UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

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SUBJECT: PP#OE2393 ®Bayleton on cucumbers and tomatoes. Evaluation of analytical methods and residue data.

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The Mobay Chemical Corp., proposes tolerances for residues of the fungicide 1-(4-chlorphenoxy)-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 cucumbers at 0.1 ppm and tomatoes (whole, fresh) at 0.2 ppm. The commodities are to be imported into the United States from Mexico.

There are no established tolerances for ®Bayleton. Tolerances are pending for grapes and melons at 0.2 ppm (PP#OF2349); apples and pears at 0.75 ppm and grapes at 1.0 ppm (PP#OG2300).

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. The method should be modified to determine the conjugated components.

3a. The residue data do not reflect total residues (free and conjugated) of Bayleton and its metabolite KWG0519. Therefore, valid conclusions on residue levels in cucumbers and tomatoes cannot be made. Residue data must be submitted for total residues in cucumbers and tomatoes.

3b. Fresh market restrictions are not generally practical for a permanent tolerance since tomatoes could be diverted to processing channels. Residue data should be submitted for the tomato by-products (paste; wet and dry pulp). If necessary, food aditive tolerances should be proposed. Alternatively, the petitioner may be able to ascertain that imported tomatoes are not processed.

4. If the fresh market restrictions are shown to be impractical and residues result in the feed item (tomato pulp), then livestock feeding studies will be necessary to show if residues occur in eggs, milk, and meat. If residues occur in eggs, milk and meat, then tolerance proposals will be necessary. 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 noted in Conclusions 2,3, and 4.

Detailed Considerations:

Manufacturing Process (PP#OG2300)

[redacted] Tech. Bayleton has the following composition.

Bayleton 92-95%

[redacted]

The impurities are not likely to produce a residue problem.

MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

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.

Tomatoes (fresh market only): apply 2.5 ozs. a.i./A as a foliar spray. A maximum of 8 applications may be made up to day of harvest.

Cucumbers: apply 1.8 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 tomatoes may be diverted to the processing market. The petitioner may be able to eliminate the need for processed tomato data if he can demonstrate that tomatoes imported from Mexico would not be processed.

Nature of the Residue:

Metabolism studies were submitted for tomatoes and cucumber in PP#OF2349. 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 anlyzed for residues of Bayleton and its metabolites.

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, 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 plants residue 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.

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 spectometry, and derivative formation with acetic anhydride.

Plant metabolism studies with radolabelled Bayleton and apples were reviewed in PP#OG2300 (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 wheathering 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% of the residue at 0-day, 50% at 14 days, and had decreased to 13% at 49 days. The principal metabolite was [1-(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%).

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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.

Animals:

Metabolism studies were performed with radiolabelled C^{14} Bayleton and various animals (rats, lactating cows, pigs, and laying hens-see PP#OG2300). 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.

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 cucumbers and tomatoes had <0.01-0.02 ppm Bayleton or KWG0519-equivalent residues. Control samples of tomatoes and cucumbers were fortified with Bayleton and its metabolite KWG0519 at levels of 0.05 ppm and 0.1 ppm. Recoveries were 80-99% for tomatoes and 87-142% for cucumbers.

All Nitrogen-containing compounds registered for use on cucumbers and tomatoes were tested as sources of inteferences in the analysis of Bayleton and KWG0519 residues. Any interferences were 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 (PP#0F2349).

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. A method tryout will need to be conducted when the questions raised are resolved.

Residue Data:

Tomatoes: samples were obtained from crops in Mexico which had been treated as proposed (8 foliar applications up to day of harvest at 2.5 oz act/A/app.). Residues of Bayleton and its metabolite were 0.08-0.15 ppm on day of harvest (0-day); 0.02-0.08 ppm at 5 days after the last application; and, 0.01-0.05 ppm at 15 days.

Tomato byproducts: the tomatoes are for the fresh market only. However, it is possible that the imported tomatoes could be diverted thru processing channels. As a result, the fresh market only restriction is not considered practical for a permanent tolerance.

Residue data should be submitted for tomato byproducts (paste, wet and dried pulp). The wet and dried pulp are used as livestock feeds. If residues in these items or paste exceed the level in fresh tomatoes, then food additive tolerances should be proposed to cover such residues.

Cucumbers: samples were obtained from crops in Mexico which had been treated as proposed (3 foliar applications at 1.8 oz act/A/app. up to day of harvest). Residues of Bayleton and its metabolite were <0.01-0.09 ppm at 0-day; <0.01-0.04 ppm at 5 day; and, <0.01-0.02 ppm at 15 days.

The residue method dos 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 cucumbers and tomatoes cannot be made.

Data for tomatoes and cucumbers which reflect analyses for free and conjugated forms of Bayleton and its metabolite KWG0519 should be submitted.

Meat and Milk

If the fresh market restriction is shown to be impractical and residues occur in the feed item tomato pulp, then livestock feeding studies will be needed to show if residues occur in eggs, milk, and meat. If residues do occur in eggs, milk, and meat, then appropriate tolerance proposals will be necessary. Additionally, a validated analytical method will be necessary for residue determinations.

TS-769:RCB:A.Smith:gs:X77324:CM#2:RM810:11/10/80
cc: RF, Circ., Smith, Watts, FDA, TOX, EEB, EFB, PP#0E2393
RDI: R.S. Quick:11/5/80

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INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Triadimefon®; Bayleton®

PETITION NO OE2393

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

Residue: beta-(4-chlorophenoxy)-alpha-(1,1-dimethylethyl)-1H-1,2,4-triazol-1-ethanol

Crop(s)	Tol. (ppm)
Cucumbers	0.1
Tomatoes (fresh)	0.2

CANADIAN LIMIT

Residue: None

Crop	Limit (ppm)
None	

MEXICAN TOLERANCIA

Residue: None

Crop	Tolerancia (ppm)
None	

Notes:

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