

US EPA ARCHIVE DOCUMENT

ADSchlosser:REley:abs  
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*Reley*

Reevaluation of Pesticide Petition No. 990768 for  
methoxychlor [2,2-bis (p-methoxyphenyl)-1,1,1-  
trichloroethane] and other isomers and reaction products  
Submitted by DuPont  
Revised September 17, 1969 Metabolite Studies  
Revised July 16, 1970 additional residue data

INTRODUCTION

See evaluation dated December 30, 1968.

See opinion dated January 17, 1969.

On July 16, 1970 petitioner submitted additional residue, metabolite  
and toxicity studies requested by the FDA.

This petition proposes that FDA Reg. No. 120.120 be amended to require  
100 parts per million in milk with 40 ppms per million in milk  
for collecting pesticide residue in milk. The latter being equivalent  
to 0.05 ppm for whole milk at 42 bacterial content.

DIRECTIONS FOR USE

See MIRA Summary pages 111-114.

Apply 1/2 to 1/4 (depending) 2 grams per acre. Repeat every 7 weeks  
if necessary.

Apply 1/2 to 1/4 (depending) 1.0 to 1.5 lbs per acre/week.

ANALYTICAL METHODS

GC-microencapsulated detection.

DISCUSSION OF DATA

Some of the residue data submitted are listed  
in the following table. The table shows the  
residue levels in milk and in other tissues  
after various treatments. The table also  
shows the results of the metabolite studies  
conducted by the petitioner.

Residue in Milk (ppm) - 100  
Residue in Milk (ppm) - 40

Feeding Studies  
Residue PPM in Whole Milk

Days of Fortified diet	100 PPM in Diet			300 PPM in Diet			Control	
	Methoxy- chlor	B	C	Methoxy- chlor	B	C	Methoxy- chlor	B
0 pre treatment	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
1	"	"	"	0.07	"	"	"	"
3	"	"	"	0.08	"	"	"	"
5	"	"	"	0.10	"	"	"	"
7	"	"	"	0.08	"	"	"	"
11	"	"	"	0.08	"	"	"	"
21	"	"	"	0.07	"	"	"	"
29	"	"	"	0.08	"	"	"	"
1 day after treatment	"	"	"	0.02	"	"	"	"
6 days after treatment	"	"	"	0.02	"	"	"	"

Data on dust application and feeding appear to support tolerance. Spray application data are at only 1/2 the maximum recommended rate.

In connection with the feeding studies analyses of feces and urine were made during the test period. For animals fed the 100 PPM methoxychlor diet, a maximum of only 11 PPM of intact methoxychlor was found in feces along with 0.05 PPM of compound B and C. Maximum in urine was 0.02 PPM each for methoxychlor and compounds B and C.

Levels of compound B (1,1,1-Trichloro-2,2,2-trihydroxyethyl) shown as high as 12 PPM were found in urine and 14 PPM in feces. Report states that methoxychlor was eliminated from treated cows in the urine as compound B, and/or as 1,1,1-trichloro-2,2,2-trihydroxyethyl.

The following are noted concerning above data:

(1) The greater part of the 300 PPM of ingested methoxychlor is metabolized for excretion as parent compound or metabolites in animal urine and feces.

(2) It is not clear whether unchanged compound B is excreted in the analytical results in this compound.

No metabolites reported for possible unidentified metabolites.

Metabolism of methoxychlor in diet:

(1) Methoxychlor is metabolized in diet by 0-methoxylation to 1,1,1-trichloro-2,2,2-trihydroxyethyl (methoxychlor), 1,1,1-trichloro-2,2,2-trihydroxyethyl (methoxychlor), 1,1,1-trichloro-2,2,2-trihydroxyethyl (methoxychlor), 1,1,1-trichloro-2,2,2-trihydroxyethyl (methoxychlor) and their respective chlorides. These compounds are highly volatile in animal urine.

(2) All of radioactively labeled methoxychlor was eliminated within 4 days.

(3) 90% of total activity was found in faces of which 85.4% was polar or soluble in diethyl ether and 14.4% was hexane soluble.

#### Degradation of methoxychlor by Ultra-Violet light and sunlight

(1) Aqueous dispersions of methoxychlor wettable powder are very stable U.V. irradiation in the laboratory.

(2) Sunlight causes a rapid degradation of a methanol solution of methoxychlor.

(3) In general methoxychlor is degraded to less toxic compounds when exposed to sunlight, ultraviolet light and heating.

(4) Author recommends toxicology tests on animals with methyl salicylate (one of the degradation products). This compound is insecticidally active.

#### Additional studies:

A 2 quart pour on application of 0.5% methoxychlor (1/2 recommended maximum dose) caused a 0.07% residue in whole milk at 3 days. Dusting of 3 beds of dairy cattle with 2.5 gms. active WP gave residue values of 0.041, 0.034 and 0.038% methoxychlor in whole milk at 1, 2 and 3 days. Authors state that it appears that any methoxychlor residue found in milk from dust application to dairy cows is from external application.

#### Action of Rat Liver Microsomes and Cow Liver Microorganisms on methoxychlor

(1) Extracts from the microsomal fraction of rat liver were incubated with  $^{14}C$  labeled methoxychlor. Metabolites identified by HPLC were: unchanged methoxychlor 40-65% of activity; 1,1-dichloro-2,2-bis(4-methoxyphenyl) ethane 1.2 - 1.5%; 1,1-dichloro-2,2-bis(4-methoxyphenyl) ethylene 2 - 4%; 1,1,1-trichloro-2,2-bis(4-methoxyphenyl) ethane 2 - 4%; 2,2-bis(4-methoxyphenyl) acetic acid 2-4%. 91 - 97% of applied activity claimed recovered.

Extracts from rumen flora similarly treated yielded no metabolites.

Unchanged methoxychlor 86.4%

1,1-dichloro-2,2-bis(4-methoxyphenyl) ethane 2.3%

1,1-dichloro-2,2-bis(4-methoxyphenyl) ethylene 2.4%

1,1,1-trichloro-2,2-bis(4-methoxyphenyl) ethane 1.5%

100% of applied activity was recovered.

#### CONCLUSIONS AND RECOMMENDATION

A favorable opinion was given on January 17, 1961. No further action is required at this time.