

US EPA ARCHIVE DOCUMENT



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

APR 10 1995

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Dietary Exposure Analysis for Fenbuconazole in/on existing stone fruits, pecans and bananas using a recalculated Q_1^* of 1.06×10^{-2} (mg/kg/day)⁻¹ PP#2FO4154.

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

Through: Elizabeth Doyle, Section Head
Dietary Risk Evaluation Section
SAB/Health Effects Division

Elizabeth A. Doyle

TO: C. Giles-Parker/J. Stone, PM Team 22
Registration Division (7505C)

WSP

Action Requested

Provide a dietary exposure analysis for the use of fenbuconazole in/on existing crops using a recalculated Q_1^* of 1.06×10^{-2} .

At a March 14, 1995 Agency meeting with Rohm and Haas, it was decided that the fenbuconazole Q_1^* should be recalculated based upon the new 3/4's power scaling factor instead of the previous 2/3's power (See memo, B. Fisher, 3/15/95). RD requested a new DRES run be performed incorporating the recalculated value in an attempt to grant the original petition on bananas.

Discussion

Under petition numbers 1F3995 and 1F3989, DRES had previously conducted a dietary analysis for proposed uses of fenbuconazole on pecans, bananas, and stone fruits (Except plums and prunes) (See memo, T. Chin, 11/22/94). The oncogenic risk for the three combined uses was 1.04×10^{-5} , which exceeded the 1×10^{-6} oncogenic risk generally considered negligible by the Agency. Under PP# 1F3898, the registrant then proposed pursuing the stone fruit tolerance only

12.8% of the stone fruit

COMMERCIAL/FINANCIAL INFORMATION IS NOT INCLUDED



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

crop, with a three year time-limited tolerance. The results of that carcinogenic analysis resulted in a cancer risk of 1.28×10^{-6} , which also exceeded the Agency's level of concern (See memo, B. Doyle, 2/8/95). Consequently, the current petition requested that another DRES analysis be performed for existing stone fruit (12.8% of crop treated) and proposed pecan and banana tolerances using a recalculated Q_1^* ($1.06 \times 10^{-2} \text{ mg/kg/day}$)⁻¹; results of this analysis follow.

Toxicological Endpoint:

The Reference Dose (RfD) used in the analysis is 0.03 mg/kg bwt/day, based on a NOEL of 3.03 mg/kg bwt/day from a two year rat feeding study with an uncertainty factor of 100 that demonstrated decreased body weights in females and increased liver weights with centrilobular to midzonal hepatocellular enlargement and vacuolation in both sexes (See memo, G. Ghali, 4/30/93).

Fenbuconazole has been classified as a group C (possible human carcinogen) based on thyroid tumors in male rats and liver tumors in female mice.

A Q_1^* of $1.06 \times 10^{-2} \text{ (mg/kg/day)}^{-1}$ was used to estimate the carcinogenic risk due to dietary exposure.

Residue Information

Since this is a new chemical, there are no published tolerances for fenbuconazole in 40 CFR. Tolerance level residues and 100 percent crop treated information were used for all commodities except stone fruits, which used the proposed tolerance and 12.8 % crop treated information. The analysis included time limited tolerances on stone fruits and pecans.

Results

A summary of the residue information considered in this analysis is attached as Table 1. A DRES carcinogenic analysis was performed to estimate the Anticipated Residue Contribution (ARC) for the general population. Summaries of the ARCs and their representations as percentages of the Reference Dose (RfD) for the general population and 22 subgroups are included as Table 2. Summaries of the carcinogenic risk and of the commodity contribution by raw agricultural commodity (RAC) for the overall U.S. population are attached as Table 3.

Upper Bound Carcinogenic Exposure:

Based on a Q_1^* of $0.01 \text{ (mg/kg/day)}^{-1}$ the upper bound cancer risk was calculated to be 9.0×10^{-7} , contributed by all the proposed and time limited uses for fenbuconazole.

Conclusions

The above analysis demonstrates that using the recalculated cancer potency factor and percent crop treated data for stone fruits incorporated into the analysis, the time limited uses on pecans and bananas and the proposed tolerance on stone fruits results in a level of risk below that which is generally considered of concern by the Agency.

Attachments

cc: DRES; Caswell 723Q; RCAB;

TABLE 1

DATE: 03/22/95

ANTICIPATED RESIDUE INFORMATION FOR CASWELL NUMBER 723Q

PAGE: 1

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Fenbutazone (Fenethanil)	2yr feeding - Rat	Decr body wts (F); incr liver wts with centrilobular to midzonal hepatocellular enlargement & vacuolation (M&F).	PADI UF -->100 OPP RfD= 0.0300000 EPA RfD= 0.0000000	Developmental tox- rabbit (current study maybe up-graded) Chemical was referred to HED Carcinogenicity Peer Review Committee.	RfD/PR reviewed 04/15/93 RfD/PR reviewed 04/29/93
Caswell #723Q	NOEL= 3.0300 mg/kg 80.00 ppm				
CAS No. 114369-43-6	LEL= 30.6200 mg/kg 800.00 ppm				
A.I. CODE: 129011	ONCO: Pending				
CFR No.					

FOOD CODE	FOOD	FOOD FORM	PET.#	TOLERANCE (ppm)	ANTICIPATED RESIDUE (ppm)	AR STATISTIC TYPE	% CROP TREATED	RES. VALUE USED IN TAS RUN (ppm)
05008AA	PECANS	10 RAW-FRESH OR NFS	1F03995	A 0.100000	0.100000		100.00	0.100000
05008AA	PECANS	21 COOKED-NFS	1F03995	A 0.100000	0.100000		100.00	0.100000
05008AA	PECANS	22 COOKED-FRESH-BAKED	1F03995	A 0.100000	0.100000		100.00	0.100000
05008AA	PECANS	23 COOKED-FRESH-BOILED	1F03995	A 0.100000	0.100000		100.00	0.100000
05008AA	PECANS	62 COOKED-FRESH OR FROZEN-BAKED	1F03995	A 0.100000	0.100000		100.00	0.100000
05001AA	APRICOTS-FRESH	10 RAW-FRESH OR NFS	1F03989	N 2.000000	2.000000		12.80	0.256000
05001AA	APRICOTS-FRESH	21 COOKED-NFS	1F03989	N 2.000000	2.000000		12.80	0.256000
05001AA	APRICOTS-FRESH	31 COOKED-FRESH OR CANNED	1F03989	N 2.000000	2.000000		12.80	0.256000
05001DA	APRICOTS-DRIED	10 RAW-FRESH OR NFS	1F03989	N 2.000000	2.000000		12.80	0.256000
05001DA	APRICOTS-DRIED	22 COOKED-FRESH-BAKED	1F03989	N 2.000000	2.000000		12.80	0.256000
05002AA	CHERRIES-FRESH	10 RAW-FRESH OR NFS	1F03989	N 2.000000	2.000000		12.80	0.256000
05002AA	CHERRIES-FRESH	21 COOKED-NFS	1F03989	N 2.000000	2.000000		12.80	0.256000
05002AA	CHERRIES-FRESH	31 COOKED-FRESH OR CANNED	1F03989	N 2.000000	2.000000		12.80	0.256000
05002AA	CHERRIES-FRESH	62 COOKED-FRESH OR FROZEN-BAKED	1F03989	N 2.000000	2.000000		12.80	0.256000
05002DA	CHERRIES-DRIED	00 NOT SPECIFIED (NO CONSUMPTION)	1F03989	N 2.000000	2.000000		12.80	0.256000
05002JA	CHERRIES-JUICE	15 RAW-FRESH OR CANNED	1F03989	N 2.000000	2.000000		12.80	0.256000
05002JA	CHERRIES-JUICE	21 COOKED-NFS	1F03989	N 2.000000	2.000000		12.80	0.256000
05003AA	NECTARINES	10 RAW-FRESH OR NFS	1F03989	N 2.000000	2.000000		12.80	0.256000
05004AA	PEACHES-FRESH	10 RAW-FRESH OR NFS	1F03989	N 2.000000	2.000000		12.80	0.256000
05004AA	PEACHES-FRESH	21 COOKED-NFS	1F03989	N 2.000000	2.000000		12.80	0.256000
05004AA	PEACHES-FRESH	31 COOKED-FRESH OR CANNED	1F03989	N 2.000000	2.000000		12.80	0.256000
05004DA	PEACHES-DRIED	51 COOKED-CANNED	1F03989	N 2.000000	2.000000		12.80	0.256000
05004DA	PEACHES-DRIED	10 RAW-FRESH OR NFS	1F03989	N 2.000000	2.000000		12.80	0.256000
05004DA	PEACHES-DRIED	22 COOKED-NFS	1F03989	N 2.000000	2.000000		12.80	0.256000
06002AA	BANANAS-UNSPEC	22 COOKED-FRESH-BAKED	2F04154	A 0.050000	0.050000		100.00	0.050000
06002AB	BANANAS-FRESH	10 RAW-FRESH OR NFS	2F04154	A 0.050000	0.050000		100.00	0.050000
06002AB	BANANAS-FRESH	21 COOKED-NFS	2F04154	A 0.050000	0.050000		100.00	0.050000
06002AB	BANANAS-FRESH	31 COOKED-FRESH OR CANNED	2F04154	A 0.050000	0.050000		100.00	0.050000
06002DA	BANANAS-DRIED	10 RAW-FRESH OR NFS	2F04154	A 0.050000	0.050000		100.00	0.050000
06002DA	BANANAS-DRIED	21 COOKED-NFS	2F04154	A 0.050000	0.050000		100.00	0.050000
06016AA	PLANTAINS	21 COOKED-NFS	2F04154	A 0.050000	0.050000		100.00	0.050000
06016AA	PLANTAINS	23 COOKED-FRESH-BOILED	2F04154	A 0.050000	0.050000		100.00	0.050000
06016AA	PLANTAINS	25 COOKED-FRESH-FRIED	2F04154	A 0.050000	0.050000		100.00	0.050000

TABLE 2

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Fenbutazone (Fenethanil) Caswell #723q CAS No. 114369-43-6 A.I. CODE: 129011 CFR No.	2yr feeding - rat NOEL= 3.0300 mg/kg 80.00 ppm LEL= 30.6200 mg/kg 800.00 ppm ONCO: Pending	Decr body wts (F); incr liver wts with centrilobular to midzonal hepatocellular enlargement & vacuolation (M&F).	PADI UF -->100 OPP Rfd= 0.0300000 EPA Rfd= 0.0000000	Developmental tox- rabbit (current study maybe up-graded) Chemical was referred to HED Carcinogenicity Peer Review Committee.	Rfd/PR reviewed 04/15/93 Rfd/PR reviewed 04/29/93

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	%RFD
U.S. POPULATION - 48 STATES	0.000000	0.000616	2.054127	2.054127	2.054127	0.000089	0.29786
U.S. POPULATION - SPRING SEASON	0.000000	0.000630	2.098630	2.098630	2.098630	0.000090	0.30154
U.S. POPULATION - SUMMER SEASON	0.000000	0.000961	3.202823	3.202823	3.202823	0.000134	0.44554
U.S. POPULATION - FALL SEASON	0.000000	0.000427	1.423033	1.423033	1.423033	0.000065	0.21776
U.S. POPULATION - WINTER SEASON	0.000000	0.000449	1.495480	1.495480	1.495480	0.000068	0.22706
NORTHEAST REGION	0.000000	0.000646	2.151707	2.151707	2.151707	0.000093	0.30954
NORTH CENTRAL REGION	0.000000	0.000656	2.187720	2.187720	2.187720	0.000094	0.31246
SOUTHERN REGION	0.000000	0.000461	1.536520	1.536520	1.536520	0.000068	0.22729
WESTERN REGION	0.000000	0.000788	2.625653	2.625653	2.625653	0.000115	0.38329
HISPANICS	0.000000	0.000671	2.238143	2.238143	2.238143	0.000103	0.34491
NON-HISPANIC WHITES	0.000000	0.000635	2.117107	2.117107	2.117107	0.000092	0.30605
NON-HISPANIC BLACKS	0.000000	0.000472	1.572533	1.572533	1.572533	0.000067	0.22274
NON-HISPANIC OTHERS	0.000000	0.000584	1.947640	1.947640	1.947640	0.000090	0.29873
NURSING INFANTS (< 1 YEAR OLD)	0.000000	0.003083	10.277767	10.277767	10.277767	0.000435	1.44953
NON-NURSING INFANTS (< 1 YEAR OLD)	0.000000	0.005216	17.386597	17.386597	17.386597	0.000715	2.38309
FEMALES (13+ YEARS, PREGNANT)	0.000000	0.000458	1.526680	1.526680	1.526680	0.000064	0.21458
FEMALES 13+ YEARS, NURSING	0.000000	0.000585	1.950250	1.950250	1.950250	0.000083	0.27799
CHILDREN (1-6 YEARS OLD)	0.000000	0.001444	4.812677	4.812677	4.812677	0.000217	0.72472
CHILDREN (7-12 YEARS OLD)	0.000000	0.000905	3.017387	3.017387	3.017387	0.000130	0.43168
MALES (13-19 YEARS OLD)	0.000000	0.000397	1.323817	1.323817	1.323817	0.000058	0.19395
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.000000	0.000398	1.325973	1.325973	1.325973	0.000057	0.19052
MALES (20 YEARS AND OLDER)	0.000000	0.000357	1.189397	1.189397	1.189397	0.000052	0.17464
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.000000	0.000433	1.444720	1.444720	1.444720	0.000062	0.20763

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

5

TABLE 3

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Fenbutazone (Fenethanil) Caswell #7230 CAS No. 114369-43-6 A.I. CODE: 129011 CFR No.	2yr feeding - rat NOEL= 3.0300 mg/kg 80.00 ppm LEL= 30.6200 mg/kg 800.00 ppm ONCO: Pending	Decr body wts (F); incr liver wts with centrilobular to midzonal hepatocellular enlargement & vacuolation (M&F).	PADI UF -->100 OPP Rfd= 0.030000 EPA Rfd= 0.000000	Developmental tox- rabbit (current study maybe up-graded) Chemical was referred to HED Carcinogenicity Peer Review Committee.	Rfd/PR reviewed 04/15/93 Rfd/PR reviewed 04/29/93

COMMODITY CONTRIBUTION BY RAC FOR: U.S. POPULATION - 48 STATES

FOOD CODE	FOODNAME/FOODFORM	TOLERANCE (PPM)	TYPE	TMRC (UG/KG/DAY)	%RFD	TMRC ONCO RISK	ANTICIPATED RESIDUE (PPM)	ARC (UG/KG/DAY)	%RFD	ARC ONCO RISK
06002AA	BANANAS-UNSPECIFIED 22 COOKED-FRESH-BAKED	0.050	A	0.000165	0.001	0.00000000165	0.05000	0.000165	0.001	0.00000000165
06002AB	BANANAS-FRESH 10 RAW-FRESH OR NFS 21 COOKED-NFS 31 COOKED-FRESH OR CANNED	0.050	A	0.011202	0.037	0.00000011202	0.05000	0.009888 0.000270 0.001044	0.033 0.001 0.003	0.0000009888 0.0000000270 0.00000001044
06002DA	BANANAS-DRIED 10 RAW-FRESH OR NFS 21 COOKED-NFS	0.050	A	0.000088	0.000	0.00000000088	0.05000	0.000027 0.000060	0.000 0.000	0.00000000027 0.00000000060
06016AA	PLANTAINS 21 COOKED-NFS 23 COOKED-FRESH-BOILED 25 COOKED-FRESH-FRIED	0.050	A	0.000082	0.000	0.00000000082	0.05000	0.000000 0.000040 0.000042	0.000 0.000 0.000	0.00000000000 0.00000000040 0.00000000042
CROP GROUP TOTALS FOR UNSPECIFIED:										
		2.000	N	0.011537	0.038	0.00000011537	0.05000	0.011536	0.038	0.00000011536
05001AA	APRICOTS-FRESH 10 RAW-FRESH OR NFS 21 COOKED-NFS 31 COOKED-FRESH OR CANNED	2.000	N	0.067379	0.225	0.00000067379	0.25600	0.001463 0.001992 0.005170	0.005 0.007 0.017	0.00000001463 0.00000001992 0.000000005170
05001DA	APRICOTS-DRIED 10 RAW-FRESH OR NFS 22 COOKED-FRESH-BAKED	2.000	N	0.004848	0.016	0.00000004848	0.25600	0.001888 0.001129 0.003211 0.002008	0.006 0.004 0.011 0.007	0.00000001888 0.00000001129 0.000000003211 0.000000002008
05002AA	CHERRIES-FRESH 10 RAW-FRESH OR NFS 21 COOKED-NFS 31 COOKED-FRESH OR CANNED 62 COOKED-FRESH OR FROZEN-BAKED	2.000	N	0.064351	0.215	0.00000064351	0.25600	0.000526 0.000094	0.002 0.000	0.00000000526 0.00000000094
05002DA	CHERRIES-DRIED 00 NOT SPECIFIED (NO CONSUMPTION)	2.000	N	0.000008	0.000	0.00000000008	0.25600	0.001888 0.001129 0.003211 0.002008	0.006 0.004 0.011 0.007	0.00000001888 0.00000001129 0.000000003211 0.000000002008
05002JA	CHERRIES-JUICE 15 RAW-FRESH OR CANNED 21 COOKED-NFS	2.000	N	0.010224	0.034	0.00000010224	0.25600	0.001200 0.000108	0.004 0.000	0.000000001200 0.000000000108
05003AA	NECTARINES 10 RAW-FRESH OR NFS 10 RAW-FRESH OR NFS 21 COOKED-NFS	2.000	N	0.025932	0.086	0.00000025932	0.25600	0.003319	0.011	0.000000003319
05004AA	PEACHES-FRESH 10 RAW-FRESH OR NFS 21 COOKED-NFS 31 COOKED-FRESH OR CANNED 51 COOKED-CANNED	2.000	N	0.430783	1.436	0.00000430783	0.25600	0.025721 0.002518 0.020450 0.006451	0.086 0.008 0.068 0.022	0.000000025721 0.000000002518 0.000000020450 0.000000006451
05004DA	PEACHES-DRIED 10 RAW-FRESH OR NFS	2.000	N	0.000694	0.002	0.00000000694	0.25600	0.000047	0.000	0.000000000047

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Fenbutazone (Fenethamil) Caswell #7230 CAS No. 114369-43-6 A.I. CODE: 129011 CFR No.	2yr feeding - rat NOEL= 3.0300 mg/kg 80.00 ppm LEL= 30.6200 mg/kg 800.00 ppm ONCO: Pending	Decr body wts (F); incr liver wts with centrilob- ular to midzonal hepato- cellular enlargement & vacuolation (M&F).	PADI UF -->100 OPP RfD= 0.0300000 EPA RfD= 0.0000000	Developmental tox- rabbit (current study maybe up- graded) Chemical was referred to HED Carcinogenicity Peer Review Committee.	RfD/PR reviewed 04/15/93 RfD/PR reviewed 04/29/93

COMMODITY CONTRIBUTION BY RAC FOR: U.S. POPULATION - 48 STATES

FOOD CODE	FOODNAME/FOODFORM	TOLERANCE (PPM)	TMRC TYPE (UG/KG/DAY)	%RFD	TMRC ONCO RISK	ANTICIPATED RESIDUE (PPM)	ARC (UG/KG/DAY)	%RFD	ARC ONCO RISK
	21 COOKED-NFS		0.604219	2.014	0.00000604219	0.25600	0.000042	0.000	0.00000000042
CROP GROUP TOTALS FOR STONE FRUITS:									
03008AA	PECANS	0.100	A	0.000482	0.00000000482	0.10000	0.000068	0.000	0.00000000068
	10 RAW-FRESH OR NFS					0.10000	0.000006	0.000	0.00000000006
	21 COOKED-NFS					0.10000	0.000111	0.000	0.00000000111
	22 COOKED-FRESH-BAKED					0.10000	0.000235	0.001	0.00000000235
	23 COOKED-FRESH-BOILED					0.10000	0.000063	0.000	0.00000000063
	62 COOKED-FRESH OR FROZEN-BAKED					0.10000	0.000063	0.000	0.00000000063
CROP GROUP TOTALS FOR TREE NUTS:									
			0.000482	0.002	0.00000000482	0.000000	0.000483	0.002	0.00000000483

GRAND TOTALS FOR U.S. POPULATION - 48 STATES

0.616238	2.054	0.00000616238	0.089357	0.298	0.00000089357
----------	-------	---------------	----------	-------	---------------

TOLERANCE TYPE: N=NEW; A=PENDING; P=PUBLISHED
 TMRC=THEORETICAL MAXIMUM RESIDUE CONTRIBUTION
 ARC = ANTICIPATED RESIDUE CONTRIBUTION
 RFD = REFERENCE DOSE