Petitioner AMVAC Exhibit 9

EPA OALJ Docket No. FIFRA-HQ-2022-0002

Update on DCPA developmental thyroid studies

Background

Two studies are planned/in progress to investigate developmental thyroid effects of DCPA:

- DCPA (Chlorthal Dimethyl): Dose Range Finding Pre and Post Natal Developmental Thyroid Study in Sprague-Dawley Rats by Oral Administration (Envigo study: BDG0204). Currently in progress.
- DCPA (Chlorthal Dimethyl): Definitive Main Pre and Post Natal Developmental Thyroid Study in CD Rats by Oral Administration (Envigo study: BDG0202). Planned Q1 2018.

This update concerns the dose range finding study (BDG0204). The study design is summarised below:

Group	Treatment	DCPA mg/kg/day	Number of animals	Animal numbers
Phase I				
1	Groups 1-5	0	10	1-10
2	dosed on Day 6	0.1	5	11-15
3	to Day 20	1	5	16-20
4	after mating	10	5	21-25
5	(initial phase)	100	10	26-35
Phase IA*				
6	Groups 6-10	0	10	101-110
7	dosed on Day 6	0.1	5	111-115
8	to Day 20	1	5	116-120
9	after mating	10	5	121-125
10	(repeated phase)	100	10	126-135
Phase II**				
11	Groups 11-15	0	5	136-140
12	dosed on Day 6	Low	5	141-145
13	after mating	Low/Intermediate	5	146-150
14	to Day 20/21	High/Intermediate	5	151-155
15	of lactation	High	5	156-160
Phase III**				
16	Groups 16-20	0	5	161-165
17	Dams dosed on Day 6	Low	5	166-170
18	after mating to Day 7 of	Low/Intermediate	5	171-175
19	lactation. Pups directly dosed	High/Intermediate	5	176-180
20	from Day 7 of age to Day 20/21 of age	High	5	181-185

* In Groups 6 to 10, blood samples from the first 5 numbered animals were taken 2h after dosing. In Groups 6 and 10, blood samples were taken from the remaining extra 5 animals 24h after dosing in order to determine the optimum sampling time.

** The last day of dosing during lactation on Phases II and III (Day 20 or Day 21) and the time of blood sampling for assessment of effects on thyroid hormone levels will be determined by the optimal time point for assessment of effects on thyroid hormone levels identified in Phase IA of the study. Dose levels for administration to Phases II and III (Groups 11-20) will be selected based on results from Phase IA.

Updates on this study were submitted on 18th January 2017 and 11th April 2017. These updates explained that Phase I had been conducted and thyroid hormones determined using a Luminex immunofluorescence assay initially developed for this work. However, values for T4 and T3 in fetuses were not detectable using this assay and therefore an LC-MS MS assay was developed. As insufficient samples remained from Phase I, this was repeated (Phase IA) and thyroid hormones were determined using the new assay.

The results of Phase IA, the intended doses for Phases II & III and sampling times for Phases II & III are described in this update.

Result summary and conclusions

The Terminal Summary from Phase IA is shown in Appendix 1. Key points relevant for conducting Phases II and III are:

- The blood sampling time will be 2h after dosing, as somewhat greater reductions in T4 in fetuses and dams were seen at this timepoint compared to 24h. Sampling at 2h also enables a simpler necropsy process.
- T4 was the most sensitive biomarker and is used as the basis for setting doses in Phases II and III. Changes in T3 followed a similar pattern to T4 but effects were seen at higher doses.
- Statistically significant reductions in T4 were seen in dams at 10 or 100 mg/kg/day, and significant reductions in T4 were seen in fetuses at 1, 10 or 100 mg/kg/day. No effects were seen at 0.1 mg/kg/day.
- TSH concentrations were generally unaffected by maternal treatment, although blood volume limitations and differences in fetal sex ratio meant that sample numbers were low.
- The doses proposed for Phases II and III of BDG0204 are the same as those used in Phase I, i.e. 0, 0.1, 1, 10 or 100 mg/kg/day, as a NOAEL was achieved for T4 whilst the other hormones were less affected.

Appendix 1

Study number:	BDG0204
Study title:	DCPA (Chlorthal Dimethyl): Dose Range Finding Pre and Post Natal Developmental Thyroid Study in Sprague-Dawley Rats by Oral Administration
Study Director:	Adam Leggett
Phases covered in the summary:	Phase IA
Date of issue:	19 May 2017

Treatment commenced:	Phase I:	15 February 2016
	Phase IA:	
Terminal sacrifice commenced:	Phase I:	29 February 2016
	Phase IA:	20 March 2017
Treatment scheduled to commence:	Phase II:	To Be Determined
	Phase III:	To Be Determined
Terminal sacrifice scheduled to commence:	Phase II:	To Be Determined
	Phase III:	To Be Determined
Draft report due:		To Be Determined

Study Design and Structure

1.1 Identity of treatment groups

Group	Treatment	Dose mg/kg/day#	Number of animals	Animal numbers
Phase I				
1	Control	0	10	1-10
2	DCPA	0.1	5	11-15
3	DCPA	1	5	16-20
4	DCPA	10	5	21-25
5	DCPA	100	10	26-35
Phase IA				
6	Control	0	10	101-110
7	DCPA	0.1	5	111-115
8	DCPA	1	5	116-120
9	DCPA	10	5	121-125
10	DCPA	100	10	126-135
Phase II*ø				
11	Control	0	5	136-140
12	DCPA	Low	5	141-145
13	DCPA	Low/Intermediate	5	146-150
14	DCPA	High/Intermediate	5	151-155
15	DCPA	High	5	156-160
Phase III*ø				
16	Control	0	5	161-165
17	DCPA	Low	5	166-170
18	DCPA	Low/Intermediate	5	171-175
19	DCPA	High/Intermediate	5	176-180
20	DCPA	High	5	181-185

Expressed in terms of test substance as supplied.

Phase I - Groups 1-5 dosed on Day 6 to Day 20 after mating

Phase IA - Groups 6-10 dosed on Day 6 to Day 20 after mating

Phase II - Groups 11-15 dosed on Day 6 after mating to Day 20/21 of lactation*

Phase III - Groups 16-20 Dams dosed from Day 6 after mating to Day 7 of lactation. Pups directly dosed from Day 7 of age to Day 20/21 of age*

* The last day of dosing during lactation on Phases II and III (Day 20 or Day 21) and the time of blood sampling for assessment of effects on thyroid hormone levels will be determined by the optimal time point for assessment of effects on thyroid hormone levels identified in Group 10 in Phase IA of the study.

ø Dose levels for administration to Phases II and III (Groups 11-20) will be selected based on results from Phase IA. It is anticipated that doses will be consistent between all phases of the study but should unanticipated effects be seen on Phase IA, dose levels for Phases II/III will be adjusted accordingly.

Laboratory investigations

Thyroid Hormone Analysis	Phase I Dams: Day 20/21 of gestation
	Phase I Fetuses: Day 20/21 of gestation
	Phase IA Dams: Day 20/21 of gestation
	Phase IA Fetuses: Day 20/21 of gestation
	Phase II Dams: Day 21 of lactation
	Phase II Neonates/Juveniles: Day 4 and Day 21 of lactation
	Phase III Juveniles: Day 21 of lactation

Results

Signs and mortality

Appendix 1

There were no signs seen at weekly physical examination that were attributable to treatment and no signs were evident following administration.

There were no deaths.

Bodyweight

Table 1

Bodyweight change was unaffected by treatment.

Food consumption

Table 2

Food consumption was unaffected by treatment.

Thyroid hormones

Tables 3, 4 and 5

Serum T3

Adult T3 concentrations were unaffected by treatment at two or 24 hours after treatment on Day 20 of gestation.

Male and female fetal T3 concentrations were statistically significantly low two hours after maternal treatment at 1 mg/kg/day (82% or 86%, respectively) and were BLQ (<5.00 pg/mL) in both sexes following maternal treatment at 10 or 100 mg/kg/day. T3 concentrations were statistically significantly low in male and female fetuses at 24 hours after maternal treatment at 100 mg/kg/day (36% or 34%, respectively). Fetal T3 concentrations were unaffected at two hours after maternal treatment at 0.1 mg/kg/day.

There is no clear difference in response at 2 or 24 hours after dosing; therefore 2 hours will be used on the next phase.

Serum T4

When compared with Control, adult T4 concentrations were statistically significantly low at 10 or 100 mg/kg/day at two hours after treatment on Day 20 of gestation (75% or 50%, respectively) and were statistically significantly low at 100 mg/kg/day at 24 hours after treatment (58%). Adult T4 concentrations were unaffected at 0.1 or 1 mg/kg/day.

Male and female fetal T4 concentrations were statistically significantly low and similar in both sexes at 1, 10 or 100 mg/kg/day at two hours after maternal treatment on Day 20 of gestation (75%, 23% or 12% and 84%, 26% or 12% of Control, respectively) and were statistically significantly low at 100 mg/kg/day at 24 hours after treatment (17% of Control). Fetal T4 concentrations were unaffected at two hours after maternal treatment at 0.1 mg/kg/day.

There is a slight increase in response at 2 hours compared with 24 hours after dosing; therefore 2 hours will be used on the next phase.

Plasma TSH

When compared with Control, adult TSH concentrations were unaffected by treatment at 0.1, 1, 10 or 100 mg/kg/day at two or 24 hours after treatment on Day 20 of gestation.

Samples for the TSH investigation were collected following sampling for T3 and T4 investigations; therefore, due to blood volume limitations and differences in fetal sex ratio, fewer samples were available for analysis and in some cases statistical analysis was not possible.

The available data shows that male and female fetal TSH concentration were low at 100 mg/kg/day (statistically significantly low in females) at two hours after maternal treatment on Day 20 of gestation and were considered to be comparable with Control at 24 hours after treatment. TSH concentrations were unaffected by maternal treatment at 0.1, 1 or 10 mg/kg/day.

Organ Weights

Table 6

There were no treatment-related effects on organ weight.

Liver weight was statistically significantly high in animals treated at 0.1 mg/kg/day.

Macropathology

There were no macroscopic findings in adults or fetuses.

1.2 Litter responses

All animals were pregnant. Therefore, five litters were assessed at 0, 0.1, 1, 10 or 100 mg/kg/day on Day 20 of gestation and five litters were assessed at 0 or 100 mg/kg/day on Day 21 of gestation.

Reproductive assessment

Table 7

Litter data, as assessed by the number of implantations, resorptions, live fetuses, sex ratio and pre- and post-implantation loss was unaffected by treatment.

1.3 Litter and fetal weights

Table 8

Mean placental weight, litter weight, litter size and fetal weights were unaffected by treatment.

TABLE 1 Request ID: 397484

Bodyweight - group mean values during gestation (g)

Group	:	6	7	8	9	10
Compound	:	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day)	:	0	0.1	1.0	10.0	100.0

Group /Sex		Day 0	Day 3	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15
6F	Mean	253	266	283	284	286	292	298	303	308	312	317	324
	SD	13.8	14.9	13.5	17.1	16.0	15.5	17.8	15.4	13.6	13.7	12.9	16.0
	N	10	10	10	10	10	10	10	10	10	10	10	10
7F	Mean	259	274	288	292	297	304	308	312	322	326	333	342
	SD	10.7	10.9	12.7	11.4	10.9	13.0	15.0	14.6	13.5	13.4	13.1	15.4
	N	5	5	5	5	5	5	5	5	5	5	5	5
8F	Mean	261	275	293	294	299	305	310	317	324	329	333	343
	SD	11.4	13.2	10.9	14.6	14.4	11.9	11.6	14.8	16.3	14.9	16.3	14.7
	N	5	5	5	5	5	5	5	5	5	5	5	5
9F	Mean	250	267	280	282	287	293	299	305	313	319	324	334
	SD	8.7	13.1	8.1	8.5	6.9	7.2	6.0	6.7	6.0	7.2	5.2	5.8
	N	5	5	5	5	5	5	5	5	5	5	5	5
10F	Mean	244	263	277	281	285	289	294	301	307	312	317	326
	SD	11.0	15.2	17.3	16.0	17.8	19.4	17.8	16.4	17.2	16.3	15.7	15.6
	N	10	10	10	10	10	10	10	10	10	10	10	10

Group	:	6	7	8	9	10
Compound	:	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day)	:	0	0.1	1.0	10.0	100.0

Group /Sex		Day 16	Day 17	Day 18	Day 19	Day 20	Change 6-20
6F	Mean	335	350	363	376	389	107
	SD	18.2	18.1	16.0	18.2	19.7	12.3
	N	10	10	10	10	10	10
7F	Mean	351	363	380	394	411	123
	SD	16.6	14.2	13.2	17.6	17.7	12.4
	N	5	5	5	5	5	5
8F	Mean	354	367	383	398	415	123
	SD	16.9	16.6	18.4	19.7	21.0	11.9
	N	5	5	5	5	5	5
9F	Mean	345	358	372	385	399	120
	SD	6.4	3.0	4.7	4.0	8.2	7.7
	N	5	5	5	5	5	5
10F	Mean	336	348	363	375	387	110
	SD	16.5	15.6	18.1	19.9	17.7	11.4
	N	10	10	10	10	10	10

TABLE 2

Request ID: 397503

Food consumption - group mean values during gestation (g/animal/day)

Group :	6	7	8	9	10
Compound :	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day) :	0	0.1	1.0	10.0	100.0

Group /Sex		Day 0-2	Day 3-5	Day 6-9	Day 10-13	Day 14-17	Day 18-19
6F	Mean	19	21	22	22	26	25
	SD	1.8	1.7	1.6	1.0	2.9	2.5
	N	10	10	10	10	10	10
7F	Mean	21	23	24	26	28	28
	SD	1.2	1.8	0.9	1.4	1.2	2.4
	N	5	5	5	5	5	5
8F	Mean	20	23	24	26	29	27
	SD	3.3	1.5	1.4	2.0	2.4	3.0
	N	5	5	5	5	5	5
9F	Mean	21	22	24	26	28	27
	SD	1.3	1.9	2.1	1.9	1.3	2.0
	N	5	5	5	5	5	5
10F	Mean	20	22	23	24	27	26
	SD	2.6	1.9	1.7	1.3	1.9	1.2
	N	10	10	10	10	10	10

TABLE 3

Serum T3 concentrations (pg/mL) - group mean values following treatment on Day 20 of gestation

Group	:	6	7	8	9	10
Compound	:	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day)	:	0	0.1	1	10	100

Group		Adult Timepoint		Female fetus Timepoint		Male fetus Timepoint	
/Sex		2 hours	24 hours	2 hours	24 hours	2 hours	24 hours
Statistics test		Wi	Tt	Wi	Tt	Wi	Tt
6	Mean	475	344	15.6	30.8	11.8	27.0
	SD	71	84	1.1	4.4	2.0	2.3
	N	5	5	5	5	5	5
7	Mean	454	-	18.7	-	13.7	-
	SD	46	-	1.3	-	2.9	-
	N	5	-	5	-	5	-
8	Mean	477	-	13.5**	-	9.63*	-
	SD	33	-	3.3	-	1.88	-
	N	5	-	5	-	5	-
9	Mean	485	-	BLQ	-	BLQ	-
	SD	98	-	-	-	-	-
	N	5	-	5	-	5	-
10	Mean	416	305	BLQ	11.1**	BLQ	9.06**
	SD	73.0	67	-	3.4	-	2.79
	N	5	5	5	5	5	5

BLQ <5.00 pg/mL

TABLE 4

Serum T4 concentrations (pg/mL) - group mean values following treatment on Day 20 of gestation

Group	:	6	7	8	9	10
Compound	:	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day)	:	0	0.1	1	10	100

Group /Sex		Adult Timepoint		Female fetus Timepoint		Male fetus Timepoint	
		2 hours	24 hours	2 hours	24 hours	2 hours	24 hours
Statistics test		Wi	Tt	Wi	lTt	Wi	Tt
6	Mean	14800	13200	3300	4650	3110	4620
	SD	1990	4720	208	843	552	387
	N	5	5	5	5	5	5
7	Mean	14500	-	3510	-	3540	-
	SD	1660	-	409	-	470	-
	N	5	-	5	-	5	-
8	Mean	15700	-	2470**	-	2600**	-
	SD	1500	-	293	-	392	-
	N	5	-	5	-	5	-
9	Mean	11100**	-	747**	-	797**	-
	SD	1910	-	117	-	78	-
	N	5	-	5	-	5	-
10	Mean	7440**	7610*	405**	740**	386**	799**
	SD	1830	2280	35	78	69	98
	N	5	5	5	5	5	5

BLQ <5.00 pg/mL

TABLE 5

Plasma TSH concentrations (pg/mL) - group mean values following treatment on Day 20 of gestation

Group	:	6	7	8	9	10
Compound	:	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day)	:	0	0.1	1	10	100

Group /Sex		Adult Timepoint		Female fetus Timepoint		Male fetus Timepoint	
		2 hours	24 hours	2 hours	24 hours	2 hours	24 hours
Statistics test		Wi	Tt	#	#	Wi	#
6	Mean	1770	926	3050	2460	3720	2070
	SD	618	544	403	505	1570	276
	N	5	5	2	3	5	3
7	Mean	641	-	2410	-	2800	-
	SD	a	-	335	-	1300	-
	N	5	-	3	-	4	-
8	Mean	1110	-	2280	-	2370	-
	SD	526	-	656	-	566	-
	N	5	-	5	-	3	-
9	Mean	1130	-	2740	-	2780	-
	SD	760	-	902	-	1570	-
	N	5	-	4	-	5	-
10	Mean	2180	903	1350	1750	1600*	2010
	SD	2140	808	184	-	277	930
	N	5	5	4	1	4	4

a_ Standard deviation and coefficient of variation are not reported when the data contains BLQ values. # Insufficient data for statistical analysis.
Where means are calculated BLQ values have been replaced by 0.5x LLOQ i.e. 61.5 pg/mL

TABLE 6

Organ weights - group mean unadjusted and adjusted values (g) on Day 20 of gestation

Group	:	6	7	8	9	10
Compound	:	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day)	:	0	0.1	1.0	10.0	100.0

Group /Sex		Terminal Bodyweight	Liver	Thyroids + Paras
Unadjusted Means				
Statistical test:		Wi		
6F	Mean	395	13.91	0.014
	SD	19	1.13	0.001
	N	5	5	5
7F	Mean	410	15.42	0.014
	SD	20	0.86	0.004
	N	5	5	5
8F	Mean	415	14.91	0.013
	SD	18	0.80	0.002
	N	5	5	5
9F	Mean	397	14.22	0.012
	SD	8	0.93	0.001
	N	5	5	5
Adjusted Means				
Statistical test:			Wi	Wi
6F	Mean		14.03	0.014
7F	Mean		15.03	0.014
8F	Mean		14.35	0.013
9F	Mean		14.26	0.012

Organ weights - group mean unadjusted and adjusted values (g) on Day 20 of gestation

Group	:	6	7	8	9	10
Compound	:	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day)	:	0	0.1	1.0	10.0	100.0

Group /Sex		Terminal Bodyweight	Liver	Thyroids + Paras
Unadjusted Means				
Statistical test:		Wi		
10F	Mean	375	13.63	0.014
	SD	10	0.52	0.002
	N	5	5	5
Adjusted Means				
Statistical test:			Wi	Wi
10F	Mean		14.42	0.015

There were no macroscopic findings in any animal on Day 20 of gestation

Organ weights - group mean unadjusted and adjusted values (g) on Day 21 of gestation

Group	:	6	7	8	9	10
Compound	:	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day)	:	0	0.1	1.0	10.0	100.0

Group /Sex		Terminal Bodyweight	Liver
Unadjusted Means			
Statistical test:		Tt	
6F	Mean	402	13.06
	SD	21	1.34
	N	5	5
10F	Mean	418	13.58
	SD	21	1.83
	N	5	5
Adjusted Means			
Statistical test:			Tt
6F	Mean		13.58
10F	Mean		13.06

There were no macroscopic findings in any animal on Day 21 of gestation

TABLE 7

Request ID: 397864

Litter data - group mean values on Day 20 of gestation

Group	:	6	7	8	9	10
Compound	:	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day)	:	0	0.1	1.0	10.0	100.0

Group /Sex		Corpora Lutea	Implantations	Resorptions Early	Resorptions Late	Resorptions Total	Live Young Male	Live Young Female	Live Young Total	Sex ratio (%M)	Implantation Loss (%) Pre-	Implantation Loss (%) Post-
6F	Mean	16.6	16.2	0.8	0.2	1.0	9.4	5.8	15.2	62.5	2.4	6.0
	SD	0.89	0.84				2.61	3.19	0.84			
	N	5	5	5	5	5	5	5	5	5	5	5
7F	Mean	17.0	16.2	1.4	0.0	1.4	8.2	6.6	14.8	56.4	5.8	8.8
	SD	1.22	1.79				2.17	3.13	2.17			
	N	5	5	5	5	5	5	5	5	5	5	5
8F	Mean	17.0	15.8	0.6	0.0	0.6	6.8	8.4	15.2	44.1	7.6	3.9
	SD	2.92	1.92				3.27	2.41	2.28			
	N	5	5	5	5	5	5	5	5	5	5	5
9F	Mean	16.4	15.6	0.2	0.0	0.2	8.0	7.4	15.4	52.0	4.6	1.3
	SD	1.14	0.55				2.00	2.07	0.55			
	N	5	5	5	5	5	5	5	5	5	5	5
10F	Mean	14.8	14.4	1.2	0.0	1.2	6.8	6.4	13.2	51.9	2.6	8.6
	SD	1.48	1.34				1.79	2.07	1.92			
	N	5	5	5	5	5	5	5	5	5	5	5

Litter data - group mean values on Day 21 of gestation

Group	:	6	7	8	9	10
Compound	:	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day)	:	0	0.1	1.0	10.0	100.0

Group /Sex		Corpora Lutea	Implantations	Resorptions Early	Resorptions Late	Resorptions Total	Live Young Male	Live Young Female	Live Young Total	Sex ratio (%M)	Implantation Loss (%) Pre-	Implantation Loss (%) Post-
6F	Mean	15.2	13.8	1.2	0.0	1.2	6.8	5.8	12.6	54.0	9.0	8.5
	SD	0.84	0.84				2.17	2.17	0.55			
	N	5	5	5	5	5	5	5	5	5	5	5
10F	Mean	16.8	14.2	0.8	0.0	0.8	7.4	6.0	13.4	55.7	13.2	5.7
	SD	3.11	1.10				1.67	2.24	1.34			
	N	5	5	5	5	5	5	5	5	5	5	5

TABLE 8

Request ID: 397863

Placental, litter and fetal weights - group mean values (g) on Day 20 of gestation

Group	:	6	7	8	9	10
Compound	:	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day)	:	0	0.1	1.0	10.0	100.0

Group /Sex		Placental Weight	Litter Weight	Litter Size	Male Fetal Weight	Female Fetal Weight	Overall Fetal Weight
6F	Mean	0.49	52.79	15.20	3.52	3.40	3.47
	SD	0.082	5.710	0.837	0.243	0.177	0.203
	N	5	5	5	5	5	5
7F	Mean	0.49	51.66	14.80	3.56	3.41	3.51
	SD	0.013	5.961	2.168	0.205	0.157	0.188
	N	5	5	5	5	5	5
8F	Mean	0.48	56.12	15.20	3.79	3.61	3.69
	SD	0.046	9.323	2.280	0.228	0.140	0.183
	N	5	5	5	5	5	5
9F	Mean	0.48	52.73	15.40	3.54	3.30	3.42
	SD	0.019	2.408	0.548	0.123	0.126	0.138
	N	5	5	5	5	5	5
10F	Mean	0.46	46.37	13.20	3.60	3.48	3.54
	SD	0.066	3.969	1.924	0.303	0.220	0.255
	N	5	5	5	5	5	5

Placental, litter and fetal weights - group mean values (g) on Day 21 of gestation

Group	:	6	7	8	9	10
Compound	:	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day)	:	0	0.1	1.0	10.0	100.0

Group /Sex		Placental Weight	Litter Weight	Litter Size	Male Fetal Weight	Female Fetal Weight	Overall Fetal Weight
6F	Mean	0.53	65.13	12.60	5.31	4.98	5.17
	SD	0.045	4.788	0.548	0.243	0.235	0.233
	N	5	5	5	5	5	5
10F	Mean	0.48	66.15	13.40	5.02	4.81	4.94
	SD	0.052	6.959	1.342	0.133	0.187	0.137
	N	5	5	5	5	5	5

Clinical signs - individual observations

Group	:	6	7	8	9	10
Compound	:	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day)	:	0	0.1	1.0	10.0	100.0

Group /Sex	Animal Number	Death Code	Day of Death	Category	Observation	Day(s)
6F	102	T	20	Staining	Abnormal Colour, Muzzle	0, 5, 12
	103	T	20	Coat	Hair loss, Forelimbs	20
				Skin	Encrustation, Fourth Digit (Left Forelimb)	5
					Encrustation, First Digit (Right Forelimb)	5, 12
	104	T	20	Staining	Abnormal Colour, Brown, Dorsal Body Surface	5
	108	T	20	Coat	Hair loss, Forelimbs	12, 18, 20
					Hair loss, Hindlimbs	12, 18, 20
	109	T	20	Coat	Hair loss, Forelimbs	18, 20-21
7F	112	T	20	Staining	Abnormal Colour, Brown, Pinna	5, 12, 18, 20
					Abnormal Colour, Brown, Muzzle	5
	113	T	20	Coat	Hair loss, Forelimbs	0, 5, 12, 18, 20
				Staining	Abnormal Colour, Brown, Dorsal Body Surface	5, 12, 18

Only animals with observations are presented

Clinical signs - individual observations

Group	:	6	7	8	9	10
Compound	:	Control	DCPA	DCPA	DCPA	DCPA
Dose (mg/kg/day)	:	0	0.1	1.0	10.0	100.0

Group /Sex	Animal Number	Death Code	Day of Death	Category	Observation	Day(s)
8F	117	T	20	Staining	Abnormal Colour, Brown, Dorsal Body Surface	5
	118	T	20	Coat	Hair loss, Forelimbs	18, 20
	119	T	20	Staining	Abnormal Colour, Brown, Dorsal Body Surface	5
9F	123	T	20	Coat	Hair loss, Forelimbs	12, 18, 20
	124	T	20	Staining	Abnormal Colour, Brown, Dorsal Body Surface	5, 12
10F	129	T	20	Staining	Abnormal Colour, Brown, Head	5
	131	T	20	Coat	Hair loss, Forelimbs	18, 20

Only animals with observations are presented