11-4-93 R.F.

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

NOV 4 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Reregistration of Chlorothalonil. **Ruminant Metabolism Study Upgrade.** List A Case No. 0097. Chemical No. 081901. CBRS No. 9417; DP BARCODE D174779; MRID 42174401.

FROM: Paula A. Deschamp, Section Head
Reregistration Section I
Chemistry Branch II: Reregistration Support
Health Effects Division (7509C)

THRU: Edward Zager, Chief
Chemistry Branch II: Reregistration Support
Health Effects Division (7509C)

TO: Lois Rossi, Deputy Division Director
Reregistration Branch
Special Review and Reregistration Division (7508W)

Attached is the review of data/information on two ruminant metabolism studies submitted in response to the 9/88 Chlorothalonil Guidance Document and a CBRS review by R. Perfetti (CBRS No. 7112 dated 1/30/91). This information was reviewed by Acurex Environmental under supervision of CBRS, HED. The data assessment has undergone secondary review in CBRS and has been revised to reflect Branch policies.

The nature of the residue in ruminants is adequately understood. The terminal residues of concern in milk and ruminant tissues consists of chlorothalonil and its hydroxy metabolite, SDS-3701. The registrant has provided additional information and adequately addressed the deficiencies in the CBRS review dated 1/30/91.

Attachment 1: Chlorothalonil CBRS No. 9417; DP BARCODE D174779. Registrant's Response to Residue Chemistry Data Requirements.

cc: PADeschamp (CBRS), Circulate, Chlorothalonil RegStd File, SF, Acurex Environmental, Microfiche
electronic media: F:\USER\CB\Chlorothalonil.2

7509C:CBRS:PDeschamp:CM#2:Rm804A:703-305-6227:11/03/93
RDI: MMetzger:11/03/93

CHLOROTHALONIL
(Chemical Code 081901)
(CBRS No. 9417; DP Barcode D174779)

TASK 3

Registrant's Response to Residue Chemistry Data Requirements

September 17, 1993

Contract No. 68-DO-0142

Submitted to:

U.S. Environmental Protection Agency
Arlington, VA 22202

Submitted by:

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CHLOROTHALONIL

(Chemical Code 081901)

(CBRS No. 9417; DP Barcode D174779)

REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY REQUIREMENTS

Task 3

BACKGROUND

The Chlorothalonil Guidance Document dated 9/88 concluded that the qualitative nature of the residue in animals is not adequately understood and required data pertaining to the nature of the residues in poultry and ruminants. The Guidance Document specified dosing animals with [^{14}C]chlorothalonil; however, the previous Guidance Document (9/84) included a requirement for dosing with the [^{14}C]hydroxy-chlorothalonil plant metabolite (4-hydroxy-2,5,6-trichloroisophthalonitrile; SDS-3701), as well as the parent compound. In response to these requirements, Fermenta ASC Corporation submitted metabolism studies on lactating goats dosed with [^{14}C]chlorothalonil (1990; MRID 41576001) and [^{14}C]4-hydroxy chlorothalonil (1990; MRID 41576002). The Agency review of these studies (R. Perfetti; CBRS No. 7112; 1/30/91) concluded that the metabolism of [^{14}C]4-hydroxy chlorothalonil in goats is adequately understood; however, the [^{14}C]chlorothalonil study was found to be deficient. In reply, ISK Biotech Corporation has submitted a response (1992; MRID 42174401) to the Agency's review of the [^{14}C]chlorothalonil goat metabolism study. This submission is reviewed here to determine its adequacy in fulfilling outstanding ruminant metabolism requirements. The Conclusions and Recommendations stated herein pertain only to data requirements for ruminant metabolism.

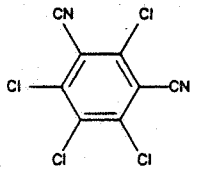
The qualitative nature of the residue in plants is not adequately understood. Metabolism data for celery (D185139) and snap beans (D195755) to support reregistration of chlorothalonil are currently under review. The existing and reviewed plant metabolism data indicate that the terminal residues in plants consist of parent chlorothalonil and its hydroxy metabolite SDS-3701 (a minor component of the residue).

The qualitative nature of the residue in livestock is not adequately understood; data depicting the metabolism of ring-labeled [^{14}C]chlorothalonil in poultry remain outstanding.

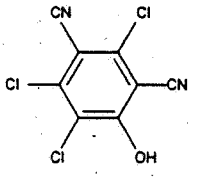
Tolerances for chlorothalonil in or on raw agricultural commodities are currently expressed in terms of the combined residues of chlorothalonil (2,4,5,6-tetrachloroisophthalonitrile) and its hydroxy metabolite (SDS-3701), 40 CFR §180.275(a) and (b). No tolerances have been established for residues of chlorothalonil or the 4-hydroxy metabolite in animal commodities.

An adequate GC/electron capture detection (ECD) enforcement method is available for determining residues of chlorothalonil and SDS-3701 in or on plant commodities and is listed as Method I in PAM, Vol. II. A more recent GC method for determining residues of chlorothalonil, SDS-3701, SDS-46851, hexachlorobenzene, and pentachloronitrobenzene on crops was reviewed by CBTS (W. Chin, 2/22/91) and recommended for inclusion in PAM, Vol. II. No methods for determining chlorothalonil residues in animal commodities are listed in PAM, Vol. II.

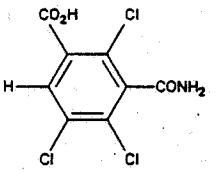
Codex MRLs for chlorothalonil residues are currently defined in terms of parent chlorothalonil. If SDS-3701 is deleted from the U.S. tolerance expression, then the U.S. tolerance definition will be compatible with the Codex definition.



Chlorothalonil



SDS-3701



SDS-46851

CONCLUSIONS

1. The nature of the residue in ruminants is adequately understood. The terminal residues of concern in milk and ruminant tissues consists of chlorothalonil and its hydroxy metabolite, SDS-3701. The registrant has provided additional information and adequately addressed the deficiencies in the CBRS review dated 1/90/91 (R. Perfetti, CBRS No. 7112).

2. Data depicting the metabolism of ring-labeled [^{14}C]chlorothalonil in poultry remain outstanding.

RECOMMENDATIONS

The registrant should be informed that the ruminant feeding study required in the 7/31/91 Chlorothalonil DCI remains outstanding. The HED Reregistration Eligibility Document (RED) for Chlorothalonil has been scheduled for 5/30/94. We wish to point out the importance of obtaining required data when due so that the Residue Chemistry RED chapters can be completed in a timely manner.

DETAILED CONSIDERATIONS

Background: Ruminant metabolism data (1990; MRIDs 41576001 and 41567002) pertaining to the metabolism of [^{14}C]chlorothalonil and [^{14}C]4-hydroxy-chlorothalonil in lactating goats were submitted by Fermenta ASC Corporation in response to the 9/84 Chlorothalonil Guidance Document and reviewed by the Agency (R. Perfetti; CBRS No. 7112; 1/30/91). CBRS concluded that data on the metabolism of [^{14}C]4-hydroxy chlorothalonil adequately described the terminal residues of this compound in goats. Little metabolism of SDS-3701 occurred in goats and the unchanged test substance accounted for 88-99% of the total radioactive residue (TRR) in milk and edible tissues. However, CBRS concluded that the ruminant metabolism study using [^{14}C]chlorothalonil was not adequate because ^{14}C-residues were not adequately characterized. CBRS requested further characterization of insoluble ^{14}C-residues in liver and kidney, and ^{14}C-residues in liver, kidney, and milk that are putatively bound to protein. Extraction and characterization of ^{14}C-residues in muscle and fat from the high-dose goat was also required. For clarity, a summary of the results from the [^{14}C]chlorothalonil study reviewed in CBRS No. 7112 are presented in Table 1.

Table 1. Distribution and characterization of ^{14}C-residues in milk and tissues from goats dosed with [^{14}C]chlorothalonil at 30 ppm (10x the maximum dietary burden) in the diet for 8 days.

Sample Fraction	%TRR	ppm[a]	Characterization/Identification
Milk Day-6 (0.146 ppm)			
Milk diluted w/ 95% EtOH	-[b]	-	Acidified with H_2SO_4 and partitioned with diethyl ether (Et_2O):hexane and Et_2O.
Organic	-	-	The organic fractions were combined and partitioned with a 10% saturated saline solution
Aqueous	-	-	Not further analyzed.
Organic	-	-	Evaporated and partitioned between hexane and ACN.
Hexane	22.8	0.034	Fractionated by Florisil column chromatography into 11 fractions. Fractions E1 and E2 (%TRR unspecified) contained the majority of radioactivity. Normal-phase HPLC analysis of E1 and E2 tentatively identified SDS-5080[c] (2.2-4.5% TRR).
ACN	44.8	0.067	Reverse-phase HPLC identified SDS-3701 accounting for 28.8% of the TRR (0.043 ppm); chlorothalonil was not detected (<0.001 ppm). The identity of SDS-3701 was confirmed by GC/MS.
Aqueous/Solids	-	-	Separated by centrifugation. The registrant reported that the pellet accounted for >97% of the ^{14}C-residues in this fraction.
Aqueous supernatant	-	-	Not further analyzed.

Table 1. Continued.

Sample Fraction	%TRR	ppm[a]	Characterization/Identification
Solids	28.2	0.042	The majority of radioactivity (%TRR unspecified) were solubilized in ammonium carbonate and analyzed by gel permeation chromatography (Sephadex G-10 column). The majority (51-98%) of the applied radioactivity had MWs of >700 amu. Registrant concluded that radioactivity consisted of chlorothalonil covalently bound to low and moderate weight proteins.
Liver (0.68 and 0.73 ppm)			
H_2SO_4/Acetone	59.1, 49.4	0.402, 0.361	Concentrated, diluted with H_2O, and partitioned with Et_2O:hexane and Et_2O.
Aqueous	25.4, 28.0	0.173, 0.204	Acid alcoholysis (2 hrs at 90 °C in butanol/HCl): 95-98% of the radioactivity in this fraction could be partitioned into ethyl acetate following alcoholysis. Subsequent HPLC analysis indicated that 48% of the radioactivity was converted to non-polar compounds, none of which were identified. Gel permeation chromatography (Sephadex G-75): the majority of ^{14}C-residues had MWs between 400-700, with about 10% of the fraction having MWs of 700-1500.
Organic	20.6, 18.3	0.140, 0.134	The organic fractions were combined and partitioned with a 10% saturated saline solution
Saline wash	12.3, 3.6	0.084, 0.026	Contained suspended insoluble and aqueous soluble material; not further analyzed.
Organic	-	-	Concentrated and partitioned between hexane and ACN
Hexane	4.2, 4.4	0.029, 0.032	Not further analyzed.
ACN	13.9, 15.1	0.095, 0.110	Reverse-phase HPLC identified SDS-3701 accounting for 3-6% of the TRR (0.03-0.04 ppm); parent chlorothalonil was not detected (<0.003 ppm).
Solids	29.7, 43.9	0.202, 0.320	Not further analyzed.
Kidney (2.1 and 2.3 ppm)[d] - Acid extraction			
H_2SO_4/Acetone	62.6, 48.1	1.31, 1.11	Concentrated, diluted with H_2O, with Et_2O:hexane and Et_2O.
Aqueous	47.9, 29.6	1.01, 0.681	Analyzed by gel permeation chromatography (Sephadex G-10). Data reported were for goat #9: 9.6% TRR (0.2 ppm) coeluted with high molecular weight proteins; 15.5% TRR (0.38 ppm) had retention characteristic of conjugated standards (400-600 mw); and 11.5% TRR (0.24 ppm) was a broad band containing strongly absorbing functional groups. These fractions were not further analyzed.
Organic	12.2, 10.1	0.256, 0.232	The organic fractions were combined and partitioned with a 10% saturated saline solution.
Saline wash	0.8, 1.9	0.016, 0.044	The aqueous soluble residues were separated from suspended solids by centrifugation; not further analyzed.
suspended solids	3.0, 11.5	0.063, 0.265	Not further analyzed.

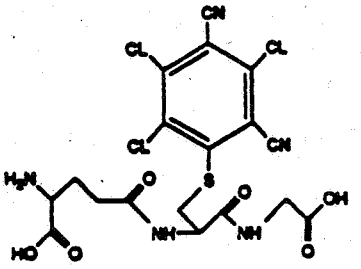
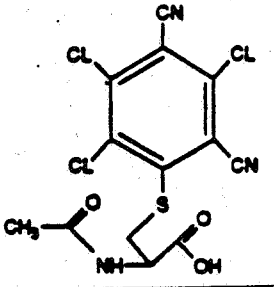
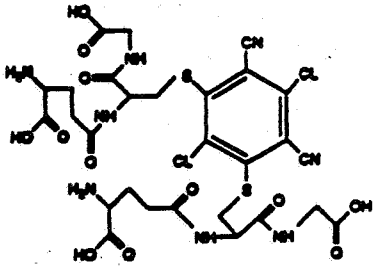
(continued)

Table 1. Continued.

Sample Fraction	%TRR	ppm[a]	Characterization/Identification
Organic	-	-	Concentrated and partitioned between hexane and ACN
Hexane	4.1, 2.8	0.086, 0.064	Fractionated by Florisil column chromatography, but fractions were not further analyzed.
ACN	8.3, 7.4	0.174, 0.170	HPLC analysis identified SDS-3701, accounting for 2.4-3.2% of the TRR (0.05-0.07 ppm). Parent chlorothalonil was not detected (<0.005 ppm).
Solids	38.2, 34.9	0.802, 0.803	Not further analyzed.
Kidney (2.1 ppm)[e] - Neutral buffer extraction			
0.05M Phosphate buffer	-	-	Centrifuged a second time.
Supernatant	47.1	0.989	HPLC analysis: identified SDS-3701 accounting for 3.8% TRR (0.08 ppm); two other peaks accounting for ca. 3.5% and 3.0% of the TRR were detected that the registrant suggested were mono- and diglutathione conjugates of chlorothalonil. Gel permeation chromatography (Sephadex G-75): isolated two regions of radioactivity; one associated with proteins (45,000-54,000 mw), and the other eluting in low molecular weight fractions (330-360 mw). HPLC analysis of this low molecular wt. fraction gave results similar to the above HPLC analysis. Acid hydrolysis (6N HCl, ~90 °C, 24 hrs): after hydrolysis 32.1% TRR was recovered in the supernatant, of which 6.4% TRR was organosoluble.
Solids (Pellet A2)	5.8	0.122	Not further analyzed.
Solids	44.6	0.937	Reextracted a second time with buffer.
Supernatant	13.9	0.292	Not further analyzed.
Solids (Pellet B)	25.1	0.527	Acid hydrolysis (6N HCl, ~90 °C, 24 hrs) released an additional 16% of the TRR of which 1.5% TRR was organosoluble.

[a]Expressed as chlorothalonil equivalents. [b]Data not provided. [c]SDS-5080 is the chemical code for 2,5-dichloro-4,6-dimethoxyisophthalonitrile. [d]Data from goats #3 and #9. [e]Data from goat #3.

The registrant proposed that the primary pathway for chlorothalonil metabolism in ruminants involves the substitution of one or more of the chlorine atoms with glutathione, and that the stable chlorothalonil-glutathione(s) conjugates undergo further modifications of the glutathione side-chains to yield a complex array of products. Three possible degradates of the glutathione pathway are given below.

9. a) SDS-66382 b) S-[2,4-dicyano-3,5,6-trichlorophenyl]-glutathione	
10. a) SDS-66430 b) S-[2,4-dicyano-3,5,6-trichlorophenyl] N-acetyl cysteine	
11. a) SDS-66432 b) 5,5'-[2,4-dicyano-3,6-dichlorophenyl] diglutathione	

In response to the CBRS review, ISK Biotech Corporation (1992: MRID 42174401) argues that the results from the [^{14}C]chlorothalonil and [^{14}C]SDS-3701 goat metabolism studies should be considered together when assessing the nature of chlorothalonil residues on ruminants. The registrant's arguments and responses to specific deficiencies are presented below followed by CBRS' conclusions.

Registrant's Response.

The registrant stated that chlorothalonil is not registered on major livestock feed items and presented data from the 1988 Residue Chemistry Science Chapter indicating that the contribution of SDS-3701 to the combined residues of chlorothalonil and SDS-3701 is 30% in soybean hulls, 35% in peanut hulls, 36-43% in dry beans, and 4.6% in tomatoes. They further explained that the selected "1x" and "10x" dosing levels (chlorothalonil at 3.2 and 31.5 ppm, and SDS-3701 at 0.27 and 2.5 ppm) were designed to reflect a worse case ratio (12:1) of chlorothalonil:SDS-3701 levels in animal feed items, and that the actual percentage of the chlorothalonil residues comprised of SDS-3701 in a ruminant diet is expected to be higher than 8%.

Based on its assessment that the ratio of chlorothalonil to SDS-3701 fed in the studies reflects the highest possible ratio in animal feed items, the registrant used data from the two goat tests (low dose groups of 0.27 ppm SDS-3701 and 3.2 ppm chlorothalonil) to estimate combined levels of ^{14}C-residues resulting from a combined feeding. The registrant presented data suggesting that the majority of the ^{14}C-residues would be accounted for by SDS-3701 even though SDS-3701 accounts for only 8% of the combined radioactivity fed because SDS-3701 accumulates to a greater degree in goats than chlorothalonil and because SDS-3701 is essentially not metabolized in goats. Based on this argument, the registrant contends that the unidentified residues derived from [^{14}C]chlorothalonil, which are of concern to the agency, would not constitute a significant percentage of the total residues if one combines the expected residues from both chlorothalonil and SDS-3701.

The registrant also calculated the contributions from chlorothalonil and SDS-3701 to the total residue in milk and tissues where SDS-3702 represented 10, 20, and 30% of the total residue in livestock feed items

CBRS Conclusions.

Using the results from goats dosed with [^{14}C]chlorothalonil and [^{14}C]SDS-3701 at approximately 30 ppm and 2 ppm, respectively, (high dose groups) CBRS has calculated the theoretical residues resulting from a combined feeding of the parent and hydroxy metabolite; these data are present in Table 2. These data support the registrant's assertion that SDS-3701 would be the principle residue in animal matrices resulting from the feeding of plants containing chlorothalonil residues.

Table 2. Total radioactive residues in milk and tissues of a goat fed for 8 days with either 30 ppm of [^{14}C]chlorothalonil or 2 ppm of [^{14}C]4-hydroxy-chlorothalonil and the theoretical combined residues.

	[^{14}C]Chlorothalonil Study[a]		[^{14}C]SDS-3701 Study[b]			Percent of combined TRR identified as SDS-3701[e]
Matrix	TRR (ppm)[c]	SDS-3701 (%TRR)[d]	TRR (ppm)[c]	SDS-3701 (%TRR)[d]	Combined TRR	
Milk[f]	0.147	28.8	0.960	100.0	1.107	90.5
Muscle	0.032	-[g]	0.138	90.2	0.170	73.2
Fat	0.038	-[g]	0.083	89.5	0.121	61.3
Liver	0.680	6.0	0.761	96.2	1.441	53.6
Kidney	2.10	3.2	1.486	94.0	3.586	40.8

[a]Data for goat #3 (30 ppm dose) from MRID 41576001. [b]Data for goat #5 (2 ppm dose) from MRID 41576002. [c]PPMs are expressed in terms of the respective test substances. [d]Percent of the TRR identified as SDS-3701 in each study. [e]Sum of SDS-3701 identified in each sample ÷ by the combined TRR. [f]Day-6 afternoon sample. [g]Not determined.

Deficiency 1

Radioactivity in the aqueous fraction of milk, accounting for up to 56% of the ^{14}C-activity was insufficiently characterized; although evidence to support a proteinaceous nature of these residues was presented, the existence of conjugated residues of concern in this fraction could not be ruled out.

Registrant's Response

The registrant stated that the review was incorrect in stating that "greater than 97% of the radioactivity in the aqueous fraction was precipitated by aqueous sodium chloride." The aqueous precipitate was the result of diluting the milk sample with ethanol and concentrated sulfuric acid, extracting with ethyl ether and ether/hexane mixtures, and high speed centrifugation of the remaining aqueous solution. Precipitation with sodium chloride was not done with the aqueous milk fraction. The chemical and physical properties of this fraction indicate that it behaves like chlorothalonil covalently bound to protein. Furthermore, when the results of both studies are considered, the unidentified portion is 4.9 and 11.8% rather than 56%

CBRS Conclusion

CBRS acknowledges the incorrect statement on p. 5 of the CBRS review but points out that the precipitating agent used is not the issue. Rather, our concern is that the determinations of molecular size and solubility characteristics were not supported by raw data and thus do not provide conclusive evidence for the characterization of ^{14}C-residues as "chlorothalonil (or its metabolite) that has become conjugated to low or moderate molecular weight proteins" as

the registrant claims. Nonetheless, CBRS accepts the argument that unidentified residues derived from [^{14}C]chlorothalonil would not constitute a significant percentage of the total residues if one combines the expected residues from both chlorothalonil and SDS-3701. This deficiency has been resolved.

Deficiency 2

Levels of 4-hydroxy chlorothalonil in liver and kidney were reported only as a range of values and the actual amount in any given sample could not be determined.

Registrant's Response

The registrant indicated that the actual values for 4-hydroxy chlorothalonil determined in kidney and liver of the two high dose goats were 2.4% and 3.2% of the TRR (0.050 and 0.074 ppm) in kidney and 3% and 6% of the TRR (0.020 and 0.044 ppm) in liver, respectively. The data were originally presented as a range to indicate that the levels were similar for each of the two high dose goats analyzed.

CBRS Conclusion

This deficiency has been resolved.

Deficiency 3

Insoluble residues in liver and kidney accounting for up to 33% of the residue in liver and 43% in kidney were not characterized.

Registrant's Response

The registrant indicated that the extraction conditions utilized for tissue samples were developed to be the most vigorous conditions possible without degrading chemical features of the chlorothalonil molecule. The registrant stated that the use of heat and acid will hydrolyze the cyano groups and the use of alkali will lead to the replacement of one or more chlorine atoms on the ring. They further stated that the conjugation of the aromatic ring by dehalogenation produces stable covalent linkages that are resistant to most chemical and enzymatic hydrolyses. In previous plant metabolism studies, acidic, alkaline, and enzymatic hydrolyses released only small amounts of organosoluble radioactivity none of which could be identified before or after methylation.

CBRS Conclusion

CBRS acknowledges that because acid and alkali hydrolyses of the insoluble residues may substantially alter the nature of the residues extracted, these technique may be unsuitable for releasing insoluble residues. CBRS also accepts the argument that unidentified residues

derived from [^{14}C]chlorothalonil would not constitute a significant percentage of the total residues if one combines the expected residues from both chlorothalonil and SDS-3701. This deficiency has been resolved.

Deficiency 4

The up to 24% of the total liver residue in the saline wash of the organosoluble fraction and the 17% of the kidney residue that appear to be low molecular weight conjugates warrant further characterization.

Registrant Response

The registrant stated that the 17% of the kidney residues cited in the review were not associated with the saline wash of the kidney organosoluble fraction. Rather, radioactive residues in the saline wash from the kidney organic fractions accounted for 0.8-1.9% of the TRR in high dose goats. The registrant indicated that the majority of radioactivity associated with the kidney saline wash fractions actually consisted of suspended solids (3-11.5% TRR for high dose goats) and are not low molecular weight conjugates. The registrant indicated that suspended solids were also associated with the saline washes from low dose kidney (6.8-8.9% TRR), high dose liver (3.6-12.3% TRR), and low dose liver (14.8-24.2% TRR) fraction.

CBRS Conclusion

There appears to be some confusion regarding this deficiency. Although the 24% figure cited in CBRS' review does pertain to the highest TRR percentage associated with the saline wash of the organic fraction from liver, the 17% of the kidney TRR cited does not refer to the saline wash fraction from kidneys. Rather, it references the radioactivity in high dose goat kidneys listed as "total conjugate" in the registrant's summary table for kidney (MRID 41576001, p. 78, Table 15). Nonetheless, based on the argument that unidentified residues in liver and kidney derived from [^{14}C]chlorothalonil would not constitute a significant percentage of the total residues if one combines the expected residues from both chlorothalonil and SDS-3701, CBRS considers this deficiency resolved.

Deficiency 5

Radioactive residues in muscle and fat samples were not characterized and should be investigated with respect to the solvent extraction properties of these residues.

Registrant Response

The registrant indicated TRR levels in these tissues were extremely low at 0.03-0.04 ppm in muscle and fat from the 30 ppm (high dose) feeding level. Based on CBRS guidance, the

registrant concluded that it was justified in not attempting further analysis of the ^{14}C-residues in these tissues.

CBRS Conclusion

Based on the metabolic profiles for milk and liver from goats dosed with either [^{14}C]chlorothalonil or [^{14}C]SDS-3701, CBRS concludes that additional analytical work on muscle and fat sample matrices from goats dosed with [^{14}C]chlorothalonil would not improve the data needed to complete an exposure and risk assessment.

Deficiency 6 -

The registrant needs to report information pertaining to the conditions and intervals of sample storage, and, if the duration of storage was greater than 6 months, a storage stability study must be conducted.

Registrant Response

The registrant stated that milk analyses were completed within 6-10 months, but characterization of ^{14}C-residues in liver and kidney required "considerably more time." The registrant also noted that the TRR levels in tissues at the time of analysis were comparable to the initial values reported by ABC Laboratories.

CBRS Conclusion

CBRS concludes that this deficiency has been adequately resolved.

References

Citations for the MRID documents referenced in this review are presented below. Submissions reviewed in this document are indicated by shaded type.

42174401 Doran, T. (1992) Response to EPA's Review of Chlorothalonil Goat Metabolism Study: Doc. No. RC-92-RPB-001-001. Unpublished report prepared by Ricerca, Inc. 42 p.

41576001 Duane, W. and T. Doran. (1990) A Study to Determine the Nature of the Residue in Meat, Milk and Tissue from Lactating Goats Fed ^{14}C-Chlorothalonil (2,4,5,6-tetrachloroisophthalonitrile): Report No. 1067-85-0080-EF-001. Unpublished report prepared by Ricerca, Inc. 183 p.

41576002 Han, H. (1990) A Study to Determine the Nature of the Residue in Milk, Meat, and Tissue from Lactating Goats Dosed with ^{14}C-4-hydroxy-2,5,6-trichloroisophthalonitrile (SDS-3701): Report No. 1183-87-0024-EF-001. Unpublished report prepared by Ricerca, Inc. 180 p.