

Memorandum

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

TO : Mr. Stokes
Petitions Control Branch (SC-13)

FROM : Drs. G. E. Whitmore & F. W.
Division of Pharmacology and Toxicology
Petitions Review Branch (SC-970)

SUBJECT: PP Nos. 8FO670 (2,4-D); 8FO669 (2,4,5-T); 8FO761 (MCPA); 8FO675 (silvex)

DATE: January 15, 1969

NACA Industry Task Force on
Phenoxy Herbicide Tolerances
Washington, D. C.

We have tried to review and unify available data for the class of phenoxy herbicides.

Based on the many evaluations of DFCT, the following generalization with reference to metabolism of this class of compounds may be made:

1. They are numerous.
2. They are not static-continuously changing.
3. They are present in varied amounts related to time of application, plant growth stage, weather conditions, and particular chemical applied.
4. Impractical, if not impossible, to identify kinds and amounts of the various metabolites for any particular crop at any particular time.
5. Known and speculated major metabolites evolve from degradation of side chains, hydroxylation of aromatic ring, and conjugation with plant constituents.
6. The ultimate fate of all metabolites has been postulated to continue to monochloroacetic acid and further to CO_2 , H_2O , and Cl .

From both the petitioner's data and DFCT evaluations, major points of interest, acting to lower total residue emerge. These are that the required long preharvest interval for crop weed control with these compounds would provide time for metabolic processes to approach end point and the use of the compounds on maturing fruits with short preharvest intervals do not involve large amounts of chemical; consequently, very little of parent compound would be available for subsequently produced metabolites.

From the toxicological point of view, the sum of total available information allows a judgement that possible metabolites would not be expected to be significantly more toxic than parent compounds. At the worst we could expect the whole spectrum of potential metabolites to be present or alternately, with time, residues would tend to be of diminishing concern toxicologically, i.e., monochloroacetic, etc. Long preharvest intervals and low application rates tend to reinforce this hypothesis. If DFCT could conclude the presence of any metabolite would be negligible or of the order of the parent residue we could conclude there is no reason to identify or quantitate metabolites in order to establish safety.

INIT: HBlumenthal

cc: SC-970 SC-440 SC-950
GEWhitmore:gr 1/15/69

VM-100

PP Nos. 8FO670, 8FO669, 8FO761, 8FO675

COST REDUCTION PROGRAM