Statistics
Special Study 71-25
Job No. 8505016

PCB RESIDUES IN BEAGLE DOGS

INTRODUCTION

Bio-Test Laboratories conducted a two-year chronic oral toxicity study on Aroclor in beagle dogs. Tissue samples were sent to Monsanto for analysis of the residues. The data were submitted for statistical analysis.

SUMMARY

Data were obtained after feeding 1, 10 and 100 ppm per day of Aroclors 1242, 1254 and 1260 to beagle dogs for 24 months. Residual PCB's were determined on muscle, liver and fat samples on dogs sacrificed at the end of this period. In addition, some of the dogs were tested after recovery periods of 30 and 60 days. Figure 1 shows the actual results obtained.

The data were fitted by multiple regression to the following mathematical model:

$$\text{Log PPM Found} = C_0 + C_1\,(\text{Recovery in Days}) + C_2\,(\text{Log Feed Level}) + C_3\,(\text{If Muscle}) + C_4\,(\text{If Liver}) + C_5\,(\text{If Fat}) + C_6\,(\%\ \text{Chlorine}) + C_7\,(\text{If Female}) + C_8\,(\text{Recovery X Log Feed Level}) + C_9\,(\text{Log Feed Level If Muscle}) + C_{10}\,(\text{Log Feed Level If Liver}) + C_{11}\,(\text{Log Feed Level X \% Chlorine}) + C_{12}\,(\text{Log Feed Level If Female}) + C_{13}\,(\%\ \text{Chlorine If Female}) + C_{14}\,(\text{Recovery If Muscle}) + C_{15}\,(\text{Recovery If Liver}) + C_{16}\,(\text{Recovery If Female}) + C_{17}\,(\text{Recovery X \% Chlorine}).$$

The criterion for determining the best coefficient was minimizing the sum of squares of the differences between the logs of the actual results and those calculated from the equation.

CONCLUSIONS

1. The model shows the following factors to be statistically significant ($\geq$95%): C_0, C_1, C_2, C_4, C_6, C_{11}, C_{12}, C_{15}, C_{17}.

2. The following coefficients improve the predictability of the equation but are not in themselves statistically significant:

   $$C_8,\ C_{14},\ C_{16}.$$

3. The residual standard deviation of the logarithm of PPM found is 0.19270, with 95% confidence limits of predictability of $\pm$ 0.38540. Converted to the ppm scale, the upper 95% limit is 2.4 times the predicted value, the lower limit is 0.42 times the predicted value. The predicted results from the equation are shown in Figure 2.

4. The values of the coefficients and their t values are given in Figure 3. A t value of >2.0 indicates significance at 95%.

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5. Figure 4 shows the relationship between the predicted and actual results, with 95% confidence limits.

DISCUSSION

After the test data had been obtained on the 24-month sacrifice, it was decided that a reduction in cost could be obtained with little loss in information by testing only a balanced subset of the recovery samples. This accounts for some of the gaps in Figure 1. In addition, some of the samples were not available for test.

The first pass through the regression program did not provide a satisfactory fit when compared with the work done on a previous study with albino rats. Additional data were obtained and calculations re-checked on several data points. This provided some improvement on the second pass, but was still not satisfactory. The data were then smoothed by eliminating results where the difference between the predicted and actual values exceeded two standard deviations. The third pass gave the equation shown in Figure 3. The residual standard deviation was comparable to that obtained on the rat study.

The predicted values shown in Figure 2, and inspection of the coefficients in Figure 3 indicate the following:

1. In general, PPM of Aroclor found decreases with recovery time. However, liver results at high feed levels and at high chlorine contents tend to increase during recovery time. This might show that PCB's are removed from muscle tissue into the blood stream and are concentrated in the liver.

2. Results on liver samples are significantly higher than muscle or fat at all times, feed concentrations and chlorine contents.

3. The difference between male and female tissues increases with increasing feed level. (No difference at low feed levels, females lower at high feed levels).

4. PPM of Aroclor found increases with chlorine level, relatively more rapidly at higher feed levels. Higher chlorinated materials show less drop off with time.

Perhaps a better fitting equation would have been obtained if larger numbers of animals had been used in the study. The 24-month results each represented a composite sample from two animals. The recovery results were from single animals. Individual differences in metabolism could have a strong effect on the reliability of the results.

db

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ppm PCB Lipid Wt Basis

Biotest Study # C 7299

Two Year Chronic Oral Toxicity Study Of Aroclor In Beagle Dog

		Comp 2 Dogs 24 Mo Sacrifice						30 Day 1 Dog Recovery Samples						60 Day 1 Dog Recovery Sacrifice					
		1 ppm		10 ppm		100 ppm		1 ppm		10 ppm		100 ppm		1 ppm		10 ppm		100 ppm	
		♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Aroclor 1242	Muscle	2	2	6	3	19	20	1	2		2	10	10				1	6	
	Liver	—	4	8	8	29	—	11	2		9	23	18		2	4			.
	Fat	2	3	1	2	6	7	1	1		2	13	3	0.6		2	2		
Aroclor 1254	Muscle	10	4	18	18	61	95	4			9			2	2				32
	Liver	8	6	23	40	110	130		9			111	[illegible]			43	.		
	Fat	5	3	6	5	128	132	3			22				2				42
Aroclor 1260	Muscle	9	7	78	20	796	100		8		66		491				37	301	
	Liver	17	13	175	43	762	268	11			135		81		21			659	.
	Fat	14	18	159	39	1261	287		20		72		439				78	238	
Control	Muscle		0.07	*					2	*					0.6				
	Liver								1						2				
	Fat		0.6						0.2						1				

* Comp on controls, one per sacrifice

FIGURE 1

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PREDICTED PCB FOUND
Lipid Wt Basis

PREDICTED RESULTS

Biotest Study # C 7299
Two Year Chronic Oral Toxicity Study Of Aroclor In Beagle Dogs

		24 hr. Sacrifice						30 Day Recovery Sacrifice						60 Day Recovery Sacrifice					
		1 ppm		10 ppm		100 ppm		1 ppm		10 ppm		100 ppm		1 ppm		10 ppm		100 ppm	
		♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Aroclor 1242	Muscle	2	2	5	4	14	9	1	1	3	2	8	5	1	1	1	1	5	4
	Liver	3	3	8	6	22	14	2	2	7	6	20	14	2	2	5	4	18	14
	Fat	2	2	5	4	14	9	1	1	3	3	10	7	1	1	2	2	5	4
Aroclor 1254	Muscle	6	6	26	21	124	76	3	3	17	15	102	70	2	2	11	10	71	55
	Liver	9	9	42	32	195	119	9	9	25	22	220	151	7	7	42	44	247	198
	Fat	6	6	26	21	121	76	4	4	19	17	114	72	3	3	12	11	90	70
Aroclor 1260	Muscle	10	10	59	46	368	224	7	7	44	39	315	216	5	5	34	33	269	207
	Liver	15	15	93	73	590	363	15	15	108	92	731	501	19	19	118	118	957	736
	Fat	10	10	59	46	368	225	8	8	50	44	347	238	7	7	42	41	327	251
Control	Muscle			*					·	*					·				
	Liver								·						·				
	Fat								·						·				

* Control animals not sacrificed

FIGURE 2

FIGURE 3
COEFFICIENTS FOR PREDICTING EQUATION
BEAGLE DOG STUDY
LOG PPM FOUND

TERM	COEFFICIENT	T VALUE
CONSTANT	-1.31543	NOT CALCULATED
DAYS AFTER SACRIFICE	-0.02145	3.6689
LOG FEED LEVEL	-0.41856	2.5798
IF LIVER	0.19697	3.4108
PERCENT CHLORINE	0.03823	7.9845
FEED LEVEL X DAYS AFTER SACRIFICE	0.00189	1.8277
FEED LEVEL X PERCENT CHLORINE	0.02021	6.4412
FEED LEVEL IF FEMALE	-0.10736	2.9391
DAYS AFTER SACRIFICE IF MUSCLE	-0.00167	1.1980
DAYS AFTER SACRIFICE IF LIVER	0.00423	2.1218
DAYS AFTER SACRIFICE IF FEMALE	0.00169	1.1192
DAYS AFTER SACRIFICE X PERCENT CHLORINE	0.00028	2.5628

Residual Standard Deviation = 0.19270
Percent of Variance Explained = 94.2%

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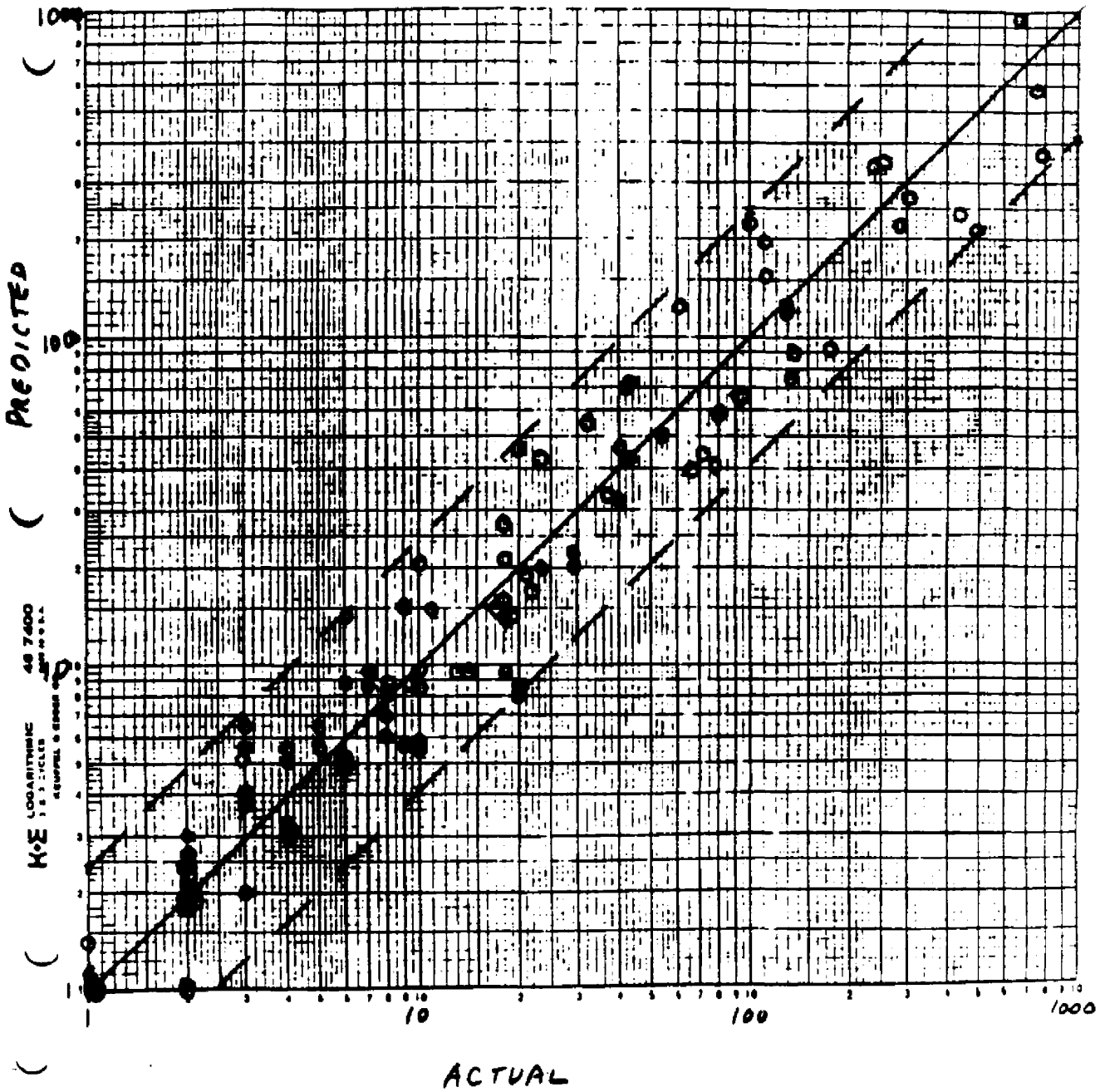
BEAGLE DOG STUDY

RESIDUALS FROM REGRESSION EQUATION

FIGURE 4



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