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

NOV 2 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Chlorothalonil Reregistration: List A Case No. 0097: Chemical No. 081901: ISK Biotech Data Waiver Request for Poultry Metabolism: CBRS No 12821: DP Barcode D196755.

FROM: William O. Smith, Chemist
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THROUGH: Edward Zager, Chief
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The registrant has requested that we reconsider previously rejected poultry metabolism/feeding studies because these studies demonstrate that residues in the feed do not transfer to eggs or meat at levels that merit any further characterization.

BACKGROUND

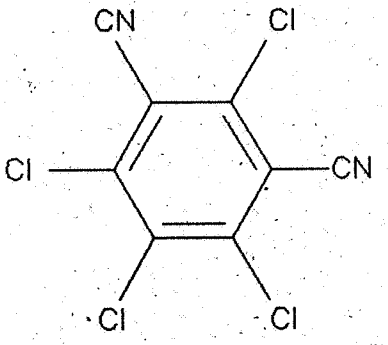
Tolerances have been established for the combined residue of chlorothalonil and its 4-hydroxy metabolite, SDS-3701, (see Fig 1 for structures) in or on numerous raw agricultural commodities ranging from 0.05 ppm to 15 ppm. No tolerances have been established for meat, milk, poultry, or eggs.

The Agency has recently accepted goat metabolism studies (P. Deschamp, D174779, 11/4/93), which included separate studies with ^{14}C-chlorothalonil and ^{14}C-SDS-3701. When ^{14}C-chlorothalonil was fed at the exaggerated level of 30 ppm in the diet, no chlorothalonil was detected in milk or tissue samples. The radioactive residues present were polar

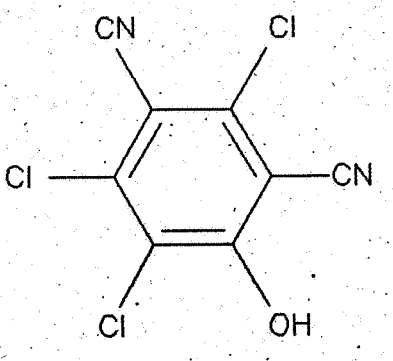
metabolites or non-extractable residues. When ^{14}C-SDS-3701 was fed at 2 ppm, considerably higher levels of radioactivity were found in milk and meat and SDS-3701 comprised 90-100% of the total radioactive residue. These data, among others, support the registrant's conclusion that chlorothalonil is extensively metabolized, probably to multiple glutathione conjugates, in animal tissues while SDS-3701 is transferred to tissues intact (see W. Smith; D199685; 10/14/94). The registrant is conducting a ruminant feeding study for purposes of establishing tolerances on meat and milk commodities.

The registrant submitted studies in 1983 under PP#3F2875 (MRID 00127866) in which separate groups of chickens were fed ^{14}C-chlorothalonil and ^{14}C-SDS-3701. These studies were rejected by the Agency because none of the radioactive residue in eggs or tissues was characterized and new poultry metabolism studies were required. The registrant is claiming that these studies should be acceptable because they were conducted at greatly exaggerated feeding rates and the transfer of total radioactive residues to eggs and tissues was so low as to not require any further characterization. Implicit in this argument is the conclusion that if no further metabolism studies are required then no tolerances will be needed for poultry commodities.

Fig. 1. Chlorothalonil Residues Regulated in Plant Commodities.



SDS-2787
CHLOROTHALONIL



SDS-3701

CBRS CONCLUSIONS

1. The previously submitted poultry feeding studies (PP#3F2875; MRID 00127866) are adequate to satisfy the poultry metabolism study required as part of reregistration (GLN 171-4(b).

2. There will be no need at the present time for further poultry feeding studies (GLN 171-4(j).

3. Analysis of the TRR from poultry fed exaggerated levels of ^{14}C-chlorothalonil and ^{14}C-SDS-3701 indicate that residues of chlorothalonil are not significantly transferred to eggs or tissues. The levels of SDS-3701 that would be transferred at a 1x feeding rate are low enough to not require any further characterization.

4. Based on present uses of chlorothalonil, we conclude that tolerances are not required for poultry commodities. If new uses are proposed on animal feed items in the future, we may require further metabolism and feeding studies and the establishment of tolerances on animal commodities.

DETAILED CONSIDERATIONS

Estimation of the Maximum Dietary Burden of Chlorothalonil and SDS-3701 for Poultry

The registrant contends that chlorothalonil is not expected to occur in significant amounts on poultry feed items and has suggested a maximum dietary burden for chlorothalonil between 0.001 ppm and 0.1 ppm depending on whether one takes into consideration such factors as actual residues monitored on feeds, the relative proximity of feed items to animals, percent crop treated with chlorothalonil, etc. They point out that corn is the major poultry feed item, comprising as much as 60% of the feed, with soybean products being the other major component of a typical diet. Less than 1% of the soybean crop in the U.S. is treated with chlorothalonil.

We agree with the registrant's assessment that corn and soybeans are the two most important ingredients in poultry diets, both in terms of the proportion of diet and widespread use. However, for purposes of setting tolerances, we must consider localized sources of residues such as dry tomato pomace and normally we base our estimates on the assumption that residues occur on feed items at tolerance levels. It should be noted that no tolerance exists for tomato pomace because residues of chlorothalonil do not concentrate in the pomace. In fact, residues have been shown to be reduced significantly in processed tomato commodities by the initial washing step and the Agency has concluded (E. Zager; 10/24/83; Appendix D to Residue Chemistry Chapter of Chlorothalonil Registration Standard) that residues in processed commodities of tomatoes are not likely to exceed 1 ppm as a result of the registered uses of chlorothalonil. Therefore, we will use a value of 1 ppm as an estimated

maximum residue for tomato pomace. Table 1 lists the potential dietary contributions of all poultry feed items for which chlorothalonil tolerances have been established or proposed.

Table 1. Potential Poultry Feed Items Treated with Chlorothalonil.

Feed Item	Max % Diet [a]	Tolerance or estimated max. residue	Potential Dietary Burden
Tomato Pomace	10	(1 ppm)[b]	**0.1 ppm**
Peanut Meal	25	0.3 ppm	0.075 ppm
Soybean Seed	20	0.2 ppm	0.04 ppm
Soybean Meal	40	0.2 ppm	**0.08 ppm**
Soybean Hulls	20	(0.4 ppm)[c]	0.08 ppm
Bean Seed	10	0.1 ppm	0.01 ppm
Cowpea Seed	10	0.1 ppm	0.01 ppm

[a] Taken from Table II (June 1994) of Subdivision O, Residue Chemistry Guidelines.

[b] A tolerance of 5 ppm has been established for tomatoes; however, processing studies have shown that residues are reduced by the initial washing step and that a maximum residue expected on pomace would be less than 1 ppm.

[c] No tolerance exists for soybean hulls at the present time but processing studies indicate that a tolerance of 0.4 ppm would be appropriate.

In the present considerations we will assume that the maximum dietary burden expected for poultry would occur from a diet containing 10% dry tomato pomace, 40% soybean meal and 50% commodities that have not been treated with chlorothalonil. Therefore, assuming that 100% of the tomato and soybean commodities in poultry feed contain tolerance level residues of chlorothalonil, a maximum dietary burden would be 0.18 ppm chlorothalonil. This is a greater dietary burden than one would reasonably expect to be present in typical poultry diets but it is consistent with the process by which the Agency sets tolerances.

We will assume that SDS-3701 comprises the same proportion of the terminal residue as assumed by the registrant in setting up ruminant feeding studies, i.e., that approximately 7% of the total chlorothalonil residue of concern is SDS-3701.

Thus, for purposes of determining the need for tolerances on poultry tissues and eggs, we

will assume a maximum potential dietary burden (1x level) of 0.18 ppm chlorothalonil and 0.013 ppm SDS-3701.

Reconsideration of Poultry Metabolism/Feeding Studies

Two poultry feeding studies were conducted with radiolabeled chlorothalonil and SDS-3701. In one study the birds were dosed daily for 21 days with 0, 2, 6 and 20 ppm ^{14}C-chlorothalonil. In the other study the birds were dosed daily for 21 days with 0, 0.1, 0.3, and 1 ppm ^{14}C-SDS-3701. Eggs were collected daily for 27 days and tissues were collected 6 hr, 3 days and 7 days after the final dose on day 21. Total radioactive residues were determined in egg and tissue samples by combustion and liquid scintillation counting. The limit of radiochemical detection, which was taken as twice background radiation, averaged about 0.03 ppm. The results of the two feeding studies are summarized in Tables 2 and 3.

Table 2. Total Radioactive Residues in Eggs and Tissues Resulting from Feeding of ^{14}C-Chlorothalonil.

	Residues in tissue (ppm)		
	Low Dose (2 ppm; 11x)	Mid Dose (6 ppm; 33x)	High Dose (20 ppm; 111x)
Egg white	<0.023-<0.041	<0.023-<0.041	<0.023-<0.041
Egg yolk	<0.021-0.048	<0.034-<0.048	0.047[a]
Liver	<0.04	0.050[b]	0.098[b]
Fat	-	<0.025	<0.042
Abductor	-	<0.025	<0.045
Pectoral	-	<0.025	<0.045
Skin	<0.04	<0.040	<0.045
Cardial	-	<0.025	<0.045

[a] During 27 days of egg collection, residues were ND (<0.029-<0.048 ppm) except for days 13 (0.047 ppm), 14 (0.044 ppm), 15 (0.041 ppm), 16 (0.039 ppm) and 17 (0.035 ppm).

[b] Residues depurated in three days.

Table 3. Total Radioactive Residues in Eggs and Tissues Resulting from Feeding of ^{14}C-SDS-3701.

	Residues in tissue (ppm)		
	Low Dose (0.1 ppm;7.7x)	Mid Dose (0.3 ppm; 23x)	High Dose (1 ppm; 77x)
Egg white	<0.022-<0.041	<0.022-<0.041	<0.022-<0.041
Egg yolk	0.04	0.119 [b]	0.415 [d]
Liver	0.056[a]	0.269 [b]	0.782 [c]
Fat	<0.038	<0.038	<0.038
Abductor	<0.034	<0.034	<0.034
Pectoral	<0.038	<0.038	<0.038
Skin	<0.034	<0.034	0.037 [a]
Cardial	<0.020	0.055 [a]	0.154 [b]

[a] Residues depurated in 3 days.
[b] Residues depurated in 7 days.
[c] Residues decreased by 30% in 3 days and 85% in 7 days.
[d] Residues decreased to 0.185 ppm by day 27.

From Table 2 it can be seen that there is no expectation of detecting residues of chlorothalonil in eggs or tissues as a result of registered uses of chlorothalonil. The only detectable residues in eggs occurred in the yolks from days 13 through 17 of the 21-day feeding period in birds that had been fed a dietary burden estimated at 111x the maximum expected dietary burden. The only tissue bearing detectable residues was liver from birds fed at the 33x and 111x rates. Extrapolating these results to a 1x feeding level indicates that residues would not be detectable.

The results summarized in Table 3 are consistent with ruminant studies in that they confirm that SDS-3701 would be the primary source of any secondary residue transferred from animal feed to the meat, milk and eggs of livestock. These results support the conclusion that residues from consumption of SDS-3701 do not concentrate in any tissue; however, residues that rapidly depurate do occur in egg yolk, liver and cardial tissue of birds that have been dosed at exaggerated rates. Egg yolks typically comprise about 35% of an egg; therefore, if the TRR in Table 3 are assumed to be 100% SDS-3701 and are extrapolated to a 1x feeding rate there is no expectation of detectable residues of SDS-3701 occurring in eggs. Likewise, extrapolation of the TRR from cardial tissue to a 1x rate indicate no expectation of detectable residues.

In the case of the liver an extrapolation of the TRR to a 1x feeding rate indicate that residues approaching 0.01 ppm might occur. These residues are approaching a level that might be detectable but given the conservative nature of our assumptions in estimating dietary burden and the transient nature of the residues in the liver we conclude that it is not likely that detectable residues of SDS-3701 would occur; therefore, the need for tolerances for residues in poultry commodities is not indicated at the present time.

cc: W. Smith, Chlorothalonil Reg. Std. File, SF, RF, circulation.

7509C:CB-II:WOS:wos:Rm805A:CM#2:X5353:10/31/94

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