Monsanto

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SUMMARY--INTERIM STATUS

CHRONIC TOXICITY WITH AROCLORS

In May and June of 1969, two year feeding studies were initiated with Aroclors 1242, 1254 and 1260. The materials are being fed to rats and dogs at levels of 1, 10 and 100 parts per million in the diet.

After 11 months there have been no clinical effects observed in the rats in the Aroclor 1242 study. Animals sacrificed at six months showed negative micropathology. There have been no clinical effects in the dogs and blood and urine chemistry studies at the one, three and six month intervals were negative.

In the case of Aroclor 1254, rats have shown a slightly depressed weight gain at 100 ppm. In the animals sacrificed at six months, thsre was slight increased liver weights in males of the animals on the 100 ppm diet. Micropathology was negative at all levels. In the dogs there have been depressed weight gains in the females at all levels fed and at the 100 ppm level in the males. Blood and urine chemistry has been negative.

With Aroclor 1260 there has been no effect on weight gain but has been increased liver weights in males at 10 and 100 ppm in the animals sacrificed at six months. Micropathology is negative. In the dogs there has been depressed weight gains in the females at 10 and 100 ppm and in the males at 100 ppm. Blood and urine chemistry has been negative.

The above data indicate that these materials are about the same order of toxicity as DDT in rats and dogs. This is reassuring in that DDT is probably the least toxic insecticide to mammalian species. Further, there is general agreement that DDT has not presented a hazard in animals or man in spite of its presence in the environment.

Interim or progress reports such as above have been provided periodically to the U. S. Food and Drug Administration, the U. S. Department of Agriculture and other governmental agencies. In addition, the data and the progress of the studies have been discussed candidly with Dr. Edward J. Burger, Jr., in the Office of Science and Technology, Executive Office of the President.

SUMMARY--INTERIM STATUS

OF

CHRONIC TOXICITY STUDIES

	Aroclor 1242	Aroclor 1254	Aroclor 1260
2 year chronic--rats at 1, 10, 100 ppm in diet			
Status--9 months	No effect clinically	Lowered weight gain at 100 ppm	No effect (see below)
Status--6 months sacrifice including micropathology	No effect clinically	Increased liver wt. in males at 100 ppm Negative pathology--all levels	Increased liver wt. in males at 10 & 100 ppm Negative pathology--all levels
2 year chronic--dogs at 1, 10, 100 ppm in diet			
Status--10 months	No effect clinically	Lowered wt. gains* all females at 1, 10 & 100 ppm Lowered wt. gains males at 100 ppm	Lowered wt. gains** females at 10 and 100 ppm Lowered wt. gains at 100 ppm
Status--6 months including blood & urine chem.	Negative	Negative	Negative**

* See report for details relative to "Mortality"
** See report for details relative to "Mortality" and "Blood Chemistry"

MONS 090115

ANIMAL LONG TERM STUDIES

INTERIM STATUS

	1242	1254	1260
2-year rat chronic			
At 1, 10, 100 ppm Status-9 months	100 ppm Poss. liver enlargement Males 10 ppm O.K.	100 ppm Poss. Liver enlargement Males 10 ppm O.K.	100 ppm Poss. liver enlargement M & F 10 ppm O.K.
2-year dog chronic			
Status--9 months	100 ppm O.K.	100 ppm Body wt. dec. 10 ppm O.K. 1M-1F died--cause unrelated to exp't	100 ppm 1M-1F died refused food--no other gross abn. 10 ppm possible body wt. effect

Presented to Meeting with FDA Scientists At Duluth Minn on 17 Mar 70

MONS 090116

3/18/70
Given to people at Dubuque

ANIMAL LONG TERM STUDIES

INTERIM STATUS

	1242	1254	1260
2-year rat chronic			
At 1, 10, 100 ppm Status-9 months	100 ppm Poss. liver enlargement Males 10 ppm O.K.	100 ppm Poss. Liver enlargement Males 10 ppm O.K.	100 ppm Poss. liver enlargement M & F 10 ppm O.K.
2-year dog chronic			
Status--9 months	100 ppm O.K.	100 ppm Body wt. dec. 10 ppm O.K. 1M-1F died--cause unrelated to exp't	100 ppm 1M-1F died refused food--no other gross abn. 10 ppm possible body wt. effect

MONS 090117

AROCLOR TOXICITY DATA

Toxicity Data	Cost	AROCLOR 1221 Have	Need	Date Begin	Date End	MCS 1016 Have	Need	Date Begin	Date End	AROCLOR 5432 Have	Need	Date Begin	Date End	AROCLOR 5442 Have	Need	Date Begin	Date End
Acute																	
Rat-LD_{50}	$ 200	X	$ (200)*	11/15 1970	12/31 1970		$ 200	11/15 1970	12/31 '70	X	$	11/15 1970	12/31 '70	X	$ (200)*	11/15 1970	12/31 '70
Rabbits-MLD (dermal)	250	X	(250)*	"	"		250	"	"	X		"	"	X	(250)*	"	"
Skin Irr. (rabbit)	100		100	"	"		100	"	"	X		"	"		100	"	"
Eye Irr. (rabbit)	125		125	"	"		125	"	"	X		"	"		125	"	"
Vapor Inhalation (Rats)	200		200	"	"		200	"	"			"	"			"	"
Fish (2 species)	600		600	"	"		600	"	"		600	"	"		600	"	"
Sub-acute																	
90-day rat **	6,000		6,000	1/2/71	6/1 '71		6,000	1/2/71	6/1 '71		6,000	1/2/71	6/1 '71		6,000	1/2 '71	6/1 '71
90-day dog	10,000		10,000	"	"		10,000	"	"		10,000	"	"		10,000	"	"
Fish (30-90 day)	3,000 (est)		3,000				3,000				3,000				3,000		
Reproduction																	
Rats	17,000		Defer				Defer				Defer				Defer		
Chickens	8,000		Defer				Defer				Defer				Defer		
Teratology																	
Rabbits	4,500		Defer				Defer				Defer				Defer		
TOTAL:	$49,975																
NEED NOW:			$20,475				$20,475				$19,600				$20,275		
DEFERRED:			$29,500				$29,500				$29,500				$29,500		

* (Repest)
** Control group cost $2,100

MONS 090118

AROCLOR TOXICITY DATA

Toxicity Data	Cost	AROCLOR 1254 Have	AROCLOR 1254 Need	AROCLOR 1254 Date Begin	AROCLOR 1254 Date End	AROCLOR 5460 Have	AROCLOR 5460 Need	AROCLOR 5460 Date Begin	AROCLOR 5460 Date End	HB-40 Have	HB-40 Need	HB-40 Date Begin	HB-40 Date End	MIPB Have	MIPB Need	MIPB Date Begin	MIPB Date End
Acute																	
Rat-LD_{50}	$ 200	X				X				X				X			
Rabbits-MLD (dermal)	250	X				X				X				X			
Skin Irr. (rabbit)	100	X				X				X				X			
Eye Irr. (rabbit)	125	X				X				X				X			
Vapor Inhalation (Rats)	200	X				X											
Fish (2 species)	600	X					$ 600	12/15 1970	1/31 '71		$ 600#	12/15 1970	1/31 '71		$ 600#	12/15 1970	1/31 '71
Sub-acute																	
90-day rat **	6,000										6,000#	11/2/70	2/15 '71		6,000#	11/2 '70	2/15 '71
90-day dog	10,000																
Fish (30-90 day)	3,000 (est.)		$ 3,000														
Reproduction																	
Rats	17,000	X					Defer										
Chickens	8,000	X				X											
Teratology																	
Rabbits	4,500		4,500	11/15 1970	2/15 '71		Defer										
TOTAL:	$49,975																
NEED NOW:			$ 7,500				$ 600				$ 6,600#				$ 6,600#		
DEFERRED:							21,500										

* (Repeat)
** Control group cost $2,100
\# Already paid

MONS 090119

AROCLOR TOXICITY DATA

Toxicity Data	Cost	MCS 1043 Have	MCS 1043 Need	MCS 1043 Date Begin	MCS 1043 Date End	Mono-Chloro Mono-Bromo Biphenyl Have	Mono-Chloro Mono-Bromo Biphenyl Need	Mono-Chloro Mono-Bromo Biphenyl Date Begin	Mono-Chloro Mono-Bromo Biphenyl Date End	Mono-Bromo Dichloro Diphenyl Have	Mono-Bromo Dichloro Diphenyl Need	Mono-Bromo Dichloro Diphenyl Date Begin	Mono-Bromo Dichloro Diphenyl Date End	AROCLOR 6062 Have	AROCLOR 6062 Need	AROCLOR 6062 Date Begin	AROCLOR 6062 Date End
Acute																	
Rat-LD_{50}	$ 200		$ 200	3rd qtr. '71	1st qtr. '72		$ 200	3rd qtr. '71	1st qtr '72		$ 200	3rd qtn '71	1st qtr. '72	X			
Rabbits-MLD (dermal)	250		250	"	"		250	"	"		250	"	"	X			
Skin Irr. (rabbit)	100		100	"	"		100	"	"		100	"	"	X			
Eye Irr. (rabbit)	125		125	"	"		125	"	"		125	"	"	X			
Vapor Inhalation (Rats)	200		200	"	"		200	"	"		200	"	"				
Fish (2 species)	600		600	"	"		600	"	"		600	"	"				
Sub-acute																	
90-day rat **	6,000		6,000	"	"		6,000	"	"		6,000	"	"				
90-day dog	10,000		10,000	"	"		10,000	"	"		10,000	"	"				
Fish (30-90 day)	3,000 (est.)		3,000	"	"		3,000	"	"		3,000	"	"				
Reproduction																	
Rats	17,000		Defer				Defer				Defer						
Chickens	8,000		Defer				Defer				Defer						
Teratology																	
Rabbits	4,500		Defer				Defer				Dafer						
TOTAL:	$49,975																
NEED NOW:			$20,475				$20,475				$20,475						
DEFERRED:			$29,500				$29,500				$29,500						

* (Repeat)
** Control group cost $2,100

AROCLOR TOXICITY DATA

Toxicity Data	Cost	Bromo-Chlorobenzene Have	Need	Date Begin	Date End	2,2 Prime Dichloro Diphenyl Ether Have	Need	Date Begin	Date End	Have	Need	Date Begin	Date End	Have	Need	Date Begin	Date End
Acute																	
Rat-LD_{50}	$ 200		$ 200	3rd qtr. '71	1st qtr. '72		$ 200	3rd qtr. '71	1st qtr. '72								
Rabbits-MLD (dermal)	250		250	"	"		250	"	"								
Skin Irr. (rabbit)	100		100	"	"		100	"	"								
Eye Irr. (rabbit)	125		125	"	"		125	"	"								
Vapor Inhalation (Rats)	200		200	"	"		200	"	"								
Fish (2 species)	600		600	"	"		600	"	"								
Sub-acute																	
90-day rat **	6,000		6,000	"	"		6,000	"	"								
90-day dog	10,000		10,000	"	"		10,000	"	"								
Fish (30-90 day)	3,000 (est.)		3,000	"	"		3,000	"	"								
Reproduction																	
Rats	17,000		Defer				Defer										
Chickens	8,000		Defer				Defer										
Teratology																	
Rabbits	4,500		Defer				Defer										
TOTAL:	$49,975																
NEED NOW:			$20,475				$20,475										
DEFERRED:			$29,500				$29,500										

* (Repeat)
** Control group cost $2,100

AROCLOR TOXICITY STUDIES--INDUSTRIAL BIO-TEST LABORATORIES

Toxicity Data	Cost	AROCLOR 1221 BTL Number	Date Begin	Date End	MCS 1016 BTL Number	Date Begin	Date End	AROCLOR 5432 BTL Number	Date Begin	Date End	AROCLOR 5442 BTL Number	Date Begin	Date End
Acute													
Rat--LD_{50}	$ 200												
Rabbits-MLD (dermal)	250												
Skin Irr. (rabbit)	100												
Eye Irr. (rabbit)	125												
Vapor Inhalation (Rats)	200												
Fish (2 species)	600												
Sub-acute													
90-day rat*	6,000												
90-day dog	10,000												
Fish (30-90 day)	?												
Reproduction													
Rats	17,000	Defer			Defer			Defer			Defer		
Chickens	8,000	Defer			Defer			Defer			Defer		
Teratology													
Rabbits	1,800	Defer			Defer			Defer			Defer		
TOTAL:	$44,275												
DEFERRED:	$26,800												

*Control group cost $2,100

MONS 090122

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Biotest Studies	Sept 1973 Protocol #	Biotest Study #	Report Date	Status
Chicken Residue		J7010	4-69	Tissues used to verify procedures
Rat Tissue Study	I	J7009	4-69	Analysis of Aroclor tissues complete
Chicken Toxicity, Reproduction and Meat and Egg Residue Study	II	J7300	6-70	~ 220 Samples at Biotest
Mallard Duck Study	III			Deleted
3-Generation Reproduction Study in Rats	IV	P7297	9-70 (15 mo)	No tissues collected?
2-Year Chronic Toxicity Study in Rats	V	B7298	9-70 (12 mo.)	~ 320 Samples 204 at So 2nd St
2-Year Chronic Toxicity Study in Dogs	VI	C7299	12-70 (18 mo.)	No tissues collected?
Subacute Fish Toxicity Study	VII	A7201	6-69	Deleted.
		A8570		69 Fish samples ~200 Water samples at So. 2nd St.

#B7298 Two Year Chronic Oral Toxicity Study Of Aroclor In Albino Rats Adverse Effects

		3 Mo. Sacrifice						6 Mo. Sacrifice						12 Mo Sacrifice						24 Mo. Sacrifice					
		1 ppm		10 ppm		100 ppm		1 ppm		10 ppm		100 ppm		1 ppm		10 ppm		100 ppm		1 ppm		10 ppm		100 ppm	
		♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Aroclor 1242	Muscle														x	x		x							
	Kidney														x	x		x							
	Liver														x	x		x							
	Fat														x	x		x							
Aroclor 1254	Muscle														x	x		A x							
	Kidney														x	x		A x							
	Liver														x	x		A x							
	Fat														x	x		A x							
Aroclor 1260	Muscle													x		x		A x							
	Kidney													x		x		A x							
	Liver													x		x		A x							
	Fat													x		x		A x							
Control	Muscle			*						*				x		*						*			
	Kidney													x											
	Liver													x											
	Fat													x											

MONS 090124

* Common control, one per sacrifice.

A) Enlarged liver

X) Samples at So 2nd St (12 mo. sacrifice)
(Samples of all tissues through 6 mo. sacrifice at So. 2nd St.)

J7300 Toxicity, Reproduction and Residue Study on Aroclor in White Leghorn Chickens, Adverse Effects

		Test Sacrifice (1)						1st wk	2nd wk	3rd wk	4th wk	1st wk	2nd wk	3rd wk	4th wk	1st wk	2nd wk	3rd wk	4th wk	Recovery Sacrifice (2)					
		1 ppm		10 ppm		100 ppm		1 ppm				10 ppm				100 ppm				1 ppm		10 ppm		100 ppm	
		♂	♀	♂	♀	♂	♀	Recovery Period												♂	♀	♂	♀	♂	♀
Aroclor 1242	Muscle	m(4)	m(4)	A m(6)	m(6)	A, B m(10)	B m(12)															A		A, C m(1)	B m(1)
	Kidney	m(4)	m(4)	A m(6)	m(6)	A, B m(10)	B m(12)															A		A, B m(1)	B m(1)
	Liver	m(4)	m(4)	A m(6)	m(6)	A, B m(10)	B m(12)															A		A, B m(1)	B m(1)
	Fat	m(4)	m(4)	A m(6)	m(6)	A, B m(10)	B m(12)															A		A, B m(1)	B m(1)
	Egg			D, E		C, D, E						D, E	D, E	D, E	D, E	D, E	D, E	D, E	D, E			D, E		C, D, E	
Aroclor 1254	Muscle	m(8)	m(8)	m(5)	m(5)	A, B m(10)	A, B m(10)															m(1)	m(1)	A, B	A, B
	Kidney	m(8)	m(8)	m(5)	m(5)	A, B m(10)	A, B m(10)															m(1)	m(1)	A, B	A, B
	Liver	m(8)	m(8)	m(5)	m(5)	A, B m(10)	A, B m(10)															m(1)	m(1)	A, B	A, B
	Fat	m(8)	m(8)	m(5)	m(5)	A, B m(10)	A, B m(10)															m(1)	m(1)	A, B	A, B
	Egg					C, D, E										D, E	D, E	D, E	D, E					C, D, E	
Aroclor 1260	Muscle	m(6)	m(6)	m(4)	m(4)	m(5)	m(5)																		
	Kidney	m(6)	m(6)	m(4)	m(4)	m(5)	m(5)																		
	Liver	m(6)	m(6)	m(4)	m(4)	m(5)	m(5)																		
	Fat	m(6)	m(6)	m(4)	m(4)	m(5)	m(6)																		
	Egg																								
Control	Muscle	m(10)	m(10)	*								*										*			
	Kidney	m(10)	m(10)																						
	Liver	m(10)	m(10)																						
	Fat	m(10)	m(10)																						
	Egg																								

* Common control
(1) Between 22nd and 26th week
(2) Between 26th and 30th week

A) Lower body weights
B) [illegible]
C) [illegible] productions

[illegible]
E) Thinner [illegible]
M) Mortalities (number)

Phase note: [illegible] are for the test groups rather than individual birds or tissues.

		3 Mo. Sacrifice					
		1 ppm		10 ppm		100 ppm	
		♂	♀	♂	♀	♂	♀
1) Aroclor 1242	Muscle	5	10	13	18	64	89
	Kidney	7	2) 72	21	16	41	40
	Liver	10	12	20	31	82	72
	Fat	6	6	13	15	53	81

1) Calculated as Aroclor 1254

2) Aroclor 1260

ppm Lipid Weight Basis

		3 Mo. Sacrifice					
		1 ppm		10 ppm		100 ppm	
		♂	♀	♂	♀	♂	♀
1.) Aroclor 1242	Muscle	5	10	13	18	64	89
	Kidney	7	(2) 72	21	16	41	40
	Liver	10	12	20	31	82	72
	Fat	6	6	13	13	53	81
Aroclor 1254	Muscle	7	12	65	107	486	1026
	Kidney	11	12	54	41	233	323
	Liver	15	20	108	122	(323)	1157
	Fat	8	3	86	66	329	2362
Aroclor 1260	Muscle	98	16	44	76	137	156
	Kidney	7	22	66	142	606	851
	Liver	20	—	112	93	1539	1815
	Fat	—	32	138	760	(1060)	672

1.) Calculated as Aroclor 1254

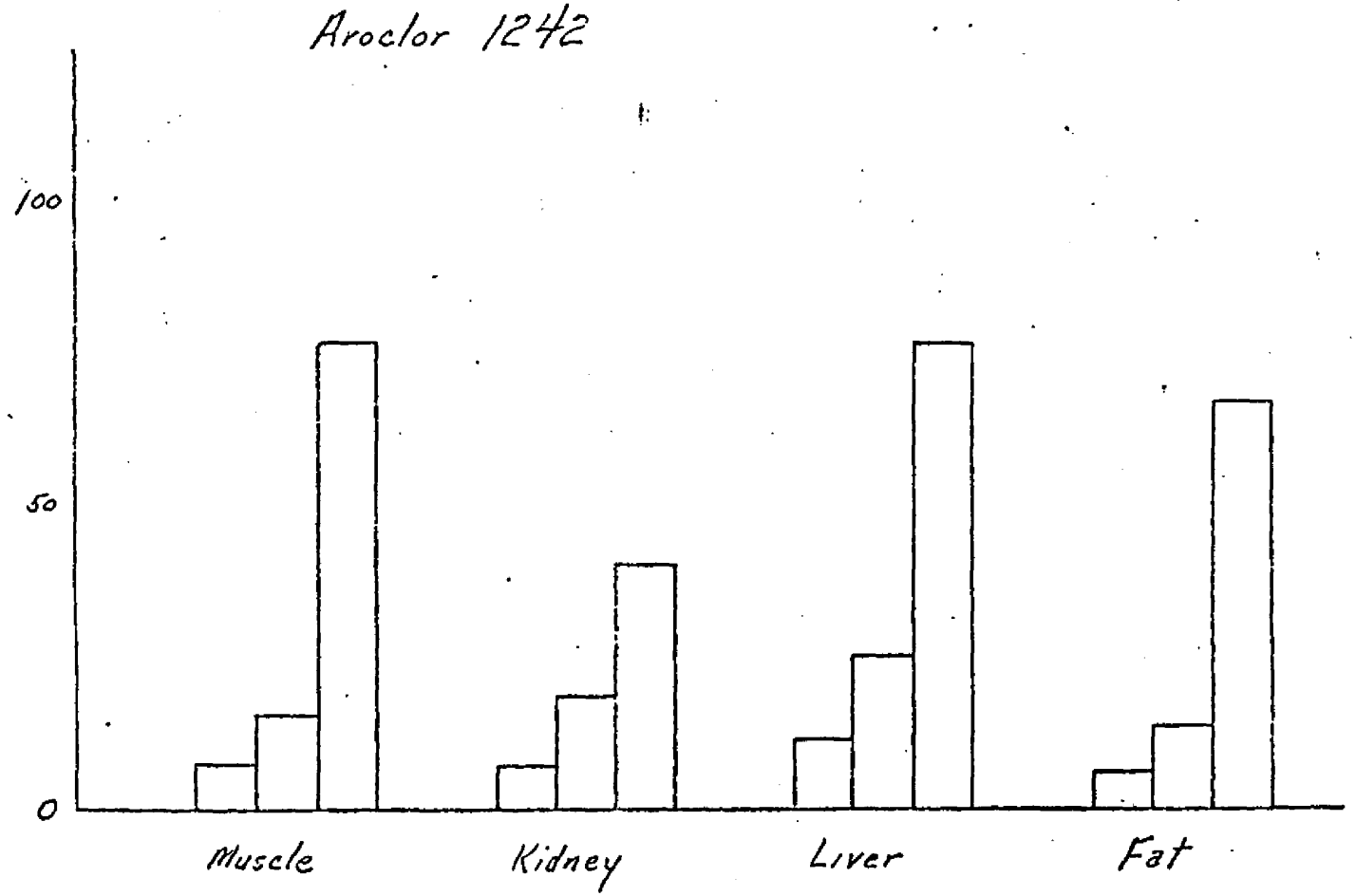
2.) Aroclor 1260

ppm Wet Weight Basis

		3 Mo. Sacrifice					
		1. ppm		10 ppm		100 ppm	
		♂	♀	♂	♀	♂	♀
1.) Aroclor 1242	Muscle	0.4	1	0.7	2	4	6
	Kidney	0.2	(2) 2	0.5	0.3	0.8	0.9
	Liver	0.1	0.1	0.2	0.3	0.9	0.9
	Fat	5	6	12	12	44	75
Aroclor 1254	Muscle	2	1	8	8	31	62
	Kidney	0.2	0.2	1	1	5	8
	Liver	0.1	0.1	1	1	18	12
	Fat	8	3	84	66	306	211
Aroclor 1260	Muscle	9	2	6	11	11	10
	Kidney	0.1	0.5	1	4	14	18
	Liver	0.2	—	1	2	18	19
	Fat	—	28	110	724	366	599

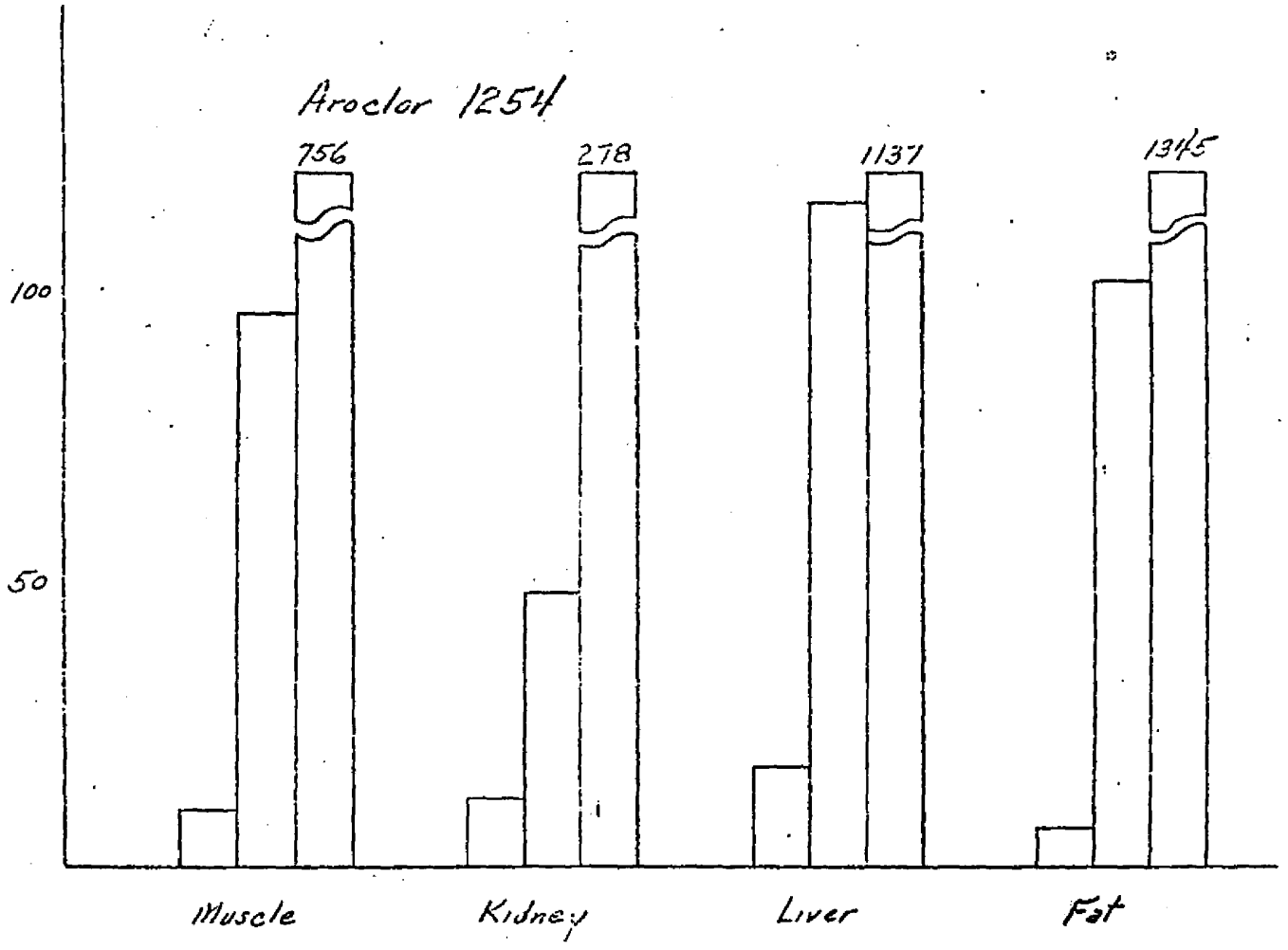
1.) Calculated as Aroclor 1254

2.) Aroclor 1260



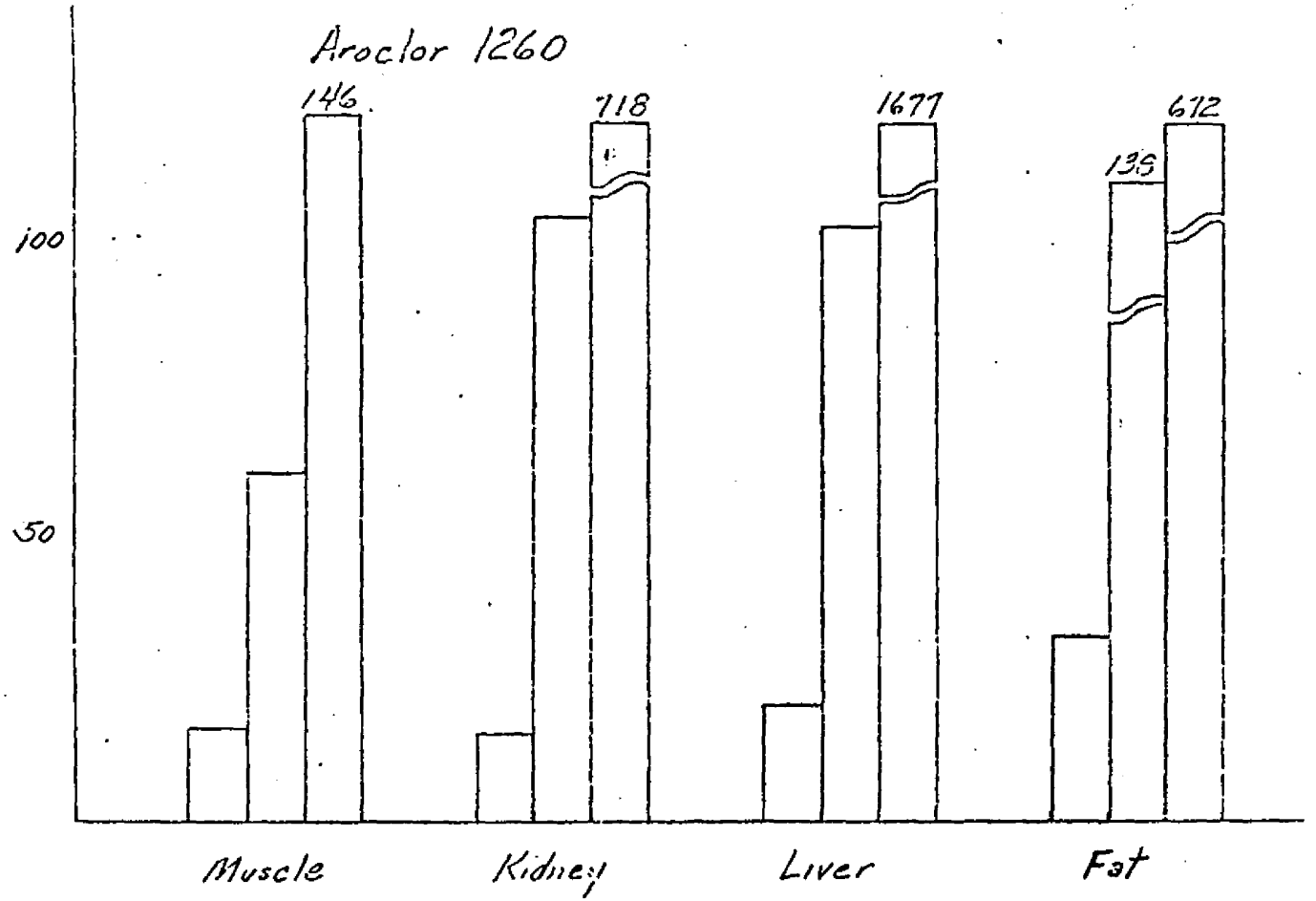
62T060 SNOW 090129

		3 Mo. Sacrifice					
		1 ppm		10 ppm		100 ppm	
		♂	♀	♂	♀	♂	♀
Residue 125I	Muscle	7	12	65	107	486	1026
	Kidney	11	12	54	141	233	323
	Liver	15	20	108	122	3239	1137
	Fat	8	3	86	66	329	2362

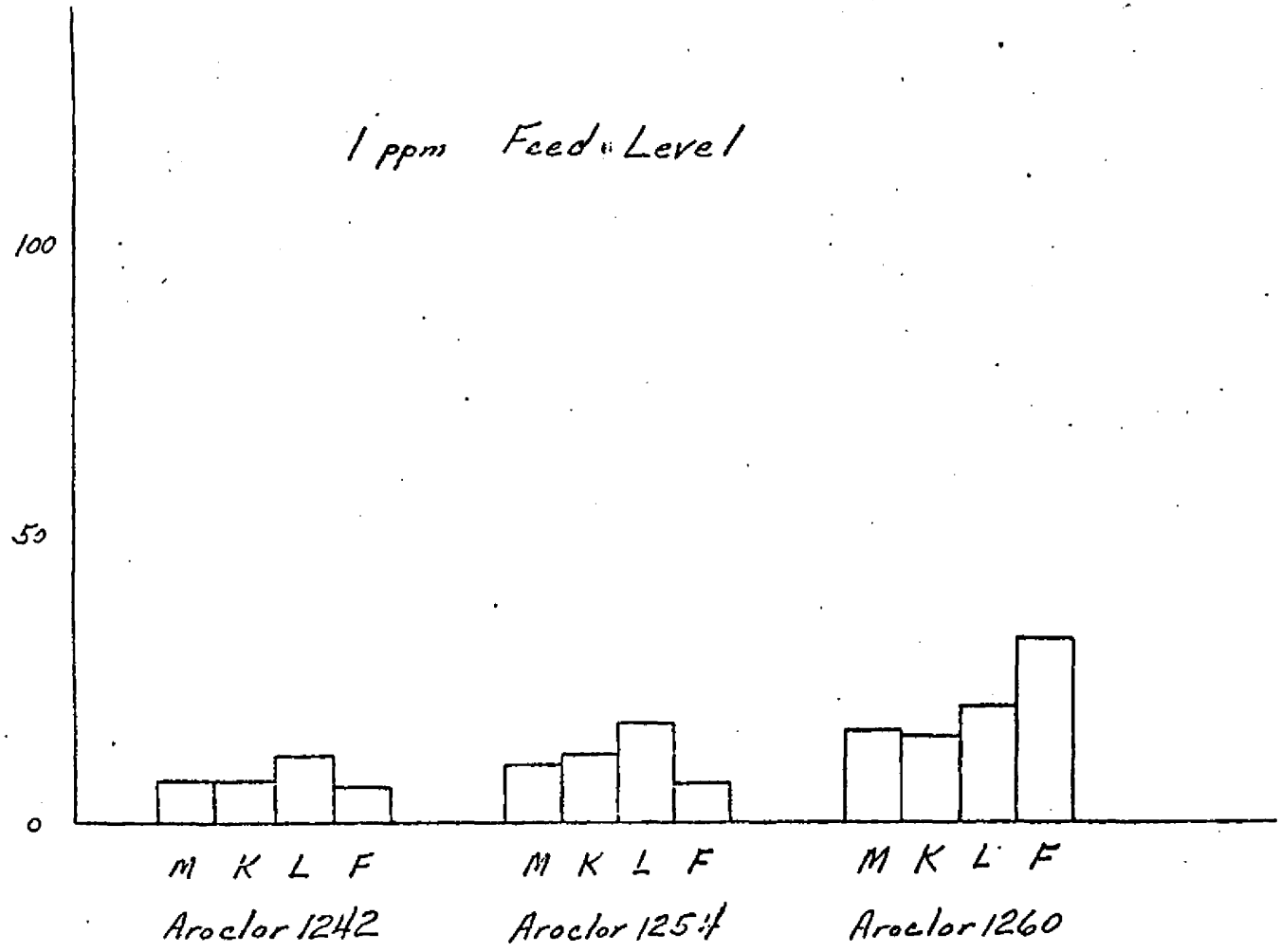

Aroclor 1254
756
278
1137
1345
100
50
Muscle
Kidney
Liver
Fat

MONS 090131

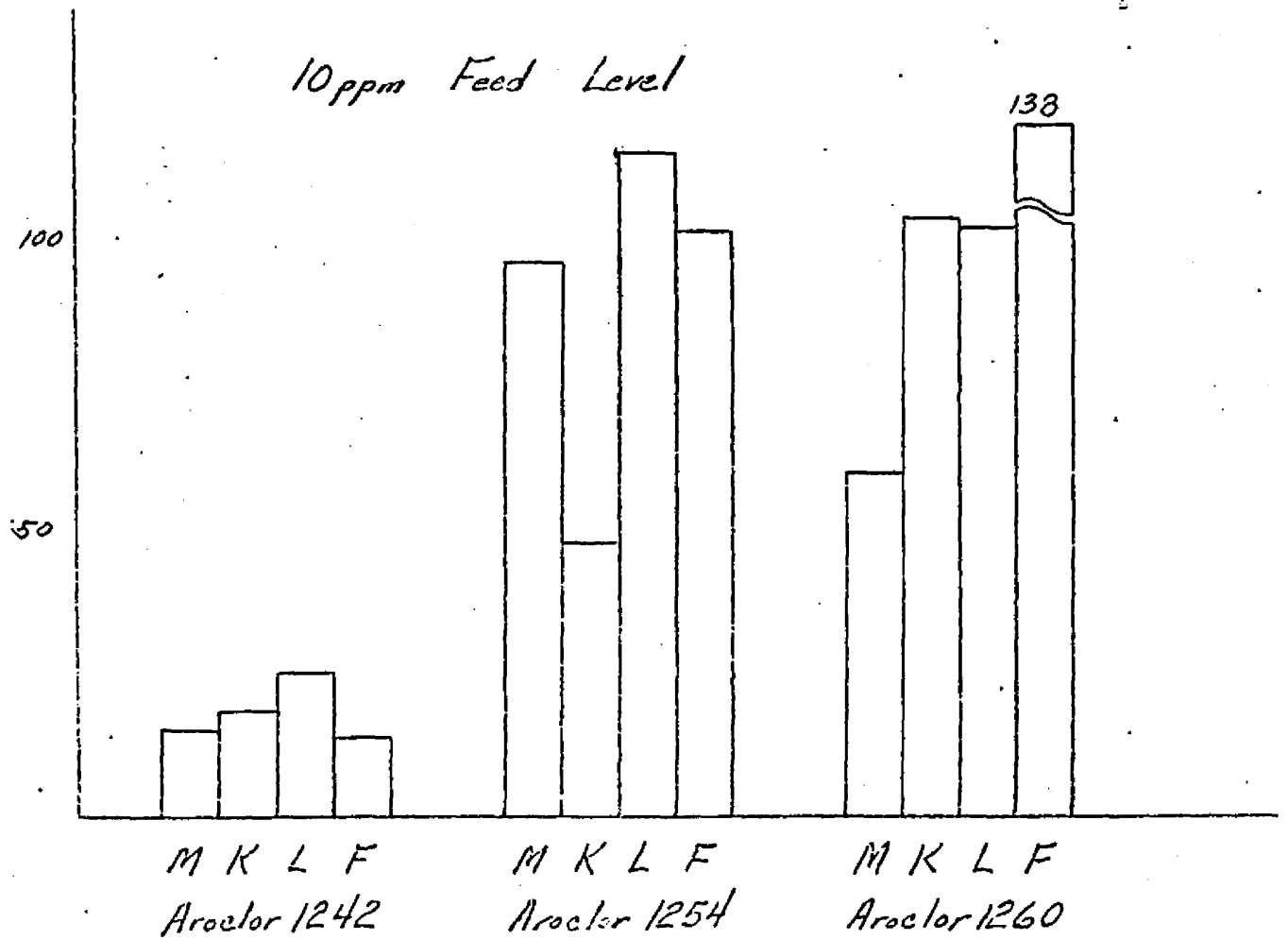
		3 Mo. Sacrifice					
		1 ppm		10 ppm		100 ppm	
		♂	♀	♂	♀	♂	♀
Aroclor 1260	Musch.	98	16	44	76	137	156
	Kidney	7	22	66	142	606	831
	Liver	20	—	112	93	1539	1815
	Fat	—	32	138	760	1060	672


Aroclor 1260
146
718
1677
672
139
100
50
Muscle
Kidney
Liver
Fat

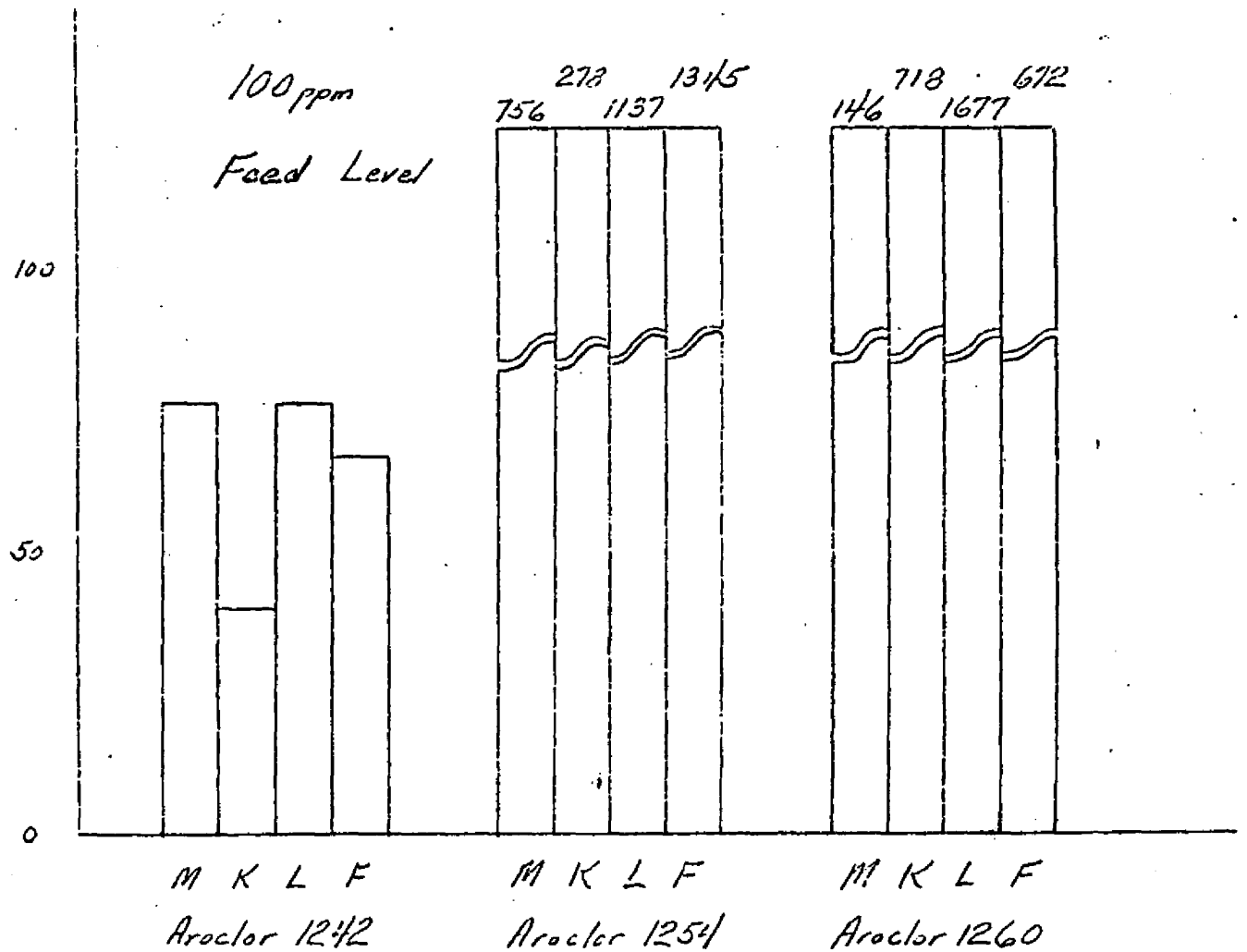
MONS 090133


1 ppm Feed Level
100
50
0
M K L F
Aroclor 1242
M K L F
Aroclor 1254
M K L F
Aroclor 1260

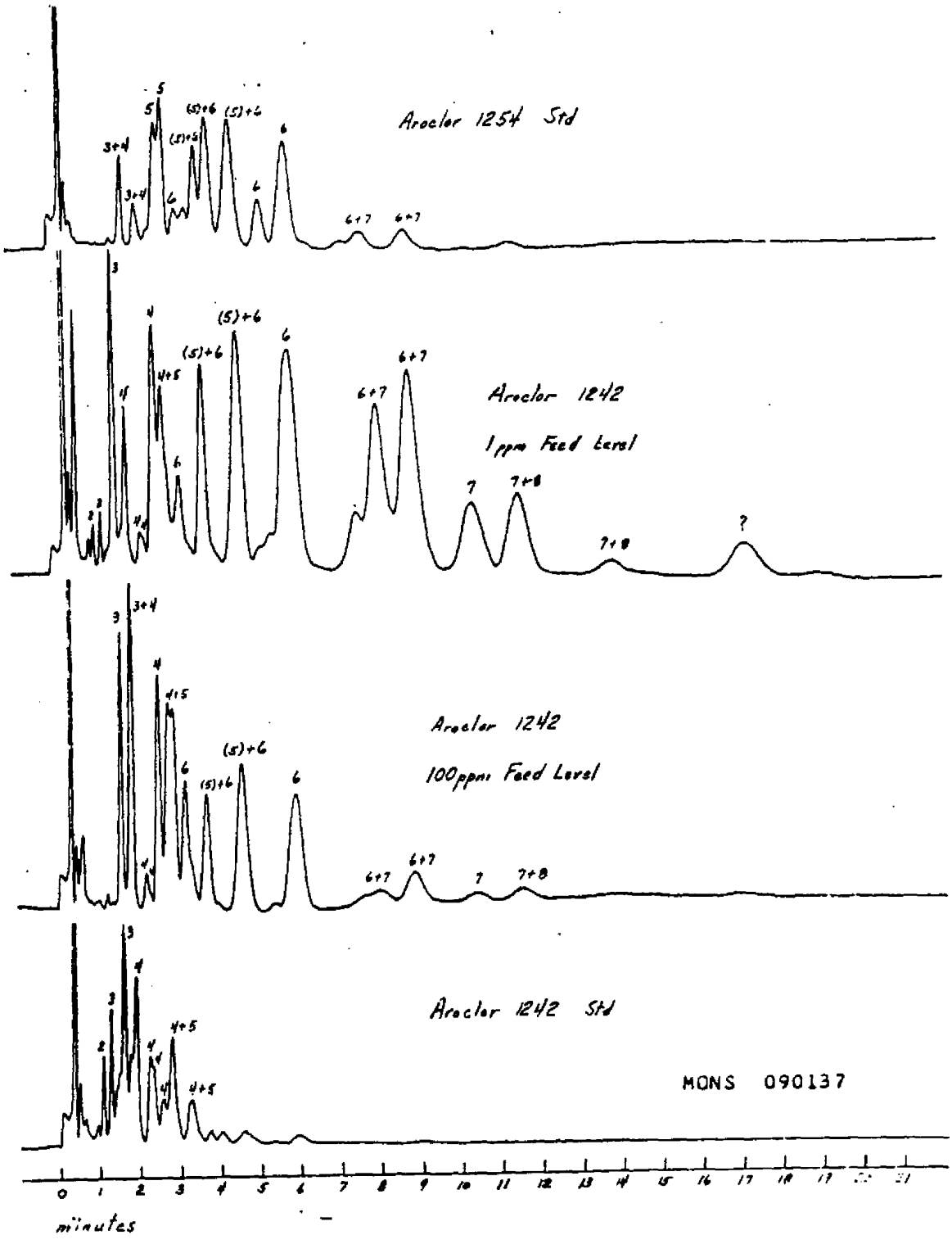
MONS 090134

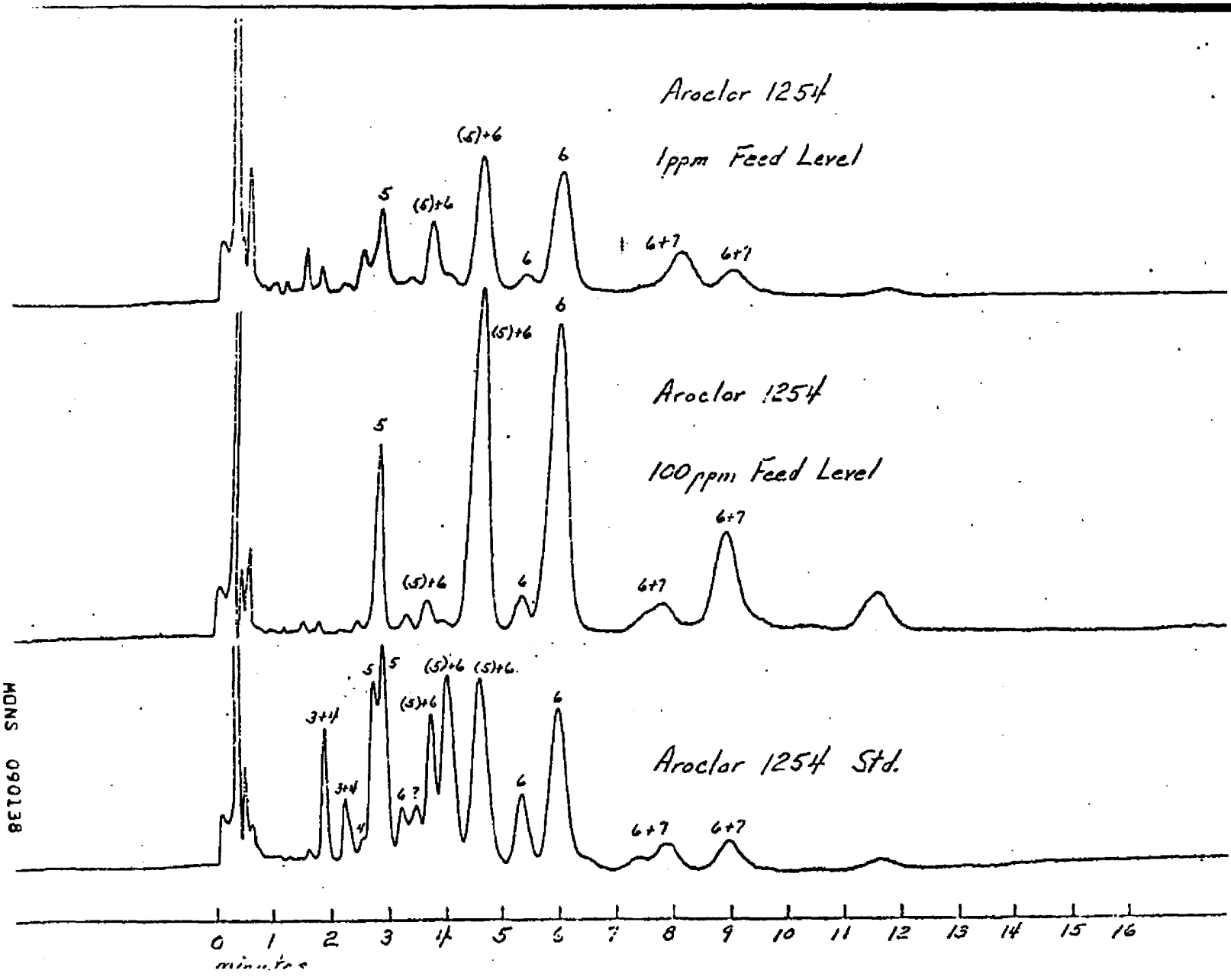

10 ppm Feed Level
138
100
50
M K L F
Aroclor 1242
M K L F
Aroclor 1254
M K L F
Aroclor 1260

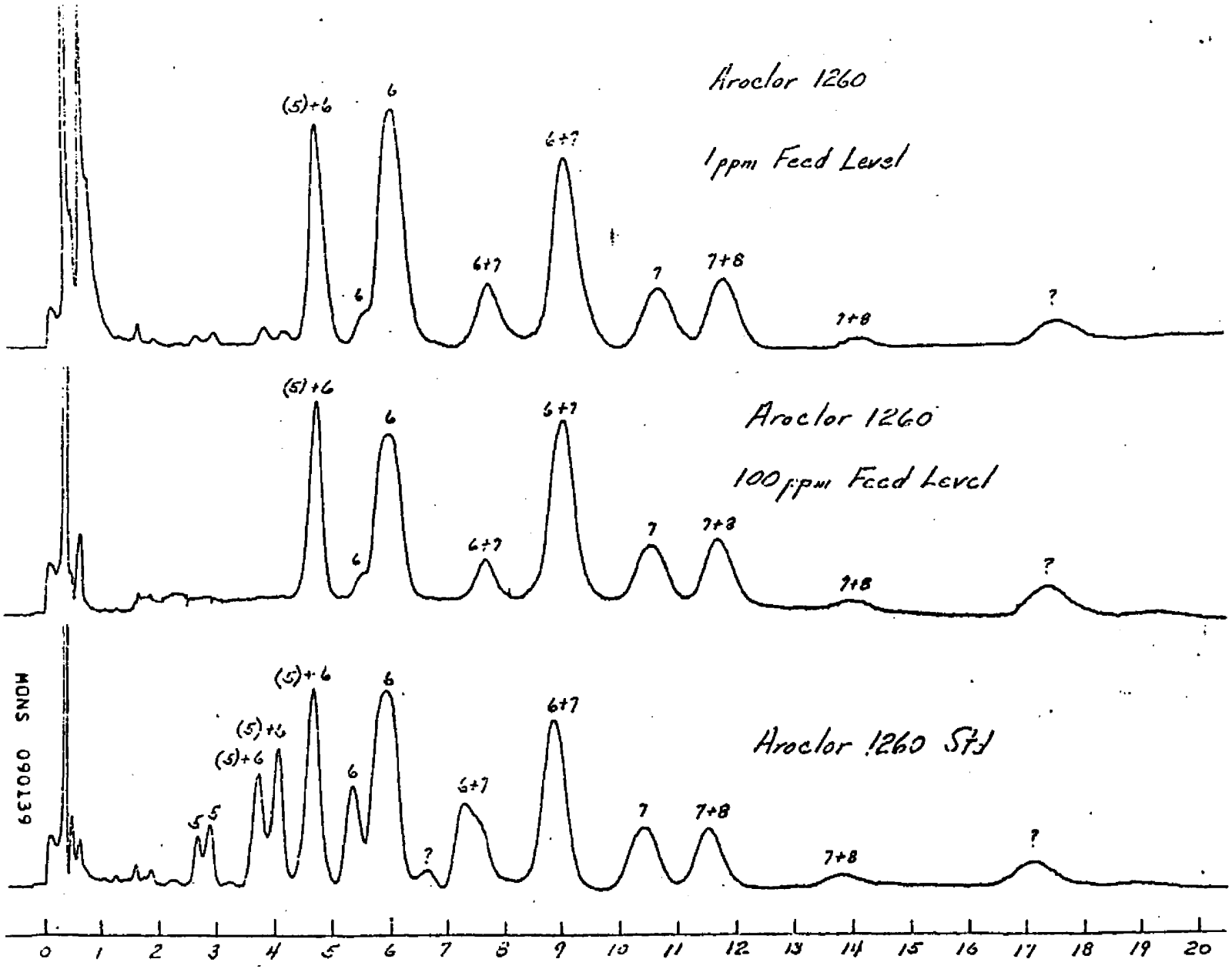
SET060 SNOW

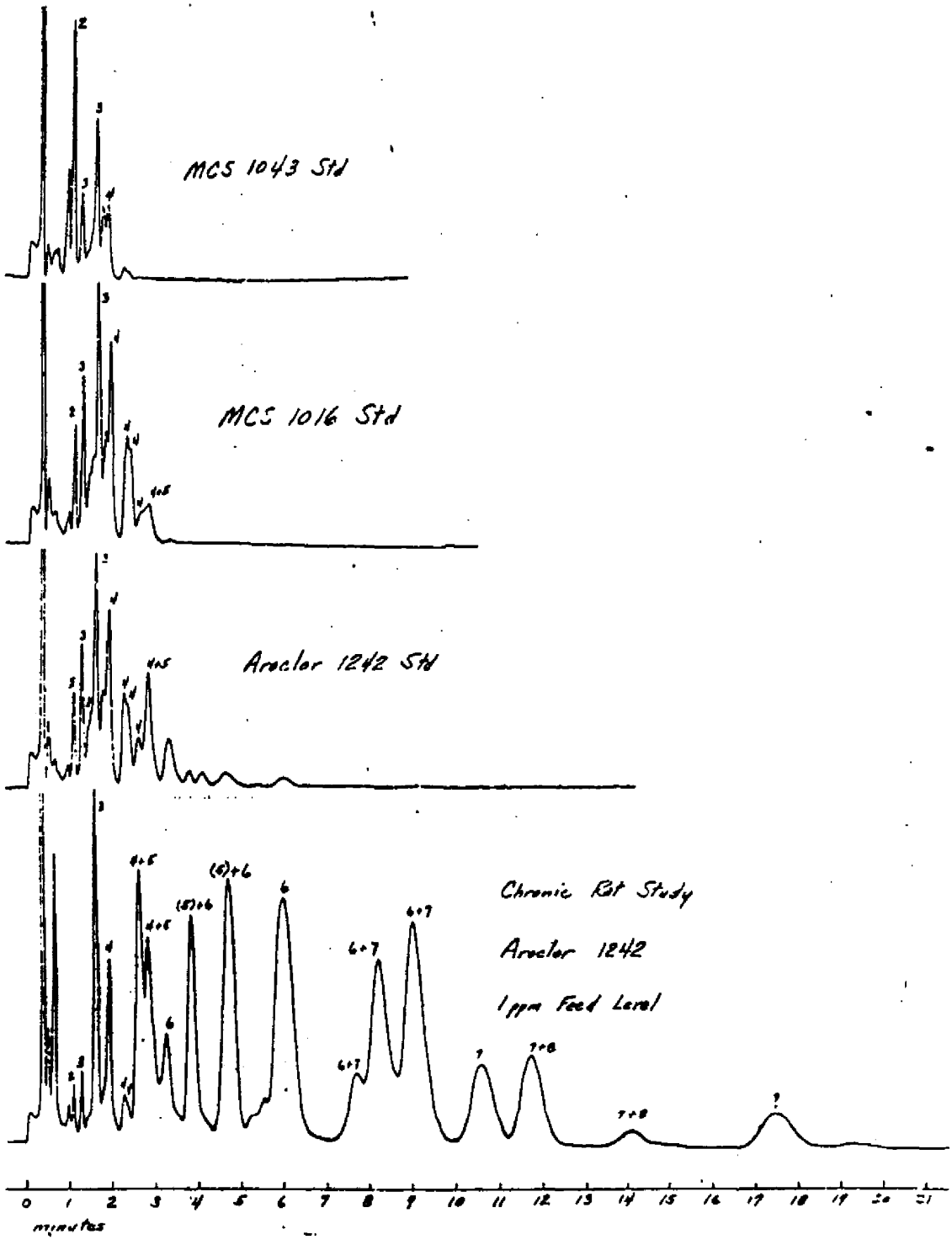

100 ppm
Feed Level
100
50
0
756
278
1137
1315
146
718
1677
672
M K L F
M K L F
M K L F
Aroclor 1242
Aroclor 1254
Aroclor 1260

MONS 090136


Aroclor 1254 Std
Aroclor 1242
1ppm Feed Level
Aroclor 1242
100ppm Feed Level
Aroclor 1242 Std
MONS 090137
minutes


Aroclor 1254
1ppm Feed Level
(5)+6
6
5
(5)+6
6
6+7
6+7
Aroclor 1254
100ppm Feed Level
(5)+6
6
5
(5)+6
6
6+7
6+7
Aroclor 1254 Std.
3+4
3+4
5
5
(5)+6
(5)+6
(5)+6
6
6
6+7
6+7
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
minutes
MONS 090138


Aroclor 1260
1 ppm Feed Level
(5)+6
6
6+7
7
7+8
?
Aroclor 1260
100 ppm Feed Level
Aroclor 1260 Std
5
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20


MCS 1043 Std
MCS 1016 Std
Aroclor 1242 Std
Chronic Rat Study
Aroclor 1242
1 ppm Feed Level
minutes

MONS 090140