3/17/71

000811

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

Date: March 15, 1971

Reply to Attn of:

Subject: Bladex (SD 15418) on corn (sweet corn kernels, corn grain) popcorn, forage and straw) 0.1 ppm.

XX

PESTICIDE PETITION NO. OFO-998

Shell Chemical Company
New York, New York
(AF 3-553)

TO: Division of Regulations and Petitions Control (BF-320)

Toxicity data supporting the safety of the granted Bladex temporary tolerance of PP 544 is summarized in memorandum August 12, 1969. These data demonstrated the following:

Two rat studies - 100 ppm diets mild effects confined to slightly reduced weight gains and slight questionable increased liver/body weight ratios.

30 ppm very slight weight gain effects.

25 ppm and below compound related effects not revealed by observations.

Dog Study - 15 mg/kg group effects confined to mild reactions during first week of experiment and very slight effects on body weight gain and liver and kidney weights in females.

5 and 1.5 mg/kg groups effects not revealed by observations.

DPI's PP 544 memorandum 29 Jan. 1970, related to some needed additional information about the toxicity experiments, concluded that they were satisfactory and that the animal toxicity feeding experiments supported the safety of the requested temporary residue tolerances.

Toxicity data presented for the support of the requested negligible residue tolerances of this petition, OFO-998, is that referred to above and in addition a rat subacute feeding study of DW 4385 (Metabolite XII), 2 year feeding studies in rats and dogs, and a 3-generation rat reproduction study for Bladex.

Subacute rat feeding study for DW 43 5 (Tunstall Lab 1969):

Groups of weanling Carworth Farms E strain rats, 12 of each sex in each group were fed [illegible] ration, 0, 1.5, 50, 200, or 800 ppm of DW 4385 (Metabolite XII).

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Observations for effects included weight gains, feed intake, behavior checks, hematology, clinical blood chemistry, gross and microscopic examination of organs and tissues. This feeding trial demonstrated a 200 ppm no-effect diet with possible minimum effects (non-degenerative liver cell reactions) in the 800 ppm fed group.

Three generation rat reproduction study (Hine Lab., 1969)

Groups of Long Evans strain of rats, 10 male and 20 females in each group, were fed 0, 3.9, 27, or 80 ppm Bladex diets for three generations. Each female produced two litters in each generation.

An examination of the furnished data did not reveal identifiable effects upon reproduction performance of the animals in this experiment.

Two year rat study (Tunstall Lab., 1970)

This was a conventional study in that numbers of rats fed, group arrangements and observations made were not unusual. The laboratory reported that 12 ppm produced no evidence of toxicological effects and effects with diets of 25 and 500 ppm were confined to slight reductions in body weights.

Two year dog feeding study (Tunstall Lab., 1970)

This was a conventional dog study. The laboratory reported an intake of 1.25 mg/kg (25 ppm)/day as not producing toxicological effects. One hundred ppm diet effects were limited to lowered growth rates, and reduced liver weights in females.

Careful reading and examination of the data in these dog and rat studies did not reveal information contrary to the conclusions of the laboratory. A detailed summary of these three long-term studies isn't needed for the support of the safety of the requested negligible residue tolerances. When the need arises via additionally requested residue tolerance, summaries will be developed.

The PEB February 8, 1971 memorandum states that residue information allows the use of this compound to fall into Category 3 of Section 420.6 with respect to meat, milk, poultry and eggs. Safety considerations for humans consequently are limited to what residue would be expected in sweet corn kernels, corn meal, and corn oil. This same memorandum states that field corn pot studies of C^{14} ring labeled Bladex demonstrated about 0.02 and 0.05 ppm of Bladex equivalent residues from a 2 and 4 pound/A application respectively. PEB stated this data extendible to sweet corn.

The PEB February 8, 1971 memorandum states that approximately 60% of the residue is comprised of the hydroxy metabolites for which there is no enforcement method. The metabolism of Bladex has been determined to be similar in corn and animals consequently the submitted toxicity data reflects laboratory animal exposure to Bladex and its metabolites that would be found as residues in the corn grain and derived products.

The low Bladex equivalent residues (Bladex and its metabolites), 0.05 ppm in the pot experiments at the 4 pound act/A presumably includes all the hydroxy metabolites including the prominent one, XII which was demonstrated to be considerably less toxic than Bladex in the submitted 13 week rat feeding study.

The petition toxicity data supports the safety of the requested negligible residue tolerances including the hydroxy metabolites.

The petition toxicity data also supports the safety of the extension of the granted temporary tolerance.

PEB defers to the toxicology group for an opinion as to whether the tolerance level should cover combined residues of Bladex and metabolites and be so expressed. It would appear from the residue information that the tolerance should be expressed as Bladex plus the metabolites.

Dr. G. E. Whitmore
Environmental Protection Agency

cc: BF-145
BF-140
BF-216
VM-300

GEWhitmore:dps 3-15-71