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

JUN 17 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TOX

243

MEMORANDUM

Subject: Addendum to Residue Chemistry Chapter for Propazine
Registration Standard: Tolerance Assessment System
Tolerance Reassessment.

To: Amy Rispin
Science Integration Staff
Hazard Evaluation Division
and
Robert Taylor PM# 25
Registration Division

From: Charles Frick
Tolerance Assessment Program
Residue Chemistry Branch, HED

c. Frick 6/15/87 DSI 6/15/87

Thru: Charles L. Trichilo Ph.D.
Chief, Residue Chemistry Branch
Hazard Evaluation Division

R.D. Schmitt for

Please find attached the Tolerance Assessment System (TAS) tolerance reassessment for Propazine, which is an addendum to the Registration Standard. This is in compliance with the recent policy established in HED that TAS will be used for all Registration Standards, Special Reviews, and tolerances on new chemicals.

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Propazine Caswell #184 CAS No. 139-40-2 A.I. CODE: 080808 CFR No. 180.243	2yr feeding- rat NOEL= 5.0000 mg/kg 100.00 ppm LEL= 50.0000 mg/kg 1000.00 ppm ONCO: Pending NOTE	Decreased body weight gain. Evidence of oncogenicity in female rats (mammary tumors), negative in mice.	PADI 300 OPP Rfd= 0.020000 EPA Rfd= 0.020000 WHO Rfd 0.000000 Type:	Chronic feeding- dog Teratology- rat (Core-Supplementary) Teratology- rabbit UF of 3 for data gaps.	TOX complete 7/18/86. ORD verified 9/29/86. TOX reassess 3/20/87. ORD verified 5/20/87.

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

FOOD CODE	FOOD NAME	TOLERANCE (PPM)		EXISTING TOLERANCES TMRC (UG/KG/DAY)	%Rfd	NEW, PENDING & PUBLISHED TOLERANCES (UG/KG/DAY)	NEW %Rfd
		NEW	PENDING				
24006AA	SORGHUM (INCLUDING MILO)		0.2500	0.0059	0.0297		
CROP GROUP TOTALS FOR CEREAL GRAINS:							
53001BA	BEEF-MEAT BYPRODUCTS	0.0500				0.0009	0.0044
53001BB	BEEF(ORGAN MEATS)-OTHER	0.0500				0.0003	0.0015
53001DA	BEEF-DRIED	0.0500				0.0001	0.0006
53001FA	BEEF(BONELESS)-FAT (BEEF TALLOW)	0.0500				0.0186	0.0930
53001KA	BEEF(ORGAN MEATS)-KIDNEY	0.1000				0.0000	0.0002
53001LA	BEEF(ORGAN MEATS)-LIVER	0.1000				0.0021	0.0103
53001MA	BEEF(BONELESS)-LEAN (W/O REMOVEABLE FAT)	0.0500				0.0581	0.2905
53002BA	GOAT-MEAT BYPRODUCTS	0.0500				0.0000	0.0000
53002BB	GOAT(ORGAN MEATS)-OTHER	0.0500				0.0000	0.0000
53002FA	GOAT(BONELESS)-FAT	0.0500				0.0000	0.0000
53002KA	GOAT(ORGAN MEATS)-KIDNEY	0.1000				0.0000	0.0000
53002LA	GOAT(ORGAN MEATS)-LIVER	0.1000				0.0000	0.0000
53002MA	GOAT(BONELESS)-LEAN (W/O REMOVEABLE FAT)	0.0500				0.0000	0.0000
53003AA	HORSE	0.0500				0.0000	0.0000
53005BA	SHEEP-MEAT BYPRODUCTS	0.0500				0.0000	0.0000
53005BB	SHEEP(ORGAN MEATS)-OTHER	0.0500				0.0000	0.0000
53005FA	SHEEP(BONELESS)-FAT	0.0500				0.0002	0.0011
53005KA	SHEEP(ORGAN MEATS)-KIDNEY	0.1000				0.0000	0.0000
53005LA	SHEEP(ORGAN MEATS)-LIVER	0.1000				0.0000	0.0000
53005MA	SHEEP(BONELESS)-LEAN (W/O REMOVEABLE FAT)	0.0500				0.0006	0.0031
53006BA	PORK-MEAT BYPRODUCTS	0.0500				0.0013	0.0063
53006BB	PORK(ORGAN MEATS)-OTHER	0.0500				0.0002	0.0010
53006FA	PORK(BONELESS)-FAT (INCLUDING LARD)	0.0500				0.0104	0.0521
53006KA	PORK(ORGAN MEATS)-KIDNEY	0.1000				0.0000	0.0000
53006LA	PORK(ORGAN MEATS)-LIVER	0.1000				0.0005	0.0024
53006MA	PORK(BONELESS)-LEAN (W/O REMOVEABLE FAT)	0.0500				0.0196	0.0978
CROP GROUP TOTALS FOR RED MEAT:							
55008LA	TURKEY-GIBLETS (LIVER)	0.1000		0.0000	0.0000	0.1129	0.5645
55013LA	POULTRY, OTHER-GIBLETS(LIVER)	0.1000				0.0000	0.0000
55015LA	CHICKEN-GIBLETS(LIVER)	0.1000				0.0000	0.0001
CROP GROUP TOTALS FOR POULTRY:							
				0.0000	0.0000	0.0005	0.0027

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TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Propazine Caswell #184 CAS No. 139-40-2 A.I. CODE: 080808 CFR No. 180.243	2yr feeding- rat NOEL= 5.0000 mg/kg 100.00 ppm LEL= 50.0000 mg/kg 1000.00 ppm ONCO: Pending NOTE	Decreased body weight gain. Evidence of oncogenicity in female rats (mammary tumors), negative in mice.	PADI 300 OPP Rfd= 0.020000 EPA Rfd= 0.020000 WHO Rfd 0.000000 Type:	Chronic feeding- dog - Teratology- rat (Core-Supplementary) Teratology- rabbit UF of 3 for data gaps.	TOX complete 7/18/86. ORD verified 9/29/86. TOX reassess 3/20/87. ORD verified 5/20/87.

TOTAL TMRC (MG/KG BODY WEIGHT/DAY)

POPULATION SUBGROUP	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	0.0000	0.0003	1.7117	1.6820		
U.S. POPULATION - SPRING SEASON	0.0000	0.0003	1.6021	1.6021		
U.S. POPULATION - SUMMER SEASON	0.0000	0.0003	1.6739	1.6739		
U.S. POPULATION - FALL SEASON	0.0000	0.0003	1.7418	1.7418		
U.S. POPULATION - WINTER SEASON	0.0000	0.0003	1.7104	1.7104		
NORTHEAST REGION	0.0000	0.0003	1.7236	1.7236		
NORTH CENTRAL REGION	0.0000	0.0003	1.7478	1.7478		
SOUTHERN REGION	0.0000	0.0003	1.5225	1.5225		
WESTERN REGION	0.0000	0.0004	1.8065	1.8065		
HISPANICS	0.0000	0.0004	2.1074	2.1074		
NON-HISPANIC WHITES	0.0000	0.0003	1.6692	1.6692		
NON-HISPANIC BLACKS	0.0000	0.0003	1.5443	1.5443		
NON-HISPANICS OTHER	0.0000	0.0004	1.8568	1.8568		
NURSING INFANTS (<1 YEAR OLD)	0.0000	0.0003	1.6967	1.6967		
NON-NURSING INFANTS (<1 YEAR OLD)	0.0000	0.0014	7.1643	7.1643		
FEMALES (13+ YEARS, PREGNANT)	0.0000	0.0002	1.2010	1.2010		
FEMALES 13+ YEARS, NURSING	0.0000	0.0003	1.4514	1.4514		
-CHILDREN (1-6 YEARS OLD)	0.0000	0.0009	4.2686	4.2686		
CHILDREN (7-12 YEARS OLD)	0.0000	0.0005	2.7466	2.7466		
MALES (13-19 YEARS OLD)	0.0000	0.0004	1.8530	1.8530		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.0000	0.0003	1.4209	1.4209		
MALES (20 YEARS AND OLDER)	0.0000	0.0002	1.1449	1.1449		
FEMALES (20 YEARS AND OLDER)	0.0000	0.0002	0.9645	0.9645		

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

DATE: 06/09/87

CHEMICAL INFORMATION FOR CASWELL NUMBER 184

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Propazine Caswell #184 CAS No. 139-40-2 A.I. CODE: 080808 CFR No. 180.243	2yr feeding: rat NOEL= 5.0000 mg/kg 100.00 ppm LEL= 50.0000 mg/kg 1000.00 ppm ONCO: Pending NOTE	Decreased body weight gain. Evidence of oncogenicity in female rats (mammary tumors), negative in mice.	PADI 300 OPP Rfd= 0.020000 EPA Rfd= 0.020000 WHO Rfd 0.000000 Type:	Chronic feeding- dog Teratology- rat (Core-Supplementary) Teratology- rabbit UF of 3 for data gaps.	TOX complete 7/18/86. ORD verified 9/29/86. TOX reassess 3/20/87. ORD verified 5/20/87.

FOOD CODE	FOOD NAME	PETITION NUMBER	NEW	TOLERANCE (PPH)	PUBLISHED
24006AA	SORGHUM (INCLUDING MILO)	8F0687			0.2500
50000DB	MILK-NON-FAT SOLIDS	2F2618	0.0200		
50000FA	MILK-FAT SOLIDS	2F2618	0.0200		
50000SA	MILK SUGAR (LACTOSE)	2F2618	0.0200		
53001BA	BEEF-MEAT BYPRODUCTS	2F2618	0.0500		
53001BB	BEEF(ORGAN MEATS)-OTHER	2F2618	0.0500		
53001DA	BEEF-DRIED	2F2618	0.0500		
53001FA	BEEF(BONELESS)-FAT (BEEF TALLOW)	2F2618	0.0500		
53001KA	BEEF(ORGAN MEATS)-KIDNEY	2F2618	0.1000		
53001LA	BEEF(ORGAN MEATS)-LIVER	2F2618	0.1000		
53001MA	BEEF(BONELESS)-LEAN (W/O REMOVEABLE FAT)	2F2618	0.0500		
53002BA	GOAT-MEAT BYPRODUCTS	2F2618	0.0500		
53002BB	GOAT(ORGAN MEATS)-OTHER	2F2618	0.0500		
53002FA	GOAT(BONELESS)-FAT	2F2618	0.0500		
53002KA	GOAT(ORGAN MEATS)-KIDNEY	2F2618	0.1000		
53002LA	GOAT(ORGAN MEATS)-LIVER	2F2618	0.1000		
53002MA	GOAT(BONELESS)-LEAN (W/O REMOVEABLE FAT)	2F2618	0.0500		
53003AA	HORSE	2F2618	0.0500		
53005BA	SHEEP-MEAT BYPRODUCTS	2F2618	0.0500		
53005BB	SHEEP(ORGAN MEATS)-OTHER	2F2618	0.0500		
53005FA	SHEEP(BONELESS)-FAT	2F2618	0.0500		
53005KA	SHEEP(ORGAN MEATS)-KIDNEY	2F2618	0.1000		
53005LA	SHEEP(ORGAN MEATS)-LIVER	2F2618	0.1000		
53005MA	SHEEP(BONELESS)-LEAN (W/O REMOVEABLE FAT)	2F2618	0.0500		
53006BA	PORK-MEAT BYPRODUCTS	2F2618	0.0500		
53006BB	PORK(ORGAN MEATS)-OTHER	2F2618	0.0500		
53006FA	PORK(BONELESS)-FAT (INCLUDING LARD)	2F2618	0.0500		
53006KA	PORK(ORGAN MEATS)-KIDNEY	2F2618	0.1000		
53006LA	PORK(ORGAN MEATS)-LIVER	2F2618	0.1000		
53006MA	PORK(BONELESS)-LEAN (W/O REMOVEABLE FAT)	2F2618	0.0500		
53006BA	PORK-MEAT BYPRODUCTS	2F2618	0.0500		
53006BB	PORK(ORGAN MEATS)-OTHER	2F2618	0.0500		
53006FA	PORK(BONELESS)-FAT (INCLUDING LARD)	2F2618	0.0500		
53006KA	PORK(ORGAN MEATS)-KIDNEY	2F2618	0.1000		
53006LA	PORK(ORGAN MEATS)-LIVER	2F2618	0.1000		
53006MA	PORK(BONELESS)-LEAN (W/O REMOVEABLE FAT)	2F2618	0.0500		
55008LA	TURKEY-GIBLETS (LIVER)	2F2618	0.1000		
55013LA	POULTRY, OTHER-GIBLETS(LIVER)	2F2618	0.1000		
55014AA	EGGS-WHOLE	2F2618	0.0200		
55014AB	EGGS-WHITE ONLY	2F2618	0.0200		
55014AC	EGGS-YOLK ONLY	2F2618	0.0200		
55015LA	CHICKEN-GIBLETS(LIVER)	2F2618	0.1000		

Table 2
PAGE 2

DATE: 06/09/87

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

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

FOOD CODE	FOOD NAME	TOLERANCE (PPM)		EXISTING TOLERANCES THRC (UG/KG/DAY)	NEW, PENDING & PUBLISHED TOLERANCES NEW THRC (UG/KG/DAY)	NEW XRFD
		NEW	PENDING			
500000B	MILK-NON-FAT SOLIDS	0.0200			0.1427	0.7136
50000FA	MILK-FAT SOLIDS	0.0200			0.0679	0.3395
50000SA	MILK SUGAR (LACTOSE)	0.0200			0.0007	0.0037
55014AA	EGGS-WHOLE	0.0200			0.0113	0.0565
55014AB	EGGS-WHITE ONLY	0.0200			0.0002	0.0009
55014AC	EGGS-YOLK ONLY	0.0200			0.0001	0.0007
CROP GROUP TOTALS FOR DAIRY PRODUCTS:				0.0000	0.2230	1.1149

TOLERANCE ASSESSMENT SYSTEM REASSESSMENT

CHEMICAL: PROPAZINE

1. The Provisional Acceptable Daily Intake (PADI) for this chemical is 0.02 mg/kg/day, and has been approved by the Toxicology Branch and Agency Reference Dose Committees.

In addition, this compound has been identified as an oncogen in rats. The potency estimate (Q^*), of Propazine is $1.7 \times 10^{-1} \text{ (mg/kg/day)}^{-1}$ (memorandum, C.J. Nelson, Toxicology Branch).

2. The food uses evaluated by the Tolerance Assessment System (TAS) were published tolerances as established under CFR 180.243, PP# 8F0697 and pending tolerances, PP# 2F2618. A list of these tolerances is appended.

3. Evaluation of proposed uses relative to the PADI: If all pending uses are approved, the TMRC for the U.S. population average will be 0.0003 mg/kg/day, equivalent to 1.7% of the PADI. The most highly exposed subgroups were non-nursing infants (0.0014 mg/kg/day, equivalent to 7.2% of the PADI and children 1-6 years of age (0.0009 mg/kg/day, equivalent to 4.3% of the PADI).

4. Calculation of oncogenic risk: Risk was calculated only for the U.S. population average, in accordance with current HED policy. This value was calculated by the relationship:

$$\text{Risk} = \text{Exposure} \times Q^*$$

For established and pending uses, the risk was calculated as:

$$0.0003 \times (1.7 \times 10^{-1}) = \underline{5.1 \times 10^{-5}}$$

For a listing of exposure by RAC for the U.S. population (published and pending) see tables 1 and 2.

5. Since this risk estimate is based on tolerances rather than actual residues in food as it is eaten, data demonstrating the effect of cooking and other processing steps may result in lower estimates of risk.

Propazine cont.

ATTACHMENT

cc. Registration Standard File
TAS File
Reading File
C. Frick (RCB)
Toxicology Branch
Circ.
PMSD