SFHoward:RENey:ow
8/31/71

Evaluation of Data for Registration for
PP No. 1F1157 for Sec-butylamine also
2-aminobutane

Submitted by Elanco, Eli Lilly
Filed June 7, 1971

INERT INGREDIENT INFORMATION IS NOT INCLUDED

I. Introduction

1. There have been two previous petitions for sec-butylamine submitted by the Petitioner: Experimental Permit 1471-EXP-19G and Petition 7F0520; both have been favorably evaluated. Petition 7F0520 established a tolerance of 35 ppm for residues of 2-aminobutane in or on oranges.

2. This proposal requests the establishment of tolerances for residues of the fungicide sec-butylamine in or on citrus fruits (oranges, lemons, grapefruits, tangerines, and tangelos) at 50 ppm; kidney of cattle at 3 ppm; and fat, liver, meat, and milk of cattle at 0.75 ppm. There are no registered tolerances for 2-aminobutane in milk or animal tissue.

3. Names and formulations of the product:

"Frucote" formerly "Tutane" is the trade name of sec-butylamine and 2-aminobutane. Reference to date with Exp. Permit 1417-EXP-19G, and Petition 7F0520, August 10, 1966.

Frucote	98%
Inert Ingredient	2.0%

Impurities in 98% product

[redacted]

4. Chemical and Physical Properties:

Structural formula	$CH_3CH_2CH(NH_2)CH_3$
Molecular formula	$C_4H_{11}N$
Molecular weight	73.14

Sec-butylamine is a clear to pale yellow liquid

Refractive index	about 1.393 at 20°C
Specific gravity	about 0.7200 at 25°C/25°C

[redacted]

Assay Method - GLC

II. Directions for Use

Dip, drench or spray citrus fruit with 1% Frucote solution. To prepare 1% solution, add 14 gallons Frucote to 1000 gallons of water. Mix and adjust to pH 8.0 - 9.0 with hydrochloric, sulfuric, acetic or phosphoric acid. Carbonated solution may also be used; prepare by bubbling compressed CO_2 through the dilute solution or by adding dry ice until pH of 8.0 -9.0 is obtained.

Dip: 1-5 minutes

Drench: Not less than 3 minutes

Spray: One gallon per 30-35 bushels of fruits

Sodium lauryl sulfate may be used as wetting agent

Fruits may be waxed following the application of Frucote by any of the recommended methods: dip, drench, or spray.

For each 0.1% reduction in concentration in the treating solution, add 11 pts. of Frucote per 1000 gallons of treating solution. Adjust to pH 8-9.

III. Analytical Method

A description of the analytical method with an evaluation have been given in the review of Petition No. 7F0520: Tolerance of 35 ppm for 2-aminobutane on oranges by R. L. Caswell, August 31, 1966.

Although the Petitioner has revised the method; we agree with the favorable evaluation of the method. The revisions are minor in nature and mainly include measures to reduce losses of 2-aminobutane. Procedure 5801350; Revised, 4-3-68 and Procedure 5801490, Revised: 3-29-68. Both revisions were by W. S. Johnson.

We do think that the method is selective and sufficiently sensitive (about 0.1 ppm-0.001) to determine sec-butylamine in or on citrus; in milk and meat particularly, if the TLC separation of interferences prior to GLC is made general in all of the procedures:

5801310 - General procedure (without TLC) Used to obtain residue data in or on citrus, meat, urine, blood, and feces

5801340 - TLC, Visual estimated

5801350 - TLC, Followed by GLC

5801360 - Citrus Oil (acid extraction) TLC and GLC

5801490 - Milk, TLC and GLC

This would probably improve cleanup of residues, lower the blanks, and facilitate interpretation of gas chromatograms.

Published methods for the determination of 2-aminobutane:

1. Electron Capture GLC method: Day, E. W. et.al, Anal. Chem. 38, 1053-1057 (1966)

2. EC-GLC method: Day, E. W. et.al., JAOAC, 51, 39-44 (1968)

Recoveries of sec-butylamine at 2 ppm were done on all citrus. They appear to be adequate for each crop except tangelos as shown in the following table.

	% Range of 2-aminobutane Recovered		
Crops	Pulp	Peel	Whole Fruit
Oranges	105-112	107-117	59-110
Grapefruits	52-119	66-103	85-118
Lemons	81-107	66-132	69-123
Tangerines	85-97	99-110	86-103
Tangelos			78%

With the exception of a few low and high results which widen the % range for grapefruits and lemons, the percision of the method appears capable of inforcing the proposed tolerance.

IV. Discussion of Data

1. Samples represent two or more geographical growing areas for all citrus except tangelos. For tangelos one geographical (Florida) location was represented. Application rates were varied between the proposed rate and two or three times this rate. In almost all cases the residues found were less than the proposed tolerance of 50 ppm. In other recoveries studies, tangerines were treated with: 2% Frucote in water emulsion wax; 2% aqueous + 2% water emulsion wax; and 2 x 2% aqueous + 2% water emulsion wax. For each sample, residues in peel exceeded the proposed tolerance. Residues in pulp and whole fruit were within tolerance. This is not, however, the proposed direction for use of Frucote.

Residues were mostly found in the peel.

Washing and brushing the raw commodity after treatment are not effective in removal of residues from citrus fruit.

2. Residue Data

Recoveries for 2-aminobutane on treated samples were carried out concurrently with recoveries on fortified samples. Results for residues on treated samples are given in the table below.

(a) 2-Aminobutane in treated Citrus

Crops	Appln.	Rate%	% Range (PPM) Pulp	Peel	Whole Fruit
Oranges	Spray	1.0	0.00-0.42	2.05-3.02	1.13-4.05
"	"	2.0	-	-	1.22-5.45
Grapefruits	Dip-Drench	0.5	0.03-0.18	0.41-8.20	0.16-4.06
"	"	1.0	0.09-0.63	1.23-18.0	0.50-8.65
"	"	2.0	0.16-4.06	3.12-25.6	1.24-12.6
Lemons	"	1.0	0.00-0.32	0.66-41.5	0.33-24.0
"		2.0	-0.03	-28.3	-16.0
"		2.0	-	1.33-24.6	0.67-14.0
Tangelos	"	1.0	-	-	16.2
		2.0	-	-	30.8
		5.0	-	-	68.5
Tangerines	Spray	0.5	0.23	7.75	2.40
		1.0	0.11	17.0	3.58
		2.0	0.26	23.3	5.85

Tables: III-B-2; III-C-1; III-D-1 and III-D-1 and III-D-2; III-E-1 and III-E-3 for oranges and tangerines respectively.

Conclusions for Citrus

1. Insufficient data was submitted to allow any conclusions as to distribution of sec-butylamine between pulp and peel in tangelos. However, the tolerance is on whole citrus so we do not have to pursue this at this time. If use was different we may ask for distribution curves.

2. Geographical location and number of samples analyzed are inadequate for tangelos, alone. Since there are data on other citrus crops in other geographical locations, this is acceptable.

3. It would be preferred that the TLC separation of 2-aminobutane from interferences before GLC analysis be made general in methodology, but this is up to Tolerance Division.

4. We recommend favorably for all citrus.

(b) Summary of Residue Data for Oranges and Grapefruits by-Products

Recoveries of 2-aminobutane (2-AB) from by-products of oranges and grapefruits treated with 1% or 2% Frucote are tabulated below. The values in the table represent the range for single or duplicate determinations for the by-products listed. Two geographical locations for oranges and one for grapefruits are represented.

	Range of ppm 2-AB Found	
By-Products	1%	2%
Whole Fruit	3.0-17.0	8.6-8.8
Juice	0.0-0.40	0.0-0.50
Chopped Peel Residue	3.60-9.3	3.80-11.6
Pressed Pell Liquor	1.73-6.6	2.72-6.8
Molasses	13.1-25.2	24.6-27.8
Dried Pulp	16.2-33.3	24.9-33.3
Cold Pressed Oil	0.0-0.46	0.0-0.5

Compiled from Tables IV-C-1; IV-C-1-1; IV-C-1-2; and IV-C-1-3.

Insufficient data was provided to show that residues would not exceed the proposed tolerance of 50 ppm in molasses and dried pulp. In one experiment with oranges treated at 0.9 rate, residues of 51.0 and 45.3 ppm were found in dried meal. (duplicate determinations). PTD will have to determine if additional data on food additive tolerance is needed.

No data was provided for residue of 2-AB on by-products of tangerines and tangelos.

The petitioner states that residue data on 2-aminobutane in lemons by-products have been obtained by the Food Division of Coca-Cola Company, Orlando, Florida and that their findings have been reported to Dr. Paul Thayer in a communication dated March 3, 1969, a copy of which is attached. We have not found the report in the submitted petition.

(c) Residue Data: Milk, Meat, Liver, Fat, Kidney, Urine, Blood and Feces

Residue data of 2-aminobutane (2-AB) in milk and meat tissue were conducted on lactating cows fed a grain ration containing 100, 20, 10, 5 and 2 ppm 2-AB. Composite milk samples taken at 24 hours intervals were analyzed for 2-AB twice a week. Samples of meat, fat, liver and kidney (at zero time withdrawal) from the 100, 10, and 2 ppm study and random samples of urine, blood and feces from the 100 and 10 ppm study were also analyzed

for 2-AB. The range of individual results for each type of sample from either the 10 ppm and/or 20 ppm feeding studies are shown in the following table.

PPM 2-Aminobutane Found at each Feeding Level

Sample	Feeding Level (ppm)	No. of Analyses	Range Individual Analyses ppm-2AB
Control (Milk)	0	116	0.000-0.320
" "	0	113	0.000-0.16
Milk	10	39	0.002-0.15
Milk	20	16	0.052-0.113
Meat (Control)	0	2	0.013-0.013
Meat	10	3	0.013-0.055
Liver (Control)	0	2	0.018-0.031
Liver	10	3	0.042-0.142
Fat (Control)	0	2	<0.01-<0.01
Fat	10	3	<0.01-<0.01
Kidney (Control)	0	2	0.02-0.198
Kidney	10	3	0.179-0.302
Urine (Control)	0	15	0.005-1.96
Urine	10	18	0.028-15.2
Blood (Control)	0	11	<0.01-0.02
Blood	10	15	0.01-0.04
Feces (Control)	0	15	0.01-0.20
Feces	10	18	0.01-0.84

Compiled from Tables: VI-D-1; VI,E,1; VI,F,2a-2, VI,F,2C-2.

Discussion of Residue Data on Cows

Low levels (0.002-1.96 ppm) of 2-aminobutane were found in most of the controls and animals treated with 10-20 ppm 2-aminobutane. Residues from animals treated with 100 ppm 2-AB were higher than residues found in animals treated at 10-20 ppm level. Differences between 10-20 ppm residues appear insignificant. Most of the residues is excreted in urine and feces.

The petitioner claims that 2-aminobutane found in most samples from control cows is endogenous. He supports his claim by submitting an IR spectra for a derivatized control milk residue which was identical to an IR spectra of the same derivative of a 2-AB standard. There are no references to other authorities substantiating his findings. We would like to have had desenting information from other authorities. The presence of 2-AB in the control samples could indicate a broad contamination problem. Isobutylamine was also reported to be present in the milk of control cows.

Conclusions on Cows

We would like to have had information from other authorities to confirm the presence of endogenous 2-aminobutane in milk.

Metabolism studies of 2-aminobutane in cows would be appropriate.

V. Conclusions

1. See citrus conclusions.

2. See meat and dairy animals conclusions.

3. The Tolerance Division set tolerance. Since this use does not involve growing crops or applications made to the environment, we cannot ask questions on deficiencies as stated in the conclusions on citrus and cows. We can only hope that they will be covered by PTD.

VI. Recommendation

1. We would like to know how the applicator would dispose the used treating solution.

We should RL this comment.