EFB

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Memorandum

SUBJECT: PP#0F2349: ®Bayleton in Grapes and Melons.
Evaluation of residue data and analytical method

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The Mobay Chemical Corp. proposes tolerances for combined residues of the fungicide ®Bayleton, 1-(4-chlorophenoxy)-3, 3-dimethyl-1-(1H-1,2,4-triazol-1-yl)-2-butanone, and its metabolite beta-(4-chlorophenoxy)-alpha-(1,1-dimethylethyl)-1H-1,2,4,- triazol-1-ethanol in or on melons at 0.2 ppm and grapes (fresh market only) at 0.2 ppm. These tolerances are to be established on grapes and melons imported into the United States from Mexico.

There are no established tolerances for the fungicide ®Bayleton. Temporary tolerances are pending for apples and pears at 0.75 ppm and grapes at 1.0 ppm (PP#0G2300); cucumbers at 0.1 ppm and tomatoes at 0.2 ppm (PP#0E2393).

Conclusions

1. The nature of the residue in animals and plants is adequately delineated. The parent compound Bayleton, its metabolite KWG0519, and their conjugates are the significant components of the residue.

2. The analytical method is not adequate for the determination of total residues (free and conjugated) of Bayleton and its metabolite KWG0519. Conjugated residues are not determined. Such components can be freed thru acid hydrolysis. The method should be modified to include this process.

3a. The residue data do not reflect total residues (free and conjugated) of Bayleton and its metabolite KWG0519. Therefore, valid conclusions on the residue levels in grapes and melons cannot be made. Residue data must be submitted for total residues (free and conjugated) in grapes and melons. Additionally, residue data must be submitted for more than one commodity in the "melon" category [see § 180.1(h)].

3b. Fresh fruit restrictions are not generally practical for a permanent tolerance since grapes could be diverted to processing channels. Residue data should be submitted for the grape byproducts (raisins, raisin waste, grape pomace). If necessary, food additive tolerances should be proposed. Alternatively, the petitioner may be able to ascertain that imported grapes are not processed.

4. If the fresh fruit restrictions are shown to be impractical and residues result in the feed items raisin waste and grape pomace, then livestock feeding studies will be necessary to show if residues occur in eggs, meat, and milk. If residues occur in meat, milk, or eggs, then tolerance proposals will be needed. A validated analytical method will also be needed to determine residues.

Recommendation

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

Detailed Considerations

Manufacturing Process (PP#0G2300)

[redacted] technical grade Bayleton. Tech. Bayleton has the following composition.

Bayleton	92-95%
[redacted]	

The impurities are not likely to produce a residue problem.

Formulation

Bayleton® is formulated as a 25% wettable powder containing 25% active ingredient (a.i.). The formulation is to be used on grapes and melons grown in Mexico as noted below. Adequate information is available on Mexican pesticide regulation.

Grapes (fresh market only): apply 1.4-2.2 ozs. a.i./A as a foliar spray. A maximum of 3 applications may be made up to 3 days before harvest.

Melons: apply 1.75 oz a.i./A as a foliar spray. A maximum of 3 applications may be made up to day of harvest.

The formulation's inert ingredients are cleared for use under § 180.1001.

Restrictions for fresh market use are generally considered not practical. Treated fruit may be diverted to the processing market. The petitioner may be able to eliminate the need for processed fruit data if he can demonstrate that grapes imported from Mexico would not be processed.

MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

Nature of the Residue

Plant metabolism studies with radiolabelled Bayleton and apples were reviewed in PP#0G2300 (memo 4/10/80, J. M.Worthington). Apples were treated with Bayleton (C^{14}-benzene and C^{14}-triazole labels) as a foliar spray at a rate approximating those proposed for grapes and melons. (The apple tree was protected from weathering by a polyethylene tent.) Apple samples were harvested at intervals of one hour thru 49 days and examined for residues of Bayleton and its metabolites.

Bayleton is metabolized and/or degraded following application to apples. Total residues decreased from 0.83 ppm at one hour after application (0-day) to 0.15 ppm at 21 days and beyond. Residues appear to be dissipated primarily thru volatilization.

The parent compound, Bayleton, was about 90% ofthe residue at 0-day, 50% at 14 days, and had decreased to 13% at 49 days. The principal metabolite was [1-(4-chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)2-butanol; KWG0519] and made up about 49% of the residue at 49 days. (This metabolite is also known as: beta-(4-chlorophenoxy)-alpha-(1,1-dimethylethyl)-1H-1,2,4,-triazole-1-ethanol. An unidentified metabolite which contained both the benzene and triazine rings was about 5% of the residue at 49 days.

The remainder of the residue was polar organic material (15%), water-soluble material (11%), and material which was not extractable from the plant solids (7%).

Bayleton is metabolized and/or degraded when applied to apples. The significant components of the residue are the parent compound, Bayleton, and its metabolite beta-(4-chlorophenoxy)-alpha -(1,1-dimethylethyl)-1H-1,2,4- triazole-1-ethanol.

Metabolism studies were submitted for tomatoes and cucumbers in this petition. In one study, young plants were grown in nutrient solution or soil containing C^{14}-Bayleton. Samples of plant parts (roots, shoots) were collected at intervals of 1-7 days after treatment and examined for Bayleton and its metabolites. In another study, leaves of tomato and cucumber plants grown in soil were treated with C^{14}-Bayleton. After 7 days the plants were removed from the soil, and the roots, shoots, and leaves were examined for residues of Bayleton and its metabolites. In a third study, tomato and cucumber plants were treated with multiple spray applications (up thru 4) of C^{14}-Bayleton and grown to maturity. Samples of fruit and foliage were collected at various intervals after treatment (up thru 28 days) and analyzed for residues of Bayleton and its metabolites.

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The metabolic behavior of Bayleton on tomato and cucumber plants was similar for the different modes of application. The differences lay in the level of residues present at different intervals after treatment. Such differences are expected and due to different rates of metabolism, degree of absorption, and growth dilution.

Bayleton is absorbed by roots and leaves of cucumber and tomato plants and translocated. Bayleton is metabolized, and the plant and fruit residues consist of the parent compound Bayleton and its metabolites KWG0519, KWG1323, KWG1342, and glucoside conjugates of the metabolites. The combined conjugates increased slowly and reached maximum levels in tomatoes at 28 days of approximately 8% and in cucumbers at 21 days of approximately 22% of the total plant residue. No single conjugated component made up more than 4% of the residue. The conjugated components are freed thru acid hydrolyses.

The significant components of plant residues is the parent compound and its metabolite and their conjugates KWG0519. The studies with apples, tomatoes, and cucumbers is sufficient to reflect the metabolic behavior of Bayleton in plants in general. This conclusion eliminates the need for a study with grapes as requested in our review of PP#0G2300.

Samples were analyzed by combustion and determination of the C^{14}-radioactivity by liquid scintillation counting techniques (LSC). Additional sample analyses were performed using liquid-liquid partitioning as cleanup procedures. The radioactivity was determined by LSC. Characterization of the residues were performed by column chromatography, thin layer chromatography, autoradiography, gas-liquid chromatography, mass spectrometry, and derivative formation with acetic anhydride.

Animals

Metabolism studies were performed with radiolabelled C^{14}-Bayleton and various animals (rats, lactating cows, pigs, and laying hens-see PP#0G2300). The studies show that Bayleton is metabolized and excreted by animals with some transfer of residues to eggs and milk and deposition in tissues.

The residue picture is similar for the different animals. The significant components of the residues in eggs, milk, and meat are the parent, Bayleton, and its metabolites KWG0519, KWG1323, and KWG1342. (See accompanying chart for structures).

The metabolic behavior of Bayleton in animals and plants is adequately understood.

Analytical Method

A ground sample is extracted by blending with acetone followed by dichloromethane. The extracts are filtered, combined, and mixed with dilute aqueous sodium chloride. The organic phase contains the Bayleton residues and is evaporated to dryness.

The residues are taken up with a petroleum ether-ethyl ether mixture and cleaned up on a florisil column. The residues are eluted with a mixture of hexane and ethyl acetate. The eluate is evaporated to dryness.

The residue is taken up with acetone and determined by gas chromatography using an alkali-flame detector sensitive to nitrogen. The detection limit for Bayleton or KWG0519 is reported to be approximately 0.01 ppm.

Untreated (control) samples of whole cantaloupe had <0.01-0.11 ppm Bayleton or KWG0519-equivalent residues. Control samples were fortified with Bayleton or KWG0519 at levels of 0.05-0.1 ppm. Recoveries were 74-109% (1 aberrant value at 128% for a 0.05 ppm level). Control cucumber samples had 0.02 ppm Bayleton-equivalent residues. Fortifications at 0.1 ppm yielded recoveries of 87-92%.

Control samples of grapes, grape juice, and grape wine had <0.01 ppm Bayleton or KWG0519-equivalent residues. Control samples, fortified at levels of 0.05 ppm with Bayleton or KWG0519, yielded recoveries of 80-107%.

61 Nitrogen-containing compounds, registered for use on apples, grapes, and grasses, were tested as sources of inteferences in the analysis of Bayleton and KWG0519 residues. Nine of 61 compounds caused some interference. However, the interferences wee eliminated through the use of a second GLC column and two different detectors.

A confirmatory procedure (tested with apples and soil) is available. The method employs p-values for confirmation of the presence of Bayleton and KWG0519.

The method appears to be adequate for the determination of free residues of Bayleton and KWG0519. However, the method is not likely to determine conjugated residues of Bayleton and KWG0519. The method should be modified to enable the determination of the conjugated components. Such bound components are often freed thru acid hydrolyses. Therefore, an acid reflux step should be tested to determine its adequacy for the determination of free and conjugated components of Bayleton and its metabolite KWG0519.

The residue method is not adequate for the determination of both free and conjugated components of Bayleton and KWG0519. The method should be, modified to include steps which free the conjugated components. An acid reflux step may free the bound components.

Residue Data

Grapes: samples were obtained from crops in Mexico which had received 3 foliar spray applications at rates of 1.42 oz act/A and 2.14 oz act/A (maximum proposed rate, 2.2 oz act/A). Samples were collected at intervals of 3-15 days after the last of 3 applications. [The grape varieties sampled were Thompson Seedless and Carignan. The Thompson Seedless represents about 43% of all grapes shipped fresh in the United States (United Fresh Fruit and Vegetable Association, September, 1968)].

Residues in grapes from the proposed 3-day PHI were 0.07-0.12 ppm. Residues decreased with time and were <0.01-0.06 ppm at 14-15 days from both rates.

Grape byproducts: the grapes are for the fresh market only. As a result, processing of the grapes to byproducts (raisins, juice, wine, jams, jellies) will not occur, and no feed items are involved.

It is possible that the imported grapes could be diverted thru processing channels. As a result, the fresh fruit restriction is not considered practical for a permanent tolerance.

Residue data should be submitted for grape byproducts (raisins, raisin waste, grape pomace). The raisin waste and grape pomace are used as livestock feed items. If necessary, food additive tolerances should be proposed for these items.

Melons: samples of cantaloupes were obtained from crops grown in Mexico. The crops had received 3 foliar spray applications at the proposed rate of 1.75 oz act/A. Residues on whole fruit at 0-day after the last treatment were 0.03-0.13 ppm. Residues were 0.05-0.08 ppm at 5 days and 0.03-0.11 ppm at 15 days.

The residue method does not determine conjugated residues of Bayleton and its metabolite KWG0519. As a result, total residues of Bayleton and KWG0519 (free and conjugated forms) are not reflected by the residue data. In the absence of such data, valid conclusions on the residue levels expected in grapes and melons cannot be made.

The petitioner must submit residue data for grapes and melons which reflect analyses for free and conjugated forms of Bayleton and its metabolite KWG0519.

Additionally, the category "melons" include the following raw agricultural commodities [§ 180.1(h)]: cantaloups, casabas, crenshaws, honeydew melons, honeyballs, muskmelons, Persian melons and hybrids of these, watermelons and their hybrids. Residue data on one of these commodities are not enough to show the residue levels likely to result on all commodities.

The residue data for melons are inadequate. Data on more than one commodity are necessary and should be submitted.

Meat and Milk

If the fresh fruit restrictions are shown to be impractical and residues result in the feed items raisin waste and grape pomace, then livestock feeding studies will be needed to show if residues occur in eggs, meat, and milk. If residues do occur in meat, milk, or eggs, then appropriate tolerance proposals will be necessary. Additionally, a validated analytical method will be necessary for residue determinations.

cc: Reading file
Circu
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TS-769:REVIEWER:A.SMITH:LDT:X77324:CM#2:RM:810:DATE:10/7/80
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INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Triadimefon® Bayleton PETITION NO OF2349

CCPR NO. None

Codex Status

[X] No Codex Proposal Step 6 or above

Residue (if Step 9): None

Crop(s)	Limit (mg/kg)
None	

Proposed U. S. Tolerances

1-(4-chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)-2-butanone and its metabolite beta-(4-chlorophenoxy)-alpha-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol

Residue: None

Crop(s)	Tol. (ppm)
Melons	0.2 ppm
Grapes (fresh market only)	0.2 ppm

Crops to be imported from Mexico.

CANADIAN LIMIT

Residue: None

Crop	Limit (ppm)
None	

MEXICAN TOLERANCIA

Residue: None

Crop	Tolerancia (ppm)
None	

Notes:

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