5.13.92

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
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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

TABLE 2

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS DATE: 05/07/92 PAGE: 1

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	

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.

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS DATE: 05/07/92 PAGE: 1

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
999ZZZ(TEBUCONAZOLE) Caswell ~~#999ZZZ~~ 463P 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
27007OA	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

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

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

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

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		