PP# 6G1689/FAP# 6H5108. Aldicarb in or on oranges and dried citrus pulp. Evaluation of analytical method and residue data.
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Special Registrations Section and
Toxicology Branch

The Union Carbide Corporation proposes the following tolerances be established for combined residues of the insecticide-nematocide aldicarb [2-methyl-2-(methylthio)propionaldehyde O-(methylcarbamoyl)-oxime] (trade name: TEMIK) and its cholinesterase-inhibiting metabolites, aldicarb sulfoxide and aldicarb sulfone:

(1) a temporary pesticide tolerance of 0.3 ppm in or on the r.a.c. oranges;

(2) a temporary food additive tolerance of 0.6 ppm in or on the animal feed dried citrus pulp from oranges, when present as a result of application of aldicarb to the growing crop.

Pesticide tolerances have been established [40 CFR 180.269] for combined residues of aldicarb and its sulfoxide and sulfone metabolites in various r.a.c.'s at levels ranging from 0.02-1 ppm; in meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep at 0.01 ppm (negligible residue); and, in milk at 0.002 ppm (negligible residue).

A food additive tolerance of 0.3 ppm for residues in cottonseed hulls has also been established [21 CFR 561.30].

No other petitions for this pesticide are co-pending.

The experimental program proposes use of 1020 lbs. of Temik 15G formulation (153 lbs a.i.) on a total of 20.4 acres in 4 states (AZ, CA, FL, TX). (Note: total quantity to be shipped - 1100 lbs Temik 15G.)

Conclusions

1. The nature of the residue is adequately understood. The residue of concern is aldicarb and its cholinesterase-inhibiting metabolites, aldicarb sulfoxide and aldicarb sulfone; these are present in oranges at a ratio of 0:5:1. Residues in oranges are located primarily in the peel (peel:pulp ratio of residues - 4:1).

2. Adequate analytical methodology is available for enforcement purposes.

3a. Residues in ripe oranges are not expected to exceed the proposed tolerance under the proposed conditions of use. (Higher residues may be found in immature oranges, but these are not purposefully harvested.)

3b. Incomplete residue data are available for citrus by-products. For dried citrus pulp, for which minimal data were submitted, residues are not expected to exceed 0.6 ppm. However, either residue data for citrus molasses or a label restriction limiting use to oranges intended for the fresh fruit market only and withdrawal of the proposed temporary food additive tolerance for dried citrus pulp is needed.

4. The general label restriction against preharvest grazing of treated areas should be expanded to preclude grazing in orange groves at any time. Alternately, residue data for ground cover crops can be submitted, and tolerances proposed.

5. If the petitioner restricts use to oranges intended for the fresh fruit market only and broadens the grazing restriction, no feed items will result from the proposed use and Sec. 180.6(a)(3) will apply. However, if the petitioner opts to submit residue data for citrus molasses and cover crops, animal feed items will be involved. Pending receipt and evaluation of such data no Sec. 180.6(a) categorization of that alternative can be conclusively made.

Recommendations.

We recommend against establishment of the proposed temporary tolerances at this time for the reasons cited in Conclusions 3b, 4, and 5.

We defer to TOX on occasional acute exposure (see below).

For further consideration of these tolerance requests, the petitioner must:

1) Either submit residue data for citrus molasses, or impose a label restriction limiting use to oranges intended for the fresh fruit market only. If the latter alternative is chosen, the proposed temporary food additive tolerance for dried citrus pulp should be withdrawn.

2) Either impose a label restriction precluding grazing (pre- and post-harvest) in treated orange groves or submit residue data and tolerance proposal(s) for the ground cover crop(s).

* * *

For consideration of a future permanent tolerance request, the petitioner should be advised we will also require:

1) Additional residue data for various varieties of oranges per se (especially Valencias and Temples), with field treatment reflecting the proposed use patterns.

2) An additional fraction study for citrus with adequate residue data for citrus by-products (e.g., dried pulp, molasses). Such data should be obtained using field-treated oranges containing residue levels at or near the proposed tolerance level.

* * *

EEE (R. E. Ney, Jr., 11/4/75) has commented that rotational crops are not involved in this use.

The question of an occasional acute toxic exposure of an individual to a residue higher than the tolerance level was raised in connection with the last aldicarb petition (potatoes, PP# 3F1414). The potential for such an exposure from potatoes rested largely on the effects of cooking and possible errors in field applications. Similar consideration presumably would apply to oranges. We defer to TOX as to whether

possible aldicarb residues of the levels cited in the following discussion would be of concern from an acute toxicity standpoint.

1. Residues in peel: Residues up to 0.7 ppm (0.55-0.60 aldicarb sulfoxide and 0.11-0.12 ppm aldicarb sulfone) may be localized in peels from normal use. This is substantially higher than residues in whole oranges and orange peels are themselves a human food item (as well as often being introduced into the mouth in the process of eating fresh oranges).

2. Possible occasional over-tolerance residues on whole fruit: Principal concern here is with Valencia oranges (which comprise 50% of the Florida crop). Valencias have an irregular fruiting/harvesting pattern, i.e., green fruit and ripe fruit may be present on a given tree at the same time. The main Florida crop is harvested in May-June, or about 2 months after the proposed "Spring flush" treatment in March-April. The residue uptake pattern shows a clearly defined increase in fruit for about 60 days and then a gradual decline. Valencias picked in May-June after a Mar-April treatment would thus be expected to have peak residues.

There were, in fact, no residues above 0.3 ppm tolerance reported in any samples described as "ripe". Residues up to 0.75 ppm (whole fruit) were reported on samples described as "green" or "immature". Whether this represents a real difference in metabolism rates of green vis-a'-vis mature oranges or vagaries of the sampling is uncertain. We are equally uncertain as to how many marginally ripe fruit would be included in the harvest, which is normally accomplished by tree shaking or bumping. From the standpoint of estimating an occasional acute exposure to an individual, we believe that 0.75 ppm (whole fruit basis) would be a reasonable figure reflecting maximum level from normal use. These figures do not take into account any miscalculation in dosages, which would be unlikely in an experimental program. The potential for such occasional acute exposure to an individual would be enhanced in commercial use and the petitioner should be advised if TOX sees a problem for the permanent tolerance.

Detailed Considerations

Manufacture and Formulation

[redacted]

The formulation to be used is TEMIK 15G Aldicarb Pesticide, a granulated product containing ca. 15% active ingredient. [redacted]

[redacted]

The [redacted] impurities present in the TEMIK 10G formulation were listed in our review of PP# 3F1414 (M. J. Nelson, 12/4/73), [redacted] Owing to the low levels of the individual impurities [redacted] and the nature of the proposed use (soil incorporation), we do not foresee any residue problems in oranges arising from their presence in the formulation.

Proposed Use

For control of various insects, mites, and nematocide pests on oranges, TEMIK 15G Aldicarb Pesticide (EPA Reg. No. 1016-78) is to be applied at 33-67 lbs (5-10 lbs a.i.)/A (based on average of 100 trees/A), with no more than one application permitted per year.

Arizona, California, Florida, Texas:

1) Apply granules in a 3-4 foot wide continuous band at outer edge of dripline on two sides of tree row. Incorporate 2-3 inches into soil. Follow immediately with 2-3 inches of irrigation. or,

2) Drill granules 3 inches deep into soil with fertilizer or grain drill shanks spaced 12"-14" apart to cover a 4-6 foot wide band at outer edge of dripline. Apply to two sides of tree row. Follow immediately with 2-3 inches of irrigation.

California (only):

1) Inject granules 2-3 inches deep into the bottom of water furrows between tree rows. Use two shanks per furrow. Follow immediately with 2-3 inches of irrigation.

Apply prior to or during Spring flush; i.e., between mid-March to mid-April in Arizona, California, and Florida, and between mid-January to mid-February in Texas (Rio Grande Valley). [Note: Spring flush = appearance of new leaves; this occurs prior to bloom].

Some varieties of oranges have a maturity period of about 14 months (eg, Valencia). Bloom and harvest will overlap in these varieties. Consequently, trees of these varieties would have fruit present in a nearly mature state at the time of Spring flush. This would mean that fruit of these varieties could be harvested as close as 30-60 days after treatment.

The labeling contains a general restriction against grazing of livestock in treated areas prior to harvest. We request an additional restriction precluding grazing of livestock in treated orange groves (either pre- or post-harvest) be added to the labeling since no data on residues in ground cover is submitted. Alternately, residue data for ground cover grasses can be submitted, and tolerances therefor proposed.

Nature of the Residue

Aldicarb is absorbed from soil and translocated in plants. It and its sulfoxide and sulfone metabolites, each of which contains the carbamoyl moiety, are potent cholinesterase inhibitors.

The metabolism of aldicarb in plants (cotton, potatoes, spearmint, lettuce, sugar beets, and peanuts) and animals (rat, cow, chickens) has been discussed in previous petition reviews; e.g., M. J. Nelson, 12/4/73, PP# 3F1414, which see.

In brief, the data show a consistent mode of degradation of aldicarb. In plants, aldicarb is rapidly oxidized to aldicarb sulfoxide. Aldicarb sulfoxide is degraded primarily by hydrolysis to sulfoxide oxime and to a lesser extent by oxidation to aldicarb sulfone. Sulfoxide oxime is further converted in the plant to the corresponding nitriles, alcohols, amides, and acids. Conjugation of the alcohols with plant sugars results in water-soluble glycosides. Aldicarb sulfone undergoes

degradation reactions similar to those described for aldicarb sulfoxide. There is no evidence of conjugated carbamate metabolites in plants.

It has been concluded (D. V. Reed, 6/13/72, PP# 2F1188) that there is no evidence of free or conjugated hydroxymethyl derivatives of aldicarb, aldicarb sulfoxide or sulfone, or their anticipated N-demethylated carbamate breakdown products in plants and that these, while present as minor metabolites in animals, are not of toxicological concern (G. E. Whitmore, D.V.M., 3/20/72, PP# 2F1188). In animals, as in plants, the residue of toxicological concern is comprised of aldicarb per se (of which little if any is present as a terminal residue), its sulfoxide and sulfone. Metabolic pathways in plants and animals have been shown to be similar.

While no metabolism studies have been submitted for any citrus, per se, we consider the available data adequate for purposes of defining the nature of the residue. Of concern will be the parent compound and the sulfone and sulfoxide metabolites. Residue data submitted with the petition show the absence of aldicarb per se as a residue in oranges: aldicarb sulfoxide and sulfone comprise the residue of toxicological concern, and these are present in a ratio of about 5:1 sulfoxide: sulfone.

The residue data submitted show that residues concentrate in the peel (4:1 ratio peel/pulp). These residues could occur in fruit through either translocation or in the harvesting process (fruit contact with treated ground during harvest). The latter source of residues would be minimized to some extent since aldicarb is incorporated into the soil upon application and followed by irrigation. In the submitted studies, the fruits appear to have been picked from the trees. Residues probably have resulted via translocation. This is supported by a finding of several ppm residue in the leaves of the treated trees.

Analytical Method

The method of analysis used for residue determinations in whole oranges, pulp, peel, and dried citrus pulp is a GLC procedure adapted from method UC21149-III, which method was discussed in our review (E. L. Gunderson, 1/26/71) of PP# 0F1008 and is our primary enforcement method (PAM II, Method I).

In brief, residues are extracted from a citrus macerate and simultaneously oxidized to aldicarb sulfone by the addition of peracetic acid to the extracting solvent, 3:1 acetone:water. Following clean-up of the extract via Florisil column, pesticide residues are determined by GLC utilizing a flame-photometric detector equipped with a filter specific for sulfur-containing compounds.

The method is specific for aldicarb and its carbamate metabolites; it determines aldicarb and its sulfoxide and sulfone without differentiating between them and expresses their total residue in terms of the sulfone. The oxime and nitrile metabolites of aldicarb, as well as the further degraded metabolites, are removed by the method clean-up and are discarded so they will not interfere.

The method was validated by fortification of oranges with aldicarb sulfoxide and aldicarb sulfone at levels of 0.02-0.44 ppm. Recoveries ranged from 73-96% and 79-109% for the sulfoxide and sulfone, respectively. Blank values from whole oranges were $\leq$0.01 ppm; where separate pulp and peel analyses were made, blank values were $\leq$0.01 and $\leq$0.02 ppm, respectively. Method sensitivity is ca. 0.01 ppm.

The specificity of the method was demonstrated in the presence of other sulfur-containing pesticides registered for use on citrus; interference was not a problem. If needed, an alternate confirmatory technique is available (colorimetric procedure of PAM II, Method A).

The basic GLC method has been tested satisfactorily in MTO's with cottonseed (PP# 9F0798) and milk (PP# 0F1008) at fortification levels of 0.05 ppm (aldicarb sulfoxide and sulfone) in cottonseed and 0.002 and 0.004 ppm (aldicarb sulfoxide) in milk.

We conclude that adequate analytical methodology is available for enforcement of the proposed tolerances.

[Note: methodology is also available whereby aldicarb, aldicarb sulfoxide, and aldicarb sulfone can be separated by selective elution from a Florisil column after extraction and prior to oxidation; this permits determination of individual components of the residue.]

Residue Data

Storage stability data show no loss of total aldicarb residues in ripe oranges held in freezer storage (-10°F) for an interval of 5 months. In fact, somewhat higher residue levels were detected following storage; this apparent increase in residues is attributed to some dehydration in the fruit during storage.

Seven field studies with oranges were submitted; of these, 1 (FL) was with Pineapple Oranges, 1(TX) with Marrs Oranges, 2 (CA) with Navel Oranges, and 3 (FL, CA, AZ) with Valencias. Groves received a single band treatment with TEMIK 15G followed by incorporation; application rate ranged from 2.5-20 lbs a.i./A (up to 2X maximum proposed rate. Samples represent fruit taken at varying intervals after treatment, from immature, green fruit to mature, orange fruit. Data are also presented for both the green and ripe fruit of the

Valencia variety which are found on the trees concurrently. Analyses were made of separate peel and pulp as well as whole fruit.

In the Pineapple Oranges study (treatment in September, not at Spring flush), data are available for oranges harvested 30, 62, 94, and 124 DAA (days after application), as maturation progressed from immature, green fruit to mature, orange fruit. The highest residue was found in the immature green fruit, 30 DAA; at the 1X rate, the residue in the whole fruit was calculated to be 0.42 ppm (based on 25% peel, 75% pulp W/W distribution); the residue was distributed predominantly in the peel. (Data from all field studies indicate that residues average approximately 4X higher in peel than in pulp, in both green and ripe fruit). As the fruit matured, residues decreased, and at the ripe orange stage (124 DAA) residues were <0.1 ppm in the whole fruit.

In the Marrs Oranges study, the grove was treated in May and representative ripe fruit were harvested 179 DAA. The residue level in whole fruit was <0.01 ppm. No data were submitted for immature, green fruit.

In the Navel Oranges studies, groves were treated either in late May or July at up to the 2X rate, and ripe fruit were harvested 178-193 DAA. Residues in whole fruit ranged up to 0.07 ppm. No data were available for immature, green fruit.

In the Valencia Oranges studies, groves were treated either in April or July at up to the 2X rate. In the most comprehensive study (FL - up to 1X rate), representative samples of green and ripe oranges (which, in this orange variety coexist on the same tree) were collected at 31, 63, 93, and 127 DAA, and ripe fruit only at 199, 234, and 244 DAA. Residues in immature, green oranges exceeded 0.3 ppm at each interval tested; the highest residue (0.75 ppm, calculated as whole fruit) was present in the 63 DAA sample. Residues in ripe oranges did not exceed 0.3 ppm (calculated on a whole fruit basis) at any time interval tested; highest residues were observed at 31 DAA (0.22 ppm) and 199 DAA (0.23 ppm), and lowest (0.11-0.13 ppm) at 63, 93, and 244 DAA. A separate study (CA - up to 2X rate) in which ripe oranges were sampled periodically between 7-164 DAA also showed no residues in excess of 0.3 ppm at any time period tested; maximum residue (<0.1 ppm) occurred at 35-71 DAA.

Conclusions: Maximum residues in ripe oranges are not reasonably expected to exceed 0.3 ppm (the proposed tolerance level) under the proposed use conditions. Above-tolerance residues may be encountered in immature, green fruit, but green fruit is not purposefully harvested (due to its low sugar content - per Telecon with Dr. H. Brooks, ARS, Beltsville, 12/11/75).

As previously noted, residues are distributed between the peel:pulp in ca. a 4:1 ratio. As discussed under Nature of the Residue, the residue in oranges is comprised of aldicarb:aldicarb sulfoxide: aldicarb sulfone, present in ratios on the order of 0:5:1. Orange peels per se are a human food item. Taking into account the proposed tolerance level, the peel:pulp residue distribution, and the peel: pulp weight distribution (1:3), we calculate that up to 0.7 ppm residues--consisting of ca. 0.55-0.60 ppm aldicarb sulfoxide and ca. 0.11-0.12 ppm aldicarb sulfone--could be present in orange peels under the proposed conditions of use.

Residue data for the processing by-product and animal feed item, dried citrus pulp, was also submitted. Orange trees were treated at the 2X rate (20 lbs a.i./A) and mature fruit harvested ca. 3 months later. Separate analyses were made of fresh wet orange pulp and peel and of dried pulp processed therefrom. The calculated whole fruit residue was 0.24 ppm, and the residue in dried citrus pulp was 0.45 ppm--approximately a 2-fold concentration. On this basis the petitioner proposes a temporary food additive tolerance of 0.6 ppm for dried citrus pulp prepared from treated oranges (which may contain up to 0.3 ppm residues, the proposed temporary tolerance level).

No residue data were submitted for citrus molasses, which is also an item of animal and poultry feed. Such data are needed to enable us to draw Sec. 180.6(a) conclusions. As an alternative, for purposes of the proposed experimental program (20.4 acres), we could accept a label restriction limiting use to oranges intended for the fresh fruit market only: this would also necessitate withdrawal of the proposed temporary food additive tolerance for dried citrus pulp.

For a permanent tolerance request the petitioner should be advised of the need for: (1) additional residue data for various varieties of oranges (especially Valencias and Temples), with field treatment reflecting the proposed use patterns, (2) an additional fraction study with residue data on all citrus by-products (e.g., dried pulp, molasses). Such data should be obtained using field-treated oranges containing residue levels at or near the proposed tolerance level.

Residues in Meat, Milk, Poultry, and Eggs

If the petitioner opts to restrict use to oranges intended for the fresh fruit market only and broaden the grazing restriction, no animal feed items will be involved in the proposed experimental program, and Sec. 180.6(a)(3) will apply.

Alternately, residue data for citrus molasses and for cover crops will need to be submitted to enable us to categorize within Sec. 180.6(a) the proposed feed uses. [Note: cattle and poultry feeding study data have been previously submitted and reviewed (e.g., M. J. Nelson, PP# 3F1414, 12/4/73); negligible residue tolerances of 0.01 and 0.002 ppm in meat and milk, respectively, are already established.]

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