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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

File: PP # 1G 2546

MEMORANDUM SEP 18 1981

DATE:

SUBJECT: 1) Bayleton Residue Tolerance in Grape Juice and Wine.

2) Bayleton Residue Tolerances in Apple and Grape Pomaces and Raisin Trash.

3) Bayleton Residue Tolerance in Milk, Eggs, Meat and Meat By-Products.

(Reg. # 3125-320, Caswell # 862 AA, PP # 0G2300 (petition # changed to 1G 2546) Revised 1 H 5282)

FROM: George Z. Ghali, Ph.D.
Toxicology Branch, HED (TS-769) G. Ghali R.H. 9-17-81

TO: Henry Jacoby, (PM 21)
Registration Division (TS-767)

Registrant: Mobay Chemical Corporation
Agricultural Chemical Division
Kansas City, Missouri 64120

Action Requested:

1) Establishment of a tolerance of 2 ppm in grape juice and deletion of previously proposed tolerance for wine as per Mobay Chemical's letter 3/31/81.

2) Establishment of a tolerance of 0.01 ppm in milk, eggs, meat and meat by-products of cattle, goats, hogs, horses, poultry and sheep.

3) Establishment of tolerances of 3.0, 4.0 and 7.0 on grape pomace, apple pomace and raisin trash respectively.

Conclusion and Recommendations:

1) The question of Bayleton residues in grape juice has been addressed before in a memo by G. Ghali to H. Jacoby dated June 25, 1981 in reference to pp # 1H5282 as follows: "Toxicology Branch recommends for the establishement of a tolerence of 2 ppm in grape juice providing that this juice is not to be used for wine making".

2) Toxicology Branch recommends for the establishment of the proposed 0.01 ppm tolerance for milk, eggs, meat, and meat by-products of cattle, goats, hogs, horses, poultry, and sheep if RCB finds the proposed tolerance adequate.

   Toxicology Branch defers to the RCB the question of whether the proposed tolerance adequately covers the residues expected to occur in these food commodities.

3) Toxicology Branch defers to the RCB the question of whether the feed additive tolerance proposed is adequate to cover possible residues in eggs, milk, meat, and meat by-products.

4) The reviewer of this petition considers that the teratology aspects are not adequately delineated until the raw data and background on historical terata incidence in the strain of rats used in this study, are submitted and reviewed as previously requested by Roger Gardner, memo of 4/16/81 to Donald Stubbs. However, an adequate margin of safety (MOS) exists to cover for this toxicity area (teratology) at the highest possible residue tolerance granted on food commodities.

Existing Tolerances:

There are Tox. approved (unpublished) tolerances for this pesticide, as follows:

Apples, fresh	1.00 ppm	pp# 1F2474
Pears, fresh	1.00 ppm	pp# 0G2300
Grapes, fresh	2.00 ppm	pp# 1E2459, 1F2474
Wheat	0.10 ppm	pp# 1G2432
Barley	0.10 ppm	pp# 1G2432
Chick Peas	0.10 ppm	pp# 1E2459
Tomatoes	0.20 ppm	pp# 0E2393
Cucumbers	0.10 ppm	pp# 0E2393
Melons	0.20 ppm	pp# 0E2349

Formulation:

Bayleton technical 55.0% (Active ingredient)

[redacted]

All inert ingredients have been cleared under 40 CFR 180.1001 c and e.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Toxicology Data:

A. Bayleton 50% W.P.:

(memo by John Doherty dated 2/15/78)

1.	Acute oral, rats,	LD_{50} 435 mg/kg
2.	Acute dermal, rats,	LD_{50} >
3.	Acute inhalation, rats,	LC_{50} > 20 mg/L
4.	Primary skin irritation,	negative
5.	Primary eye irritation,	corneal damage, reversible.

B. Bayleton, technical:

(memo by J. Doherty 1/9/80, A. Arce 1/24/80)

1. Acute oral, rats, LD_{50} 568 mg/kg (male), 363 mg/kg (female), Core minimal.

2. Acute I.P. rats, LD_{50} 293 (female) 321 mg/kg (male), Core minimal.

3. Acute dermal, rats, LD_{50} > 1000 mg/kg, Core minimal.

4. Acute inhalation, mice, rabbits, hamsters and rats. LC_{50} > 174 mg/m^3, Core minimal.

5. Primary skin irritation, rabbits, negative, Core minimal.

6. Skin irritation, human, Not irritant.

7. Primary eye irritation, invalid study, dose was not reported.

8. Embryotoxicity and teratology:

In an oral administration study in rats, occasionally cleft palates were seen in the groups treated with 75 mg/kg/day and above. These equaled only 4 of the 211 fetus of one experiment and 3 of 183 in another experiment. However, this deformity is seldom seen in this strain. A no-effect level for embryonic and fetal development/teratology was considered to be at least 50 mg/kg/day (J. Doherty, 2/15/1978).

In a later memo by Roger Gardner dated 4/16/81 it was concluded that the cleft palates observed in this study may not be attributable to Bayleton treatment. However, the memo also indicated that the raw data and background on the historical terata incidence in this strain of rats are needed to further evaluate the significance of this effect.

From the information available until now, the compound is questionably positive with a clear-cut no-effect level for teratogenic effect of 50 mg/kg/day.

Inhalation administration, rats, negative for terata and embryotoxicity at dose level of 113.6 mg/m^3, Core minimal.

Oral administration, rabbits, negative up to and including 50 mg/kg (highest dose tested), Core minimal.

9. Mutagenicity:

Dominant lethal test, mice negative for mutagenicity.

Micronucleus test, mice, negative for mutagenicity.

Ames test, negative at doses from 5 to 1000 ug/ml.

10. Subchronic toxicity:

Twelve-week feeding, rats, NOEL > 2000 ppm.

Thirteen-week feeding, dogs, NOEL > 2400 ppm.

11. Subacute toxicity:

Thirty-day oral administration, rats, NOEL 3mg/kg (male), 10 mg/kg (female).

Four-hours inhalation, rats, 15 exposure, NOEL 78.7 mg/m^3.

Cumulative subacute dermal application for four weeks, rabbits, NOEL 250 mg/kg.

12. Chronic Toxicity

(memo by G. Z. Ghali, 3/80, 7/80)

Two-year feeding (oncogenicity) in rats; not oncogenic, NOEL 50 ppm.

Two-year feeding study in dogs, not oncogenic, NOEL 100 ppm.

Multigeneration reproduction study, rats, NOEL 50 ppm.

Two-year feeding (oncogenicity) study in mice; not oncogenic,

NOEL 50 ppm

C. Toxicology Data Gap:

1. An adequate and appropriate metabolism study in mammals.

2. The raw data and background on the historical terata incidence in the strain of rats used in the teratology study as requested by Roger Gardner, memo of 4/16/81 to Donald Stubbs.