108501

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PP#6F1741. Pendimethalin in peanuts. Amendment of 10/31/80

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The amendment is in response to our letter of 10/8/80 in which a question was raised concerning the need for validated analytical methods for the metabolites CL 113,068 and CL 113,072. The petitioner believes that a reevaluation of the peanut metabolism study would aid in the resolution of questions on the metabolic residue picture.

We have again reviewed the peanut metabolism study and the characterization of the residue in the peanut hull. We conclude that while residues of the metabolite CL 113,068, 4-[(ethyl-3-hydroxypropyl) amino]-2-methyl-3,5-dinitro benzyl alcohol, does occasionally appear in the residue of the hull, it does not represent a significant level. As a result a validated analytical method for the determination of CL 113,068 is not necessary.

However, the metabolite CL 113,072, 4-[(1-ethyl-2-hydroxypropyl)amino]-3, 5-dinitro-o-toluic acid, does respresent a significant component of the residue in the hull.

In the petitioner's addendum of 4/20/80 (Section D18, Exhibit 1, Table III, p. 56), the amount of pendimethalin and its metabolites recovered from peanut hulls grown in treated soil is noted. Four analyses are presented. The total residue levels were: 0.09 ppm; 0.10 ppm; 0.20 ppm; 0.30 ppm. The total quantity of metabolite CL 113,072 ranges from 0-40% of the total residue. By comparison, the metabolite CL 217,146, 3-[(1-ethylpropyl)amino]-6-methyl-2, 4-dinitro benzyl alcohol, ranges from 23 - 56% of the total residue. (Levels of CL 113,072 were 0.04 ppm and 0.11 ppm. Levels of CL 217,146 were 0.05 ppm, 0.05 ppm, 0.07 ppm, and 0.07 ppm.)

In view of the foregoing, we reiterate our previous conclusion that the metabolite CL 113,072 (bound and free forms) is a significant component of the residue in peanut hulls.

Meat, Milk, and Eggs

We have indicated that no detectable residues of pendimethalin (<0.05 ppm) would result in other peanut feed items (peanuts, vines, hay, meal, soapstock). This alleviatess our concern over the transfer of pendimethalin residues from these items to meat, milk, and eggs of livestock (see our review of 5/25/76, A. Smith).

The hulls alone can make up 5% of the diet of beef cattle and 25% of the diet of horses. The whole peanut (nutmeat plus hulls) can make up 10-15% of the diet of beef and dairy cattle; 5% of the poultry diet; and, 10% of the diet of horses. An estimate of the maximum level of residues which could be ingested can be calculated using the percentage of hulls in the diet and the proposed tolerance level for hulls (0.25 ppm). The calculated ingestion levels are: cattle (0.04 ppm); poultry (0.01 ppm); horses (0.04 ppm).

Livestock feeding studies were performed in which pendimethalin was fed to lactating goats and lactating cows at levels of 0.5 - 20 ppm (PP#5F1556). The studies show that no pendimethalin or benzyl alcohol metabolite residues are likely to occur in milk, eggs, meat, fat, and meat by-products of cattle, goats, hogs, horses, poultry, and sheep due to the proposed tolerances on peanuts, peanut vine hay, and peanut hulls [§180.6(a)(3)].

A large animal metabolism study with C^{14} labeled pendimethalin did show activity deposition in animal tissues (PP#5F1556). Presumably this activity is comprised of pendimethalin metabolites.

Conclusions

1. The nature of the residue in peanut hulls is adequatley delineated. The components of hull residues are the parent compound pendimethalin (CL 92,553) and its metabolites CL 202,347; CL 217,146; and bound and free CL 113,072. The bound forms are freed thru acid hydrolysis.

We defer to the Toxicology Branch on the toxicological significance of the metabolites CL 113,072 and CL 217,146 and if such components need to be regulated.

2. Adequate methods are available for the determination of pendimethlin and the metabolites CL 202,347 and CL 217,141. However a validated method trail may be necessary for this metabolite if it needs to be regulated. The need for such data is continzent upon TOX's response in 1 above.

3. Total residues of pendimethlin and its metabolites are not likely to exceed the proposed tolerance of 0.25 ppm for peanut hulls. (This is based on results of studies with radiolabelled C^{14} pendimethalin.) However, the field residue data for hulls obtained with the residue methods are inadequate since it does not reflect residues of the metabolite CL 113,072. The need for such data is continzent upon TOX's response to Conclusion 1.

4a. No pendimethalin and benzyl alcohol metabolite residues are likely to occur in milk, eggs, meat, fat, and meat by-products of livestock due to the proposed tolerances for peanuts, peanut vine hay, and peanut hulls [§180.6(a)(3)].

4b. If TOX concludes that metabolites CL 217,146 and CL 113,072 need to be included in the tolerance, livestock feeding studies may be required for these metabolites.

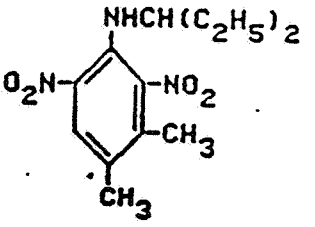
Recommendation

We recommend against the proposed tolerances. A favorable recommendation is contingent upon the resolution of questions raised in Conclusions 2, 3, and 4b.

TS-769:RCB:A. SMITH:LDT:X77377:CM#2:RM.810:2/7/81
cc: RF, CIRC., SMITH, WATTS, TOX, FDA, EEB, EFB, PP#6F1741
RDI: Quick, 2/4/81: Schmitt, 2/4/81
RETYPED:2/13/81:gs

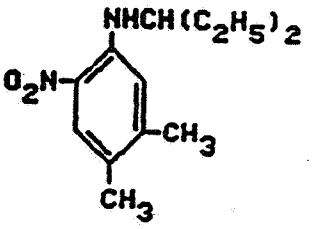
CL 92,553

2,6-Dinitrobenzenamine, N-(1-ethylpropyl)-3,4-dimethyl-



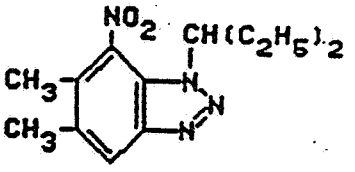
CL 94,049

3,4-Xylidine, N-(1-ethylpropyl)-6-nitro-



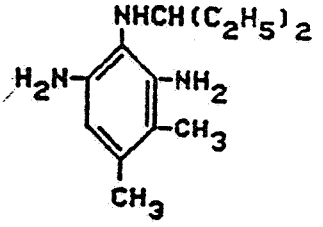
CL 94,163X

1H-Benzotriazole, 1-(1-ethylpropyl)-5,6-dimethyl-7-nitro-



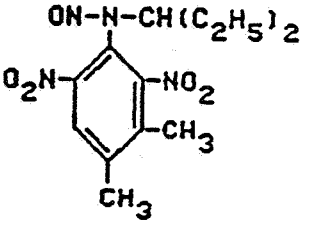
CL 94,211

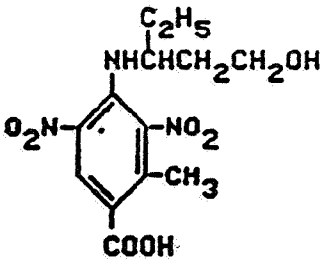
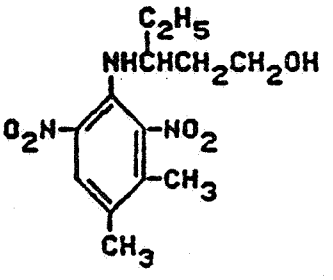
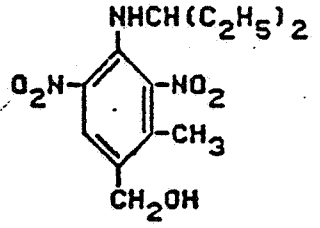
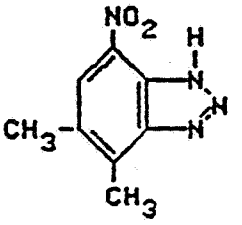
o-Xylene-3,4,5-triamine, N4-(1-ethylpropyl)-

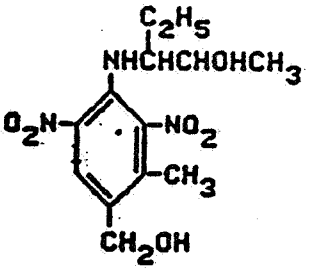
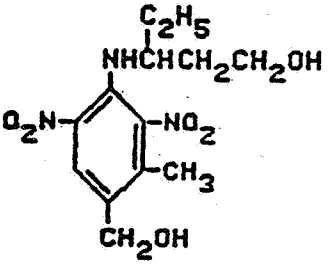
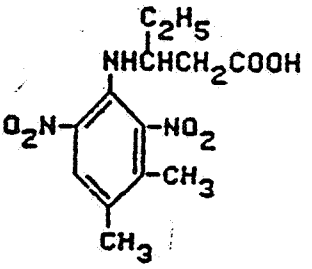
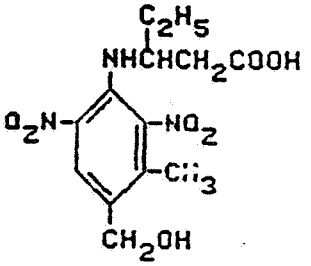


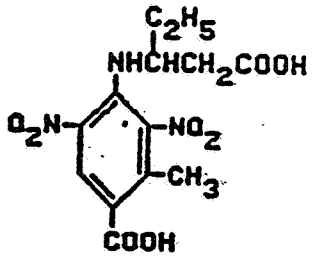
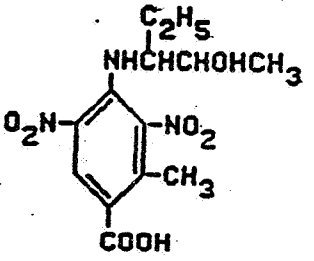
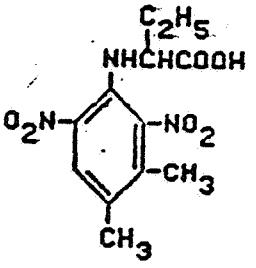
CL 94,269

3,4-Xylidine, N-(1-ethylpropyl)-2,6-dinitro-N-nitroso



CL Number	Chemical Name	Structure
CL 202,345	o-Toluic acid, 4-[(1-ethyl-3-hydroxy-propyl)amino]-3,5-dinitro-	
CL 202,346	1-Pentanol, 3-(2,6-dinitro-3,4-xylidino)-	
CL 202,347	Benzyl alcohol, 4-[(1-ethylpropyl)-amino]-2-methyl-3,5-dinitro-	
CL 202,348	1H-Benzotriazole, 4,5-dimethyl-7-nitro-	

CL Number	Chemical Name	Structure
CL 113,067	Benzyl alcohol, 4-[(1-ethyl-2-hydroxypropyl) amino]-2-methyl- 3,5-dinitro-	
CL 113,068	Benzyl alcohol, 4-[(1-ethyl-3-hydroxypropyl) amino]-2-methyl- 3,5-dinitro-	
CL 113,069	Valeric acid, 3-(2,6-dinitro- 3,4-xylidino)-	
CL 113,070	Valeric acid, 3-[α^4-hydroxy-2,6- dinitro-3,4-xylidino)-	

CL Number	Chemical Name	Structure
CL 113,071	o-Toluic acid, 4-{[1-(carboxymethyl)propyl]amino}-3,5-dinitro-	
CL 113,072	o-Toluic acid, 4-[(1-ethyl-2-hydroxypropyl)amino]-3,5-dinitro-	
CL 113,112	Butyric acid, 2-(2,6-dinitro-3,4-xylidino)-	
CL 113,113	Butyric acid, 2-(α^4-hydroxy-2,6-dinitro-3,4-xylidino)-