAY	TOTAL EXPOSURE LIFE TIME RISK (Q*= 0.015000)
U.S. POP - 48 STATES - ALL SEASONS	0.000015	2.23E-07
U.S. POPULATION - SPRING SEASON	0.000015	2.18E-07
U.S. POPULATION - SUMMER SEASON	0.000016	2.42E-07
U.S. POPULATION - AUTUMN SEASON	0.000015	2.26E-07
U.S. POPULATION - WINTER SEASON	0.000014	2.03E-07
NORTHEAST REGION	0.000013	1.97E-07
NORTH CENTRAL REGION	0.000018	2.71E-07
SOUTHERN REGION	0.000013	1.88E-07
WESTERN REGION	0.000017	2.51E-07
HISPANICS	0.000007	1.10E-07
NON-HISPANIC WHITES	0.000016	2.39E-07
NON-HISPANIC BLACKS	0.000009	1.28E-07
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000021	3.10E-07
FEMALES (13+/PREGNANT/NOT NURSING)	0.000008	1.13E-07
FEMALES (13+/NURSING)	0.000008	1.17E-07
MALES (13-19 YEARS)	0.000012	1.78E-07
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000008	1.25E-07
MALES (20+ YEARS)	0.000008	1.23E-07
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000008	1.16E-07

Table 4. Registrant's dietary exposure analysis and lifetime carcinogenic risk determination <u>without</u> an assumed feeding restriction. (Table obtained from Miles, 1992, Appendix 3, Table 2)

MILES
EXPOSURE 1-87 ANALYSIS FOR TEBUCONAZOLE (NFCS87/88 DATA)
RESIDUE FILE NAME: TEBUC2AN ADJUSTMENT FACTOR #2 NOT USED
DATE 04-08-1991 DATE RESIDUE FILE LAST UPDATED: 04-06-1992/12:42:00/1

COMMENT 1: TOLERANCES, INCLUDING MMPE - Q*=0.015

TOTAL EXPOSURE BY POPULATION SUBGROUP

POPULATION SUBGROUP	TOTAL EXPOSURE MG/KG BODY WT/DAY	TOTAL EXPOSURE LIFE TIME RISK (Q*= 0.015000)
U.S. POP - 48 STATES - ALL SEASONS	0.000015	2.28E-07
U.S. POPULATION - SPRING SEASON	0.000015	2.23E-07
U.S. POPULATION - SUMMER SEASON	0.000017	2.48E-07
U.S. POPULATION - AUTUMN SEASON	0.000015	2.31E-07
U.S. POPULATION - WINTER SEASON	0.000014	2.08E-07
NORTHEAST REGION	0.000013	2.01E-07
NORTH CENTRAL REGION	0.000018	2.75E-07
SOUTHERN REGION	0.000013	1.93E-07
WESTERN REGION	0.000017	2.57E-07
HISPANICS	0.000008	1.16E-07
NON-HISPANIC WHITES	0.000016	2.44E-07
NON-HISPANIC BLACKS	0.000009	1.34E-07
NON-HISPANIC OTHER THAN BLACK OR WHITE	0.000021	3.16E-07
FEMALES (13+/PREGNANT/NOT NURSING)	0.000008	1.17E-07
FEMALES (13+/NURSING)	0.000008	1.22E-07
MALES (13-19 YEARS)	0.000012	1.83E-07
FEMALES (13-19 YRS/NOT PREG. OR NURSING)	0.000009	1.29E-07
MALES (20+ YEARS)	0.000008	1.27E-07
FEMALES (20+ YEARS/NOT PREG. OR NURSING)	0.000008	1.19E-07

B. Results of EPA/HED's Calculations

An independent calculation of Q_1^* values was performed by HED/SSSR. Tumor data were tabulated as combined hepatocellular adenomas and carcinomas, separate Q_1^* values for adenomas or carcinomas were not calculated.

The analyses to obtain the Q_1^* values were done using the pooled data for the first and second studies and using the data for the second study only. Q_1^* values obtained with the first study only appear to be of dubious significance as there was neither a statistically significant or historically significant incidence of tumors for the HDT vs controls in the first study.

Table 5. Mouse liver tumor data[a] (EPA count, including Interim sacrifice)

Dose (ppm)	Combined adenomas/carcinomas
Males	
Pooled First and Second Studies	
0	6/96
20	2/49
60	5/50
180	6/49
500	2/43
1500	27/48***
Second Study Only	
0	3/46
500	2/43
1500	27/48***
Females	
Pooled First and Second Studies	
0	2/87
20	0/46
60	0/47
180	1/46
500	0/40
1500	14/44***
Second Study Only	
0	1/43
500	0/40
1500	14/44***

[a] Data from the first study were obtained at 0, 20, 60, and 180 ppm and for the second study at 0, 500, and 1500 ppm. *** $p << 0.001$, Fisher's Exact Test, by the reviewer.

Based on the data in Table 5 and the TOX-Risk Version 3 (Clement Assoc. Inc) software package, the Agency obtained the values for the Q_1^* for combined hepatocellular adenomas/carcinomas (linearized multistage model) shown below in

7

Table 6. The value of Q_1^* equal to 3.06×10^{-2} $(mg/kg\ BW/day)^{-1}$ (the highest), corresponding to combined adenomas/carcinomas in pooled studies 1 and 2 for males, was used for the risk calculations corresponding to a worst case scenario.

It is noted that the above Agency Q_1^* calculations for tebuconazole are preliminary pending further Agency assessment of the carcinogenic potential of the subject chemical.

Table 6. EPA values for Q_1^* for combined hepatocellular adenomas/carcinomas in treated mice.

Source of Data	Q_1^* $(mg/kg\ BW/day)^{-1}$	Goodness of Fit (p)
Males		
Pooled first & second studies	3.06×10^{-2}	0.44
Second study only	2.19×10^{-2}	0.10
Females		
Pooled first & second studies	1.02×10^{-2}	0.54
Second study only	1.55×10^{-2}	0.11

b. EPA's Exposure Assessment and Preliminary Risk Calculations

A dietary exposure analysis has been performed by HED/SACB assuming a feeding restriction as specified in the draft label. The results of this HED/SACB analysis are included as Appendix 1 [EPA memorandum from S. Schaible (HED/SACB) to S. Lewis/J. Fairfax (FHB/RD), dated 5/13/92].

As noted in Appendix 1, for the proposed used on peanuts:

- The Theoretical Maximum Residue Contribution (TMRC) for the overall U.S. population is 0.000010 mg/kg BW/day, which is approximately 0.1% of the RfD.
- The subgroup most highly exposed, children aged one through six years old, has a TMRC of 0.000027 mg/kg BW/day, which is approximately 0.27% of the RfD.
- The exposure assessment represents an overestimate, since it includes tolerance level residues and 100% of crop treated.

Using the Agency dietary exposure estimates (TMRC in Appendix 1) and the preliminary Q_1^* value of 3.06×10^{-2} $(mg/kg\ BW/day)^{-1}$, (Table 6), Table 7 depicts the life time risks associated with the various exposures.

As shown in Table 7, the group with the highest dietary exposure, children 1-6 years old, have a preliminary lifetime carcinogenic risk estimate of 8.26×10^{-7} (i.e. 0.83×10^{-6}), which is approximately 17% below the 1×10^{-6} de minimis risk acceptable to the Agency.

It is noted that the present estimate of risk is an overestimate due to an overestimation of the exposure (for the reasons discussed in Appendix 1) and also as noted in Appendix 1, due to the assuming of an exposure over 70 years while the temporary tolerance and experimental use permit (EUP) for tebuconazole on peanuts would be only one growing season.

The present de minimis risk assessment for temporary tolerance and EUP for tebuconazole on peanuts (PP#9F3724/2H5628) pertains only to the subject action and may be modified pending further Agency assessment of the carcinogenicity potential of tebuconazole.

C. Conclusion

It is recommended that the EUP and temporary tolerance on peanuts, with feeding restriction as specified in the draft label, be granted to the Registrant. This petition is granted based on the above calculations which indicate that the resulting exposures pose a de minimis risk from dietary exposure.

D. Reference

Miles, Inc. 1992. Dietary Exposure and Risk Assessment for the Use of Tebuconazole on Peanuts. Prepared by C.B. Sandusky, A.C. Katz, S.L. Graham, F.J. Hawk, and J.C. Eickoff (Technical Assessment Systems, Inc., Washington D.C.) for W. Carlson (Miles Inc., Kansas City, MO), dated April 10, 1992.

cc: SACB/HED; Caswell #463.

Table 7. Lifetime risks associated with dietary exposure estimates in Appendix 1[a].

Population Subgroup	TMRC mg/kg BW/day	Preliminary lifetime carcinogenic risk [b]
U.S. Population - 48 States	0.000010	3.06×10^{-7}
U.S. Population - Spring season	0.000010	3.06×10^{-7}
U.S. Population - Summer season	0.000010	3.06×10^{-7}
U.S. Population - Fall season	0.000009	2.75×10^{-7}
U.S. Population - Winter season	0.000009	2.75×10^{-7}
Northeast Region	0.000010	3.06×10^{-7}
North Central Region	0.000010	3.06×10^{-7}
Southern Region	0.000008	2.45×10^{-7}
Western Region	0.000011	3.36×10^{-7}
Hispanics	0.000006	1.84×10^{-7}
Non-hispanic whites	0.000010	3.06×10^{-7}
Non-hispanic blacks	0.000006	1.84×10^{-7}
Non-hispanic others	0.000008	2.45×10^{-7}
Nursing infants (< 1 year old)	0.000002	0.61×10^{-7}
Non-nursing infants (< 1 year old)	0.000003	0.92×10^{-7}
Females (13+ years, pregnant)	0.000007	2.14×10^{-7}
Females (13+ years, nursing)	0.000010	3.06×10^{-7}
Children (1-6 years old)	0.000027	8.26×10^{-7}
Children (7-12 years old)	0.000020	6.12×10^{-7}
Males (13-19 years old)	0.000010	3.06×10^{-7}
Females (13-19 years old, not pregnant or nursing)	0.000007	2.14×10^{-7}
Males ($\geq$ 20 years old)	0.000006	1.83×10^{-7}
Females ($\geq$ 20 years old, not pregnant or nursing)	0.000005	1.53×10^{-7}

[a] TMRC data from Table 2 of Appendix 1.

[b] Carcinogenic risk calculated by reviewer as follows:
Carcinogenic risk = TMRC x Q_1^*; where $Q_1^* = 3.06 \times 10^{-2}$ $(mg/kg\ BW/day)^{-1}$

10

Appendix 1

CASWELL FILE

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

MEMORANDUM

MAY 13 1992

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Dietary Exposure Analysis and De Minimis Risk Assessment for Temporary Tolerance and Experimental Use Permit for Tebuconazole on Peanuts (PP#9F3724/2H5628)

FROM: Stephen A. Schaible
Dietary Exposure Section
SACB/HED (H7509C)

TO: Susan T. Lewis/Julie Fairfax, PM 21
Fungicide-Herbicide Branch
Registration Division (H7505C)

THROUGH: James P. Kariya, Chief
Dietary Exposure Section
Health Effects Division

Action Requested

The Dietary Exposure Section (DES) was requested by Registration Division to perform a dietary exposure analysis and carcinogenic risk assessment for the chemical tebuconazole, to see whether the Agency's de minimis value for negligible risk would be exceeded by the carcinogenic risk posed by this Experimental Use Permit (EUP) and temporary tolerance on peanuts. Tebuconazole is a new chemical with no registered uses.

Since it is only recently submitted data that suggest this chemical may be a carcinogen, it has not yet gone to the HED Carcinogenicity Peer Review Committee, nor has its possible upper bound carcinogenic potency factor (Q_1^*) been determined. Without the appropriate Q*, a carcinogenic risk analysis cannot be performed by DES. In order to respond to the expedited review request by RD, an alternate analysis was performed instead, in which DES assumed the de minimis value of 10^{-6} for the carcinogenic risk and calculated the Q* that would be necessary to arrive at that de minimis value given the exposure value contributed by the EUP on peanuts.

Toxicological Endpoints

The Dietary Risk Evaluation System (DRES) chronic exposure analysis used a Reference Dose (RfD) of 0.01 mg/kg body weight/day, based on a no observed effect level (NOEL) of 1 mg/kg bwt/day and an uncertainty factor of 100. The RfD is based on a one year feeding

study in dogs which demonstrated as effects lenticular and corneal opacity and hepatic toxicity. This RfD has been approved by the HED RfD Peer Review Committee (3/5/91).

Toxicology Branch II recently received 6(a)(2) data concerning an oncogenicity study in mice which showed significant incidences of carcinomas and adenomas at the high dose in males and females (personal communication, A. Protzel, 5/7/92), but at this time tebuconazole is not considered a carcinogen.

Residue Information

The food use evaluated in this analysis was the temporary tolerance and EUP for tebuconazole on peanuts. The commodities listings in DRES which relate to peanuts are "peanuts-whole" and "peanuts- oil". For the purpose of this temporary tolerance request, tolerances reflecting secondary residues in animal commodities from the use of peanuts as a feed item are not necessary. Since the draft label dated 10/1/91 included a restriction against feeding treated peanut hay/vines to livestock (G. Otakie, 3/18/92), secondary residues are not expected in animal commodities . Tebuconazole is a new chemical and has no registered uses. A summary of the residue information used in this analysis is attached as Table 1.

Exposure Analysis

The DRES chronic exposure analysis used tolerance level residues and 100% crop treated to estimate the Theoretical Maximum Residue Contribution (TMRC) for the overall U.S. population and 22 population subgroups. A list of the TMRCs and their representations as percentages of the RfD are attached as Table 2.

The TMRC for the overall population from the proposed use on peanuts is 0.000010 mg/kg bwt/day, which represents approximately 0.1% of the RfD. The subgroup most highly exposed, children aged one through six years old, has a TMRC of 0.000027 mg/kg bwt/day, or 0.27% of the RfD. None of the subgroups has a TMRC that exceeds even one percent of the RfD, so it appears that the chronic risk from this EUP is minimal.

De Minimis Risk Assessment

As was mentioned before, no upper bound potency factor (Q*) has been determined for tebuconazole. Upper bound carcinogenic risk is calculated using the formula

Upper bound carcinogenic risk = Exposure (TMRC) x Q*

If the Q* is unknown, it is not possible to calculate the upper bound carcinogenic risk. However, by assuming the Agency's de minimis value of 10^{-6} as the upper bound carcinogenic risk value in the equation, we can arrive at a "reference Q*", the Q* which would be necessary to contribute a cancer risk of 10^{-6}, given the known

exposure from the EUP on peanuts. In other words, we reshuffled the equation to read as follows

Reference Q* = Carcinogenic risk (10^{-6})/ Exposure (TMRC)

The Q* arrived at using this analysis is the highest value that could be determined for the upper bound potency factor and still have the cancer risk posed by this EUP not exceed the de minimis value. Using this formula, the "reference Q*" for this action is approximately 0.1 $(mg/kg/day)^{-1}$. If the Q* that Toxicology Branch and the statisticians in SACB determine is less than this value, the resulting upper bound carcinogenic risk will be less than the de minimis value.

There are several assumptions that possibly make this "reference Q*" a more sensitive value than it actually should be. Assumptions made in calculating the exposure value, such as tolerance level residues and 100 percent of crop treated, in all likelihood overestimate the exposure, especially the percent of crop treated assumption, since the acreage that this chemical will be applied to through this EUP probably only represents a small percent of the total acreage that peanuts are grown on. Also, this risk assessment was performed assuming exposure over 70 years while the duration of the temporary tolerance and experimental use permit for tebuconazole on peanuts would be only one growing season. If there were a way to incorporate refinements to these sources of possible overestimation, one would expect that the reference Q* would be a higher value, thus allowing the determined Q* to be more potent than 0.1 $(mg/kg/day)^{-1}$ and still not contribute to an upper bound carcinogenic risk of more than 10^{-6}.

Attachments

cc: DES, Tox 1, CBTS, C. Frick, Caswell # 463P

TABLE 1

CHEMICAL INFORMATION FOR CASWELL NUMBER 999ZZZ DATE: 05/07/92 PAGE: 1

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
999ZZZ(TEBUCONAZOLE) Caswell #999ZZZ CAS No. A.I. CODE: CFR No. 180.	NOEL= 1.0000 mg/kg 0.00 ppm LEL= 0.0000 mg/kg 0.00 ppm ONCO:		PADI UF -->100 OPP RfD= 0.010000 EPA RfD= 0.000000	test run for temp tol for tebuconazole on peanuts	

FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED
15006AA	PEANUTS-WHOLE	9G3817	0.100000		
270070A	PEANUTS-OIL	2H5628	0.500000		

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
999ZZZ(TEBUCONAZOLE) Caswell #999ZZZ CAS No. A.I. CODE: CFR No. 180.	NOEL= 1.0000 mg/kg 0.00 ppm LEL= 0.0000 mg/kg 0.00 ppm ONCO:		PADI UF -->100 OPP RfD= 0.010000 EPA RfD= 0.000000	test run for temp tol for tebuconazole on peanuts	

LISTING OF EXPOSURE BY RAC FOR: U.S. POPULATION - 48 STATES

FOOD CODE	FOOD NAME	TOLERANCE (PPM) NEW	TOLERANCE (PPM) PENDING	TOLERANCE (PPM) PUBLISHED	EXISTING TOLERANCES TMRC (UG/KG/DAY)	EXISTING TOLERANCES %RfD	NEW & PENDING TOLERANCES TMRC (UG/KG/DAY)	NEW & PENDING TOLERANCES %RFD
15006AA	PEANUTS-WHOLE	0.10000					0.006958	0.0695
270070A	PEANUTS-OIL	0.50000					0.002613	0.0261
CROP GROUP TOTALS FOR LEGUME VEGETABLES:							0.009571	0.0957

GRAND TOTAL TMRC: 0.009571 GRAND TOTAL % OF THE RfD: 0.0957

POPULATION SUBGROUP TOTALS	0.000000	0.0000	0.009571	0.0957

POPULATION TOTAL TMRC 0.009571 POPULATION TOTAL % OF THE RfD 0.0957

Q_1^* × exposure = upper bound carcinogenic risk

$$\text{reference } Q_1^* = \frac{\text{upper bound carcinogenic risk}}{\text{exposure (TmRC)}}$$

$$= \frac{10^{-6}}{\sim 10^{-5}}$$

$$= 0.1 \text{ (mg/kg/day)}^{-1}$$

16

TABLE 2

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS DATE: 05/07/92 PAGE:

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
999222(TEBUCONAZOLE) Caswell #999222 CAS No. A.I. CODE: CFR No. 180.	NOEL= 1.0000 mg/kg 0.00 ppm LEL= 0.0000 mg/kg 0.00 ppm ONCO:		PADI UF -->100 OPP RfD= 0.010000 EPA RfD= 0.000000	test run for temp tol for tebuconazole on peanuts	

POPULATION SUBGROUP	TOTAL TMRC (MG/KG BODY WEIGHT/DAY) CURRENT TMRC*	NEW TMRC**	NEW TMRC AS PERCENT OF RFD	DIFFERENCE AS PERCENT OF RFD	EFFECT OF ANTICIPATED RESIDUES ARC	%RFD
U.S. POPULATION - 48 STATES	0.000000	0.000010	0.095710	0.095710		
U.S. POPULATION - SPRING SEASON	0.000000	0.000010	0.098220	0.098220		
U.S. POPULATION - SUMMER SEASON	0.000000	0.000010	0.103360	0.103360		
U.S. POPULATION - FALL SEASON	0.000000	0.000009	0.092520	0.092520		
U.S. POPULATION - WINTER SEASON	0.000000	0.000009	0.088720	0.088720		
NORTHEAST REGION	0.000000	0.000010	0.101130	0.101130		
NORTH CENTRAL REGION	0.000000	0.000010	0.100000	0.100000		
SOUTHERN REGION	0.000000	0.000008	0.078640	0.078640		
WESTERN REGION	0.000000	0.000011	0.111720	0.111720		
HISPANICS	0.000000	0.000006	0.057530	0.057530		
NON-HISPANIC WHITES	0.000000	0.000010	0.104470	0.104470		
NON-HISPANIC BLACKS	0.000000	0.000006	0.058870	0.058870		
NON-HISPANIC OTHERS	0.000000	0.000008	0.080160	0.080160		
NURSING INFANTS (< 1 YEAR OLD)	0.000000	0.000002	0.019130	0.019130		
NON-NURSING INFANTS (< 1 YEAR OLD)	0.000000	0.000003	0.034070	0.034070		
FEMALES (13+ YEARS, PREGNANT)	0.000000	0.000007	0.072230	0.072230		
FEMALES 13+ YEARS, NURSING	0.000000	0.000010	0.101440	0.101440		
CHILDREN (1-6 YEARS OLD)	0.000000	0.000027	0.268600	0.268600		
CHILDREN (7-12 YEARS OLD)	0.000000	0.000020	0.200080	0.200080		
MALES (13-19 YEARS OLD)	0.000000	0.000010	0.102390	0.102390		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.000000	0.000007	0.074680	0.074680		
MALES (20 YEARS AND OLDER)	0.000000	0.000006	0.064050	0.064050		
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.000000	0.000005	0.049860	0.049860		

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