Data Evaluation Report of Degradation Kinetics

PMRA Submission Number {......} **EPA MRID Number 46936101**

Test material: Fipronil
IUPAC name: 5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-4-trifluoromethylsulfinylpyrazole-3-carbonitrile
CAS name: 5-amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-[(trifluoromethyl)sulfinyl]-1*H*-pyrazole-3-carbonitrile

Primary Reviewer: James Hetrick, Ph.D. Signature: James C. Hetrick
EPA Date: 3/12/08

Secondary Reviewer: Thuy Nguyen Signature: Thuy L Nguyen
EPA Date: 5/6/08

CITATION: Tang, Z. and T.S. Ramanarayanan. 2006. Degradation of Fipronil and Its Major Metabolites Following Application of Chipco TopChoice® Leachate to Outdoor Simulated Ponds: Kinetics modeling. Sponsored by Bayer Crop Science, RTP, NC. Performed by Bayer Crop Science, Stillwell, KS, MRID 46936101.

EXECUTIVE SUMMARY:

The non-guideline study provides ancillary data on the estimation of degradation rates for fipronil and its degradation products in an outdoor pond study (Hoberg, J. 2005. Chipco® TopChoice™ Effects on Aquatic Fauna in Outdoor Simulated Ponds). Because the modeling assumed the presence of the sulfide degradation product (MB 45950) as the primary biological degradation product, it implies the model water sediment system is anaerobic. Such conditions are not expected to be present in water/sediment systems capable of supporting a viable population of invertebrates.

First-order half-lives for fipronil and its degradation products were estimated for an outdoor pond study. Degradation rates were determined using ModelMaker 4.0 (2) with the Marquardt method of optimization with ordinary least squares. The modeling assumed the MB 45950 and MB 46513 were the primary degradation products of fipronil. MB 46136 occurrence was attributed as a by-product in the fipronil formulation rather than an in-situ degradation product. The summed biolysis and photolysis degradation fipronil half-life was 3.4 day (0.204 day^{-1}). The photolysis half-life of fipronil was estimated at 9.9 days (0.070 $days^{-1}$). The half-life of fipronil degradation products was 26.7 days (0.026 day^{-1}) for MB 46513, 43.3 days (0.016 $days^{-1}$) for MB 45950, and 27.7 days (0.025 $days^{-1}$) for MB 46136.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: The SETAC-Europe: Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides (March 1995; pp. 1, 34) is not applicable.

COMPLIANCE: This study was not conducted in compliance with USEPA FIFRA Good Laboratory Practices (40 CFR Part 160).

A. Material and Methods:

The objective of the study was to determine first-order degradation rates of fipronil and its degradation products in an outdoor sediment-water system.

The registrant used ModelMaker Version 4.0 (2) to estimate simultaneous first-order degradation rates for fipronil and its degradation products from a simulated outdoor pond study. Data were taken from Hoberg, J. R., Chipco TopChoice™ Effects on Aquatic Fauna in Outdoor Simulated Ponds (**Appendix 2**). The modeling strategy employed known degradation pathways of fipronil (**Figure 1, pp 11 and Figure 2, pp 13**). The formation and decline of MB 46136 was not considered because the registrant believes MB 46136 formation was associated with the fipronil formulation rather than in situ formation in the pond. Estimation of first-order degradation rates was conducted using the Marquardt method of optimization with ordinary least squares. Chemical rate constants were estimated used to estimate first-order half-lives.

The modeling employed a mass balance approach where the concentration of residue in sediment and water was used to calculate the mass at each time interval (**Appendix 3**).

B. Results and Discussion

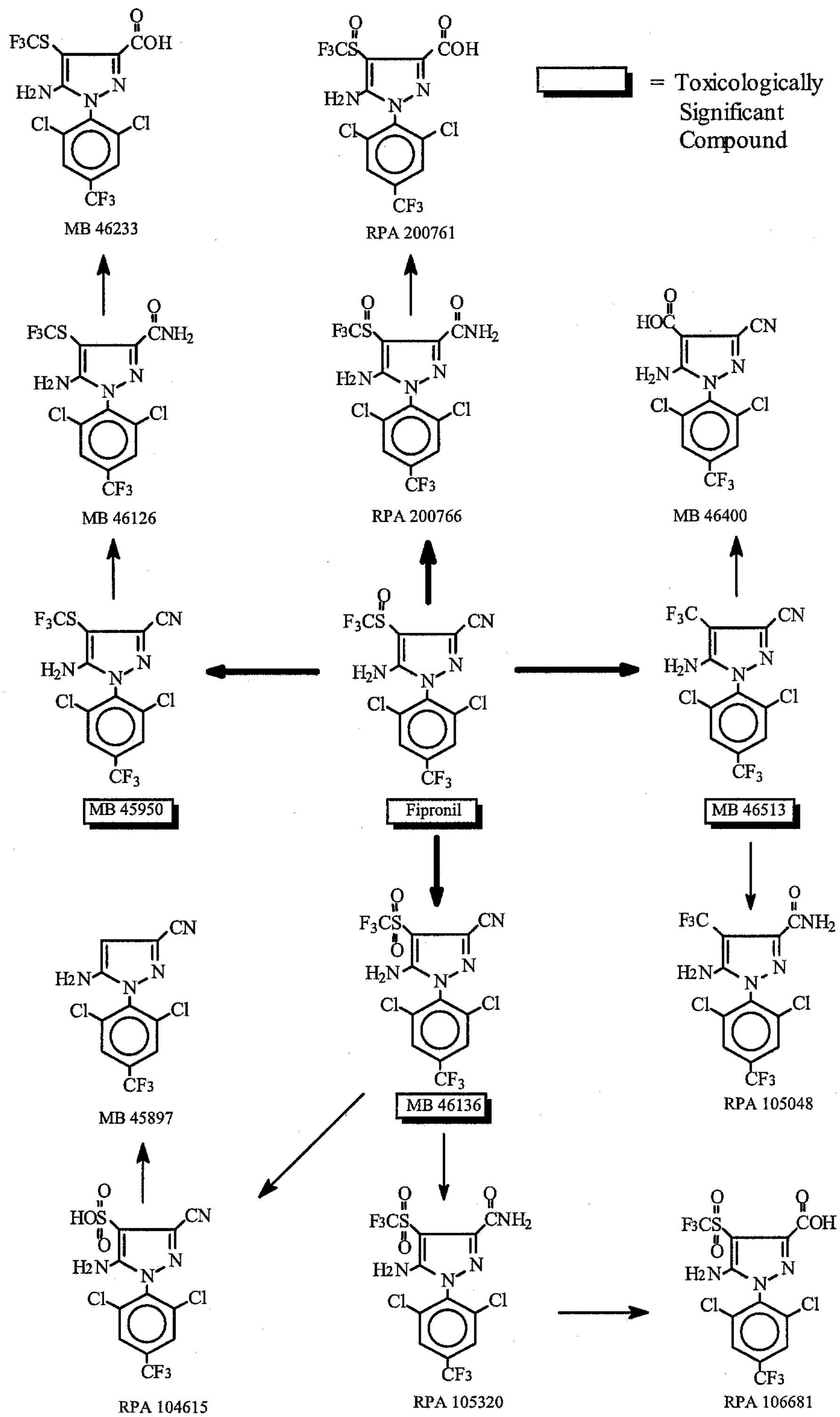
First-order half-lives for fipronil and its degradation products were estimated (**Table 1, Figures 4 and 5**). The summed biolysis and photolysis degradation fipronil half-life was 3.4 day (0.204 day^{-1}). The photolysis half-life of fipronil was estimated at 9.9 days (0.070 $days^{-1}$). The half-life of fipronil degradation products was 26.7 days (0.026 day^{-1}) for MB 46513, 43.3 days (0.016 $days^{-1}$) for MB 45950, and 27.7 days (0.025 $days^{-1}$) for MB 46136. [The reviewer notes the fipronil degradation half-life in aerobic aquatic metabolism is 33 days. The half-lives for fipronil degradation products are estimated from aerobic soil metabolism half-lives (2x aerobic soil metabolism half-life). The estimated half-live is 1320 days for MB46513, 1400 days for MB 45950 and MB 46136.]

C. Review Comments

1. The registrant did not discuss the implications of redox potentials on the formation of MB 45950 and MB 46136. The modeling strategy assumes the total system redox potential is anaerobic because MB 45950 is the major degradation product from biological degradation. Under aerobic conditions, MB 46136 is expected to be the major degradation product. The reviewer does not understand how the outdoor pond could be anaerobic and still maintain any viable population of invertebrates for toxicity testing.

2. The half-lives estimated from Model Maker are not unique values because they were derived using numerical integration methods. Estimates of half-life values may vary due different numerical techniques and convergence conditions.

Figure 1 Fipronil Degradation Pathway in the Environment



$F6 = k'_{12} * MB46136$ [6]

Figure 2 Kinetics model to describe the degradation of fipronil and its metabolites: MB 46513 and MB 45950

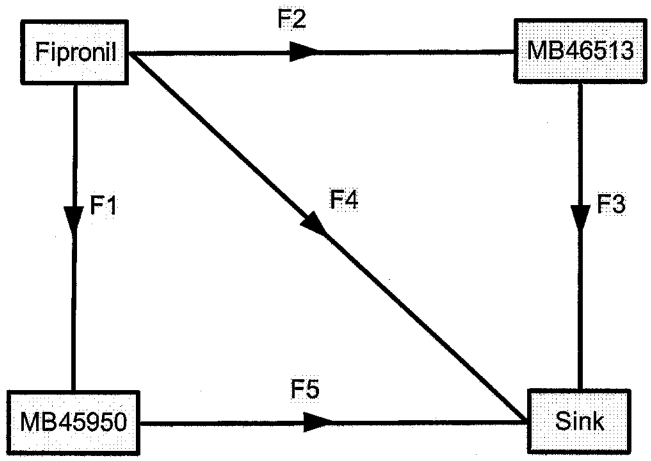
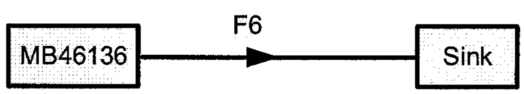


Figure 3 Kinetics model to describe the degradation of metabolite MB 46136



4.3 Goodness of Fit

The goodness of fit for the kinetics model and its parameters to fit the observed data was evaluated using the coefficient of determination (r^2). The coefficient of determination was calculated as:

$$r^2 = \left\{ \frac{\sum_{i=1}^{n} (O_i - \bar{O})(C_i - \bar{C})}{\sqrt{\sum_{i=1}^{n} (O_i - \bar{O})^2 \sum_{i=1}^{n} (C_i - \bar{C})^2}} \right\}^2 \qquad (1)$$

where:

n = total number of observations

O_i = i[th] observed value (with i = 1,2,…,n)

C_i = i[th] value calculated with selected model (with i = 1,2,…,n)

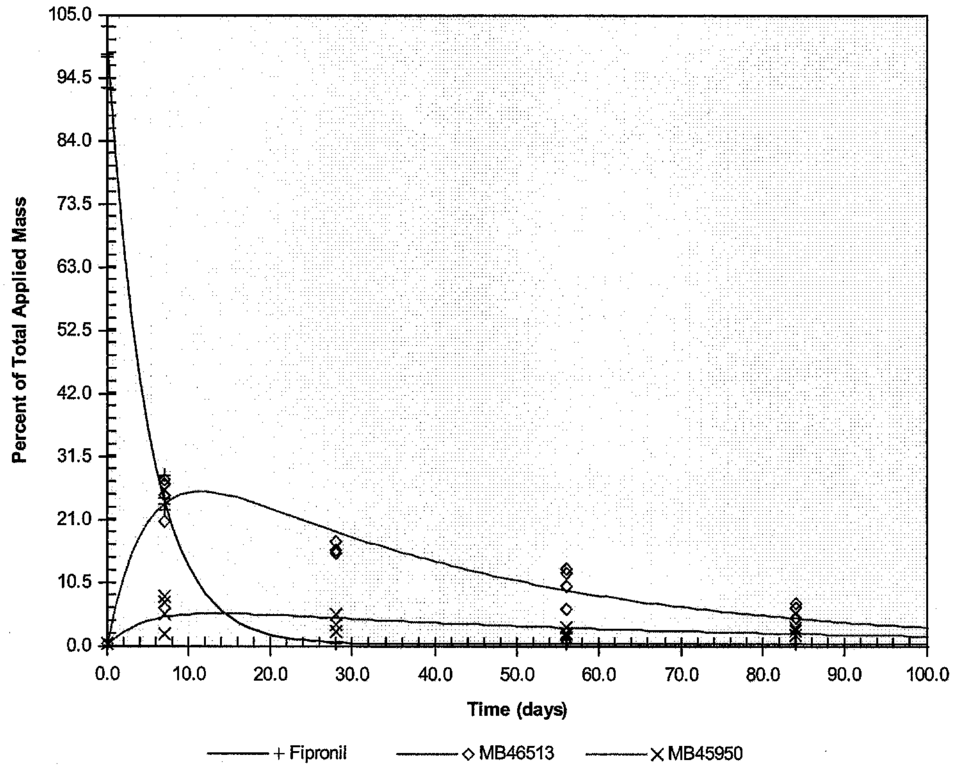
$\bar{O}$ = mean of all observed values

Table 1 Parameters describing the degradation of fipronil and its metabolites in the simulated ponds

Compound	First-Order Rate Constant (d^{-1})	Half-life (d) (Equation 2)
Fipronil		
k_{13}	0.013	
k_{14}	0.121	
$k_{13} + k_{14}$	0.134	5.2
k_{12}	0.070	9.9*
$\sum k_{1j}$	0.204	3.4**
MB 46513		26.7
k_{24}	0.026	
MB 45950		43.3
k_{34}	0.016	
Overall r^2	0.99	
MB 46136		27.7
k'_{12}	0.025	
r^2	0.76	

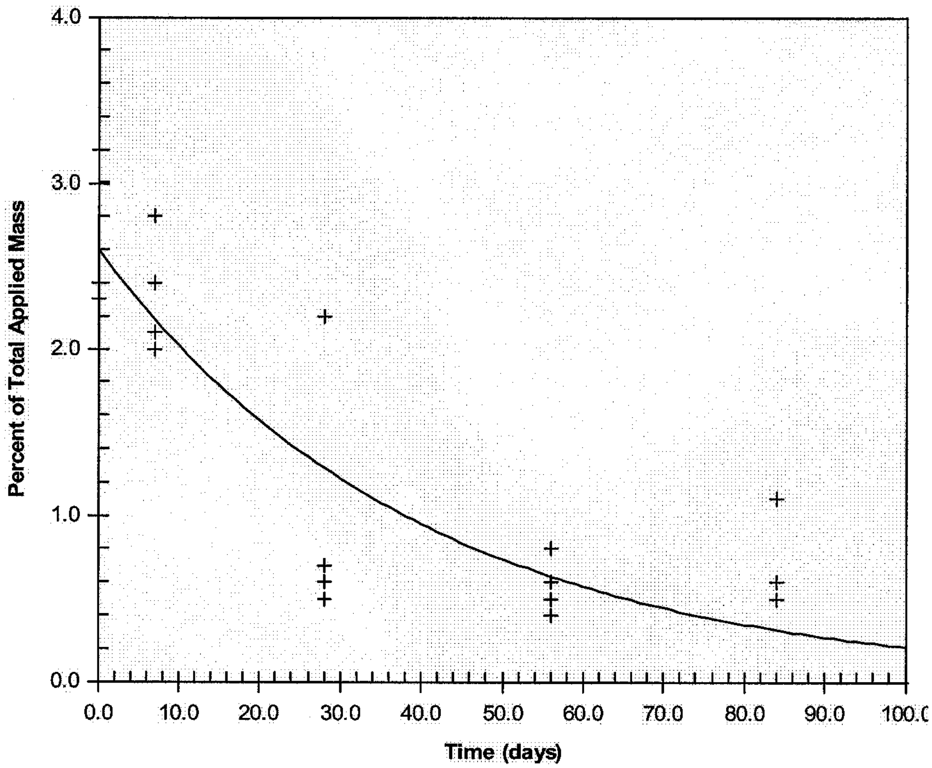
* photolysis half-life
** overall half-life: biolysis and photolysis

Figure 4 Comparison of observed and calculated residue concentrations of fipronil, MB 46513, and MB 45950 in the simulated ponds



Note: The symbols in the above graph are observed and the solid lines are calculated from kinetics modeling

Figure 5 Comparison of observed and calculated residue concentrations of MB 46136 in the simulated ponds



Note: The symbols in the above graph are observed and the solid line is calculated from kinetics modeling

6. CONCLUSIONS

The kinetics model developed in this study adequately characterized the degradation of fipronil in the sediment-water system in the simulated ponds. Using the fitted parameters of the model, simple first-order degradation rates of fipronil and its metabolites MB 46513, MB 45950, MB 46136 were estimated.

Appendix 2 Measured concentrations and calculated mass for fipronil and metabolites in the simulated ponds

Day	Concentration[a] (ng/L)								Mass[b] (ng)								Total Mass (water + sed.) (ng)			
	Rep. 1		Rep. 2		Rep. 3		Rep. 4		Rep. 1		Rep. 2		Rep. 3		Rep. 4					
	Water	Sed.	Water	Sed.	Water	Sed.	Water	Sed.	Water	Sed.	Water	Sed.	Water	Sed.	Water	Sed.	Rep. 1	Rep. 2	Rep. 3	Rep. 4
Fipronil																				
0	407		366		388		386		1139600	0	1024800	0	1086400	0	1080800	0	1139600	1024800	1086400	1080800
7	81	536	106	236	82	329	84	593	226800	31190	296800	13733	229600	19145	235200	34507	257990	310533	248745	269707
14	18		16		24		18		50400		44800		67200		50400		NA	NA	NA	NA
28	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	0	0	0	0	0	0	0	0	0	0	0	0
56	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	0	0	0	0	0	0	0	0	0	0	0	0
84	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	0	0	0	0	0	0	0	0	0	0	0	0
MB 46136																				
0	13		10		10		10		36400	0	28000	0	28000	0	26880	0	36400	28000	28000	26880
7	7	192	7	59	7	104	6	204	20720	11172	19320	3433	18480	6052	15400	11871	31892	22753	24532	27271
14	5		5		6		5		14560		14560		15960		14000		NA	NA	NA	NA
28	BDL	119	BDL	433	BDL	130	BDL	108	0	6925	0	25196	0	7565	0	6285	6925	25196	7565	6285
56	BDL	86	BDL	104	BDL	155	BDL	125	0	5004	0	6052	0	9019	0	7274	5004	6052	9019	7274
84	BDL	125	BDL	221	BDL	103	BDL	108	0	7274	0	12860	0	5994	0	6285	7274	12860	5994	6285
MB 46513																				
0	BDL		BDL		BDL		BDL		0	0	0	0	0	0	0	0	0	0	0	0
7	82	691	68	194	81	312	82	545	229600	40209	190400	11289	226800	18155	229600	31714	269809	201689	244955	261314
14	73		77		71		77		204400		215600		198800		215600		NA	NA	NA	NA
28	41	599	42	856	45	716	43	600	114800	34856	117600	49811	126000	41664	120400	34914	149656	167411	167664	155314
56	27	331	9	556	27	823	27	704	75600	19261	24920	32354	75600	47890	75600	40966	94861	57274	123490	116566
84	11	486	5	881	12	434	5	499	30800	28280	15120	51265	33600	25254	13440	29037	59080	66385	58854	42477
MB 45950																				
0	BDL		BDL		BDL		BDL		0	0	0	0	0	0	0	0	0	0	0	0
7	2	1393	BDL	332	2	1181	BDL	935	5600	81059	0	19319	5880	68722	0	54408	86659	19319	74602	54408
14	3		2		3		BDL		9240		6720		7000		0		NA	NA	NA	NA
28	BDL	420	BDL	932	BDL	644	BDL	425	0	24440	0	54233	0	37474	0	24731	24440	54233	37474	24731
56	BDL	256	BDL	356	BDL	555	BDL	391	0	14897	0	20716	0	32295	0	22752	14897	20716	32295	22752
84	BDL	572	BDL	970	BDL	307	BDL	440	0	33285	0	56444	0	17864	0	25604	33285	56444	17864	25604

[a] From Table 6 and Table 8 of the simulated pond study report (1).
[b] Pond water volume: 2800L; Total sediment mass: 58.19 kg.

Appendix 3 Percent of the total applied mass for fipronil and metabolites (fipronil equivalent) used in the kinetic models

Day	Fipronil	MB 46136	MB 45513	MB 46950
0	102.8	3.2	0.0	0.0
0	92.4	2.4	0.0	0.0
0	98.0	2.4	0.0	0.0
0	97.5	2.3	0.0	0.0
7	23.3	2.8	27.3	8.1
7	28.0	2.0	20.4	1.8
7	22.4	2.1	24.8	7.0
7	24.3	2.4	26.5	5.1
28	0.0	0.6	15.2	2.3
28	0.0	2.2	17.0	5.1
28	0.0	0.7	17.0	3.5
28	0.0	0.5	15.7	2.3
56	0.0	0.4	9.6	1.4
56	0.0	0.5	5.8	1.9
56	0.0	0.8	12.5	3.0
56	0.0	0.6	11.8	2.1
84	0.0	0.6	6.0	3.1
84	0.0	1.1	6.7	5.3
84	0.0	0.5	6.0	1.7
84	0.0	0.5	4.3	2.4