SC-330

PUBLIC HEALTH SERVICE

AF 25-202

March 3, 1969

~~Alpert~~
~~Barrack~~
~~Cummings~~
~~Diffy~~
~~Rathman~~

File: PP#9F0743

Pesticide Petition No. 9F0743

Mr. Don E. Stallard
T. R. Evans Research Center
Post Office Box 348
Painesville, Ohio 44077

Dear Mr. Stallard:

This refers to Pesticide Petition No. 9F0743 proposing a tolerance of 0.1 part per million for the combined negligible residues of the fungicide Daconil and its metabolite 4-hydroxy-2,5,6-trichloroisophthalonitrile in or on potatoes.

We have completed our review of the above-referenced petition and find that we cannot act favorably on it for the following reasons:

1. Data on the metabolism and degradation of Daconil in the plant are insufficient, and, therefore, no conclusion can be drawn regarding the presence of other metabolites, particularly trichlorodicyanoaniline and 2,4,5-trichloroisophthalonitrile, in potatoes. This was brought to your attention in our letter of October 30, 1967, concerning Pesticide Petition No. 7F0599.

2. The proposed analytical method is unsatisfactory for enforcement purposes because (1) it does not determine all of the possible metabolites including trichlorodicyanoaniline and 2,4,5-trichloroisophthalonitrile; (2) the modified method has not been validated for Daconil with the usual recovery experiments. The method has been validated for the 4-hydroxy metabolite but we will need some representative chromatograms to resolve questions on the sensitivity for this compound; (3) while there is no confirmatory method, we believe that the gas-liquid chromatographic procedure may be sufficiently specific if evidence or a rationale can be presented showing that other pesticide residues, for which tolerances have been established on potatoes, will be separated either on the Florisil column, in the gas-liquid chromatographic column, or excluded by virtue of the alternative electron capture-microcoulometric detectors to the extent that they will not interfere with the determination of Daconil and/or its metabolites.

3. The subacute rat toxicity experiment, Project 200-205, did not demonstrate a no-effect level; the lowest fed level, 4 ppm, resulted in slight kidney cell lesions in female rats that increased in degree of change in both sexes as the compound diet increased. A

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decision about the significance of these cell changes, related to the safety of the requested residue tolerance, will depend upon the following additional Project 200-205 studies:

a. The kidneys, esophagi, stomachs, thyroids, livers, and all other grossly abnormal organs of all rats surviving the 2-year experimental period, as well as all those dying (except the ones markedly autolyzed) at any period, should be examined microscopically.

b. All other organs from at least 10 rats of each sex per dosage level should be similarly sectioned and studied microscopically.

c. The chemical nature of the pigment prominent in both dogs and rats should be investigated.

d. In the event Daconil should be proven to have no chronic effects in rats at these low levels, a similar microscopic investigation of the first chronic rat feeding study (Project 200-148) and possibly the second one (Project 200-154) also will be necessary to determine the compound induced organic effects at 0.15% (1500 ppm).

e. The present format for reporting is good except that we would like listing and grading of individual lesions in individual animals in addition to the group evaluations now being submitted.

f. The criteria for diagnosing chronic nephritis should be stated since these can differ somewhat from one pathologist to another.

You may amend the petition by submitting the necessary data, or you may withdraw the petition without prejudice to a future filing. Otherwise, we may need to establish a zero tolerance for residues of Daconil and/or its metabolites on potatoes. Please let us have your reply within 30 days.

Sincerely yours,

James B. Lamb
Petitions Control Branch
Bureau of Science

cc: Pesticides Regulation
Division, ARS, USDA
cc: SC-13 SC-330 SC-970
JBLamb:mmn 3/3; ctb 2/18/69
R/D Init:HBlumenthal 2/19/69
JAlpert 2/27/69
DMBaker 2/28/69
GJBeusch 2/26/69
FJMcFarland 2/28/69