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OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

MEMORANDUM

**SUBJECT:** New Chemical/First Permanent Food Use:  
Carcinogenic and Chronic Dietary Risk Analysis  
for the Proposed Use of Fenbuconazole  
(Fenethanil) a.k.a Indar™ 2F  
in or on bananas.  
(PC Code 129011; CAS No. 114369-43-6;  
Caswell # 723Q)

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

*Teung F. Chin*

**TO:** Cynthia Giles-Parker / Dolphine Wilson, PM-22  
Fungicide-Herbicide Branch  
Registration Division (7505C)

**THROUGH:** Elizabeth Doyle, Ph.D., Acting Section Head  
DRES/SAB  
Health Effects Division

*E.A. Doyle*

Action Requested

The Fungicide-Herbicide Branch has requested that a Dietary Risk Evaluation System (DRES) analysis be performed assessing the chronic dietary and carcinogenic risks resulting from proposed use of the herbicide fenbuconazole ((ANSI/ISO) or RH-7592 [alpha-(2-(4-chlorophenyl)-ethyl)-alpha-phenyl-3-(1H-1,2,4-triazole)-1-propanenitrile] and its metabolites RH-9129 and RH-9130, at a tolerance of 0.3 ppm on raw agricultural commodity bananas (whole fruit) of which not more than 0.05 ppm is contained in the banana pulp (8/1/94 and 8/8/94 CBTS memos W.D. Wassell to C. Giles-Parker and A. Kocialski). Rohm and Haas Company, Philadelphia, PA filed the petition for permanent tolerance (PP# 2F04154) amended 3/31/94, 6/30/94, and 7/19/94.



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## Discussion

1. Toxicological Information: For chronic toxicity, the reference dose (RfD) (rats, strain not indicated) was 0.03 mg/kg/day, based on body weight decrease in females and increased liver weights with centrilobular to midzonal hepatocellular enlargement and vacuolization in males and females. An uncertainty factor of 100 was used for the inter-species extrapolation and intra-species variability (4/25/94 TB2 memo; M. Van Gamert to J. Kariya et al. and 7/7/93 RfD/QA Peer Review Memo; G. Z. Ghali to C. Giles-Parker).

No acute dietary risk assessment was necessary (4/25/94 TB2 memo; M. Van Gamert to J. Kariya et al.).

The chemical was classified as a Group C carcinogen (possible human carcinogen) (4/25/94 TB2 memo; M. Van Gamert to J. Kariya et al.). The unit risk,  $Q_1^*$  (mg/kg/day)<sup>-1</sup> of fenbuconazole, based upon male rat (Sprague-Dawley) thyroid follicular cell (adenomas and/or carcinomas) tumor rates, is  $1.65 \times 10^{-2}$  (mg/kg/day)<sup>-1</sup> in human equivalents (2/7/94 SAB memo; H. M. Pettigrew to S. Williams).

2. Residue Information: Bananas and plantain were the food uses evaluated in this analysis. Since this is a new chemical, there are no tolerances listed in §186 for meat, milk, poultry and eggs covering possible secondary residues resulting from feed additives and no § 185 tolerances, resulting its from use as a food additive. A new tolerance, set at 0.05 ppm in the pulp was incorporated into the DRES for the following foods: bananas - fresh; bananas - unspecified; bananas - dried; and plantains. Not included in the assessment was 0.3 ppm since it relates to the whole banana (i.e. with skin on). A summary of the residues used in the chronic exposure analysis is attached as Table 1.

Exposures being calculated in this analysis are from fenbuconazole (RH-7592) and its metabolites RH-9129 and RH-9130, expressed as parent equivalent residues (8/1/94 and 8/8/94 CBTS memos W.D. Wassell to C. Giles-Parker and A. Kocialski). It is also noted that CBTS recommended a tolerance with an expiration date only, at this time (8/8/94 CBTS memo W.D. Wassell to C. Giles-Parker and A. Kocialski). For a permanent tolerance, samples from additional field trials should be analyzed for the metabolite RH-4911 in addition to the other metbolites RH-9129 and RH-9130.

No processing studies were mentioned in the CBTS memos.

i. Percent Crop Treated - No percent crop treated information was utilized for the carinogenic risk assessment 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 bananas and plantains were treated with fenbuconazole.

ii. Anticipated Residues (AR) - No anticipated residues (AR) were utilized for the carcinogenic risk assessment and chronic exposure analyses. None would be available since this is a new chemical/new use pattern.

## Discussion of Results

### 1. Chronic Exposure

The DRES chronic exposure analysis used tolerance level residues and 100 percent crop treated to estimate the Theoretical Maximum Residue Contribution (TMRC) for the overall U.S. population and 22 population subgroups. Because fenbuconazole 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 as 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 2. It should be noted again that the residue of interest in this analysis is the parent compound (RH7592) and the two metabolites, RH-9129 and RH-9130.

The TMRC from the proposed new use of fenbuconazole for the general population of the 48 states is 0.000011 mg/kg bwt/day, which represents less than 1% of the RfD. The TMRC for the most exposed subgroups, non-nursing infants (< 1 year old), nursing infants (< 1 year old) and children (1-6 years old), was, respectively, 0.000054, 0.000046, and 0.000036 mg/kg bwt/day; neither exposure scenario exceeds 1% of the RfD. Therefore, minimal risk is expected from chronic dietary intake of fenbuconazole since the RfD is not exceeded for either the general population or any subgroup.

### 2. Carcinogenic Risk

Upper bound cancer risk from the proposed use of fenbuconazole on bananas does not exceed the de minimis value of  $10^{-6}$  that the Agency generally considers negligible. Table 3 provides the total oncogenic risk from each commodity for the entire U. S. Population (48 states). A value of  $1.89 \times 10^{-7}$  was derived.

## Attachments

cc: DRES, FHB, CCB, Tox 2, CBTS, Caswell # 723Q

TABLE 1: Food-Tolerances

CHEMICAL INFORMATION FOR CASWELL NUMBER 723Q DATE: 10/20/94 PAGE: 1

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES		DATA GAPS/COMMENTS	STATUS
			PADI	UF		
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).	OPP RfD= 0.030000 EPA RfD= 0.000000	-->100	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

FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM)		
			NEW	PENDING	PUBLISHED
06002AA	BANANAS-UNSPECIFIED	2F04154	0.050000		
06002AB	BANANAS-FRESH	2F04154	0.050000		
06002DA	BANANAS-DRIED	2F04154	0.050000		
06106AA	PLANTAINS	2F04154	0.050000		

4

TABLE 2: Theoretical Maximum Residue Contributions

DATE: 10/20/94

PAGE: 1

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Fenbutazone (Fenethaniol) 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= 0.0300000 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)		NEW TMRC AS PERCENT OF RFD	DIFFERENCE AS PERCENT OF RFD	EFFECT OF ANTICIPATED RESIDUES	
	CURRENT TMRC*	NEW TMRC**			ARC	%RFD
U.S. POPULATION - 48 STATES	0.000000	0.000011	0.038183	0.038183		
U.S. POPULATION - SPRING SEASON	0.000000	0.000011	0.036097	0.036097		
U.S. POPULATION - SUMMER SEASON	0.000000	0.000012	0.039023	0.039023		
U.S. POPULATION - FALL SEASON	0.000000	0.000012	0.038677	0.038677		
U.S. POPULATION - WINTER SEASON	0.000000	0.000012	0.038933	0.038933		
NORTHEAST REGION	0.000000	0.000011	0.036600	0.036600		
NORTH CENTRAL REGION	0.000000	0.000011	0.035113	0.035113		
SOUTHERN REGION	0.000000	0.000010	0.033700	0.033700		
WESTERN REGION	0.000000	0.000016	0.052613	0.052613		
HISPANICS	0.000000	0.000019	0.063673	0.063673		
NON-HISPANIC WHITES	0.000000	0.000011	0.038240	0.038240		
NON-HISPANIC BLACKS	0.000000	0.000007	0.023997	0.023997		
NON-HISPANIC OTHERS	0.000000	0.000016	0.053767	0.053767		
NURSING INFANTS (< 1 YEAR OLD)	0.000000	0.000046	0.153633	0.153633		
NON-NURSING INFANTS (< 1 YEAR OLD)	0.000000	0.000054	0.180627	0.180627		
FEMALES (13+ YEARS, PREGNANT)	0.000000	0.000006	0.020767	0.020767		
FEMALES 13+ YEARS, NURSING CHILDREN (1-6 YEARS OLD)	0.000000	0.000036	0.021427	0.021427		
CHILDREN (7-12 YEARS OLD)	0.000000	0.000015	0.121543	0.121543		
MALES (13-19 YEARS OLD)	0.000000	0.000008	0.049613	0.049613		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.000000	0.000007	0.025823	0.025823		
MALES (20 YEARS AND OLDER)	0.000000	0.000007	0.022040	0.022040		
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.000000	0.000007	0.024063	0.024063		
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.000000	0.000007	0.024533	0.024533		

\*Current TMRC does not include new or pending tolerances.

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

5

TABLE 3: Oncogenic Risk

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

DATE: 10/20/94

PAGE: 1

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Fenbutonazole (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 centrilob- ular to midzonal hepato- cellular 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

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

FOOD CODE	FOOD NAME	-----TOLERANCE (PPM)-----		--EXISTING TOLERANCES--		-NEW & PENDING TOLERANCES-		TOTAL ONCOGENIC RISK
		NEW	PENDING	PUBLISHED	TMRC (UG/KG/DAY)	%RFD	TMRC (UG/KG/DAY)	
06002AA	BANANAS-UNSPECIFIED	0.05000			0.000165	0.0005	0.000000003	0.000000003
06002AB	BANANAS-FRESH	0.05000			0.011202	0.0373	0.000000185	0.000000185
06002DA	BANANAS-DRIED	0.05000			0.000088	0.0002	0.000000001	0.000000001
06106AA	PLANTAINS	0.05000			0.000000	0.0000	0.000000000	0.000000000
CROP GROUP TOTALS FOR UNSPECIFIED:								
GRAND TOTAL TMRC:	0.011455	GRAND TOTAL % OF THE Rfd:	0.0382					

POPULATION SUBGROUP TOTALS								
POPULATION TOTAL TMRC	0.011455	POPULATION TOTAL % OF THE Rfd	0.0381					

6