MR# 313651

AR226-3822

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CXR Biosciences Ltd.
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REPORT

13-WEEK STUDY TO INVESTIGATE THE REVERSIBILITY OF PERFLUOROOCTANE SULFONATE (PFOS)-INDUCED EFFECTS IN MALE SPRAGUE DAWLEY RATS.

CXR STUDY NUMBER:	CXR0486s
Sponsor:	3M
Sponsors Representative:	Dr John Butenhoff 3M Medical Department 3M Center Building 220-06-W-08, St. Paul, Minnesota 55144-1000
Sponsor's study identifier:	06-301
Sponsor's material identifier:	MTDID-208
Study Director:	B M Elcombe, CXR Biosciences
Test facility	CXR Biosciences, James Lindsay Place, Dundee Technopole, Dundee, DD1 5JJ. and Biological Sciences Resource Unit (BSRU), Dundee University, Dundee, DD1 5EH.
"In Life" Start Date:	29th November 2006
"In Life" Finish Date:	28th February 2007
CIRCULATION	Signed Original: Study File/Archives Sponsor Copies to: Study Director Sponsor

Author _____ 22 July 2008
Barbara Elcombe, Study Director — Date

Approved _____ 22 July 2008
Director, CXR Biosciences — Date

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SUMMARY

- The mean ingested doses of Test Items calculated for the 7 days of administration were: 1.93 ± 0.01 (PFOS 20ppm) and 9.65 ± 0.08 (PFOS 100ppm) mg Test Item / kg bwt / day.

- No adverse clinical observations were made throughout the study.

- Administration of dietary PFOS (20ppm or 100ppm) to rats for 7 days did not affect body weights.

- Absolute liver weights were increased following exposure to PFOS 100ppm for 7 days, reaching 115% of control values. After 28 days on control diet, following exposure to PFOS 20ppm for 7 days, absolute liver weights were decreased to 87% of control values. Relative liver weights were increased following exposure to both PFOS 20ppm and PFOS 100ppm for 7 days to approximately 112% and 120% of control values, respectively. After 28 and 56 days receiving control diet relative livers weights had returned to control values. However, after 84 days on control diet, following exposure to both dietary concentrations of PFOS, relative liver weights were again increased, to approximately 113% of control values. The biological significance, if any, of this is unclear.

- A lack of overt hepatotoxicity was indicated for all compounds by the absence of toxicologically significant increases in plasma ALT and AST.

- Mean plasma cholesterol concentrations were decreased, in a dose dependant manner, by PFOS 20ppm and PFOS 100ppm after 7 days of treatment. Following a return to control diet for 28 days, plasma cholesterol concentrations were still decreased in a dose dependant manner. After 56 days reversal, cholesterol concentrations had recovered to near control levels in animals administered both concentrations of PFOS; however plasma cholesterol concentrations were still decreased after 84 days reversal in animals treated with PFOS 100ppm.

- Administration of PFOS 100ppm to rats for 7 days led to a small increase (127% of control) in hepatic peroxisomal β-oxidation, as determined by measurement of CN-insensitive palmitoyl CoA oxidation (PCO). This increase was maintained after 28 and 56 days return to control diet. Eighty-four days after withdrawal of PFOS 100ppm, PCO activity was returning to control levels. Administration of PFOS 20ppm did not increase PCO activity.

- Administration of PFOS 20ppm and PFOS 100ppm to rats for 7 days resulted in

marked increases in hepatic total P450, in a dose dependent manner, to 124% and 190% of control values, respectively. Reversal to control diet for up to 84 days had no effect on the increased hepatic total P450 content.

- Lauric acid 12-hydroxylation (12-OH LAH) is used as a marker for cytochrome P450 4A activity. PFOS administration at 20ppm had no effect on 12-OH LAH after 7 days on diet, whilst administration at 100ppm increased the 12-OH LAH by approximately 2-fold after 7 days on diet, and 3-fold after 28 and 56 days on control diet (Table 15). After 84 days on control diet, however, 12-OH LAH activity had returned to control values.

- Pentoxyresorufin-*O*-dependentylation (PROD) is used as a marker for cytochrome P450 2B activity. PFOS administration at 20ppm initially decreased the PROD activity by approximately half the control value after 7 days on diet. Reversal to control diet for up to 84 days had no effect, and the decrease in activity was maintained throughout. PFOS administration at 100ppm increased the PROD activity by approximately 3.5-fold after 7 days on diet. Reversal to control diet resulted in increased activity of approximately 1.5-fold relative to control values after 28 days; a return to control values after 56 days; and a decrease of approximately half the control value after 84 days. The decreases in PROD are believed to be incidental and not of biological significance.

- Testosterone 6β-hydroxylation (Test-6β-OH) is used as a marker for cytochrome P450 3A activity. PFOS administration at 20ppm had no effect on the Test-6β-OH activity until, after 84 days on control diet, a slight increase was seen. This is not considered to be biologically significant. PFOS administration at 100ppm initially increased the Test-6β-OH activity by 2.3-fold after 7 days on diet. Reversal to control diet resulted in a return to control values after 28 days followed by an increase in activity of approximately 2.2- and 1.9-fold after 56 days and 84 days, respectively.

- In the liver, histopathology revealed slightly decreased glycogen vacuolation in animals treated with 20ppm and 100ppm PFOS at each sacrifice period.
  A minimal to moderate, centrilobular hepatocellular hypertrophy was noted, dose related in severity, in animals treated with 20ppm PFOS and 100ppm PFOS for 7 days. This finding was still present after a 4-, 8- or 12-week treatment-free recovery period. An unequivocal difference in the severity and incidence of this finding between the various recovery periods was not observed, indicating an incomplete reversibility during the various recovery periods used.

- Administration of PFOS 20ppm and PFOS 100ppm for 7 days decreased the hepatic apoptotic index to approximately 70% and 40% of control values, respectively. Reverting to control diet did not reverse this decrease in hepatic apoptotic index, and

the decrease continued, reaching a minimum of 30% of control values after 84 days for PFOS 20ppm treated animals, and 20% of control values after 56 days for PFOS 100ppm treated animals.

- PFOS 20ppm and PFOS 100ppm administration for 7 days both increased the hepatocellular labelling index (S-phase) by 2.5- and 5.9-fold, respectively. Reversal to control diet resulted in a return to control values after 28 days.

- In the thyroid gland, no microscopic findings considered to be related to the treatment with the test items were recorded. The number of apoptotic cells found in all treatment groups, at all time points, was minimal. Regardless of treatment, it was usual to find either no cells or just one cell per thyroid staining in the TUNEL assay as apoptotic.

- 20ppm PFOS and 100ppm PFOS treatment had no effect on thyroid S-phase activity at any time point studied.

1. INTRODUCTION

A variety of non-genotoxic chemicals elicit hepatocellular adenomas and carcinomas when administered to rats in long-term studies. The appearance of tumours is preceded by the rapid and early stimulation of hepatomegaly.

The liver enlargement seen following the administration of such "liver growth carcinogens" to rats is a result of both hypertrophy and hyperplasia. Depending on the particular chemical, the hypertrophy in characterised by proliferation of peroxisomes and/or smooth endoplasmic reticulum, induction of peroxisomal enzymes and induction of cytochrome P450 isoforms. The hyperplasia is characterised by stimulation of hepatocellular proliferation (S-phase, labelling index) and inhibition of apoptosis.

PFOS has previously been shown to elicit marked liver growth in rats, and this study aims to characterise the reversibility of this hepatomegaly in these terms. The reversibility of thyroid effects, following the administration of PFOS to rats, will also be investigated.

This study used liver, serum, thyroid and duodenal (for assessing BrdU labelling) samples generated over a time course including exposure for 7 days followed by withdrawal of treatment for 4, 8 and 12 weeks.

The following parameters were studied:

- Bodyweights
- Liver weights (relative and absolute)
- Clinical chemistry (5 parameters).
- Haematoxylin and eosin (H&E) histopathology (liver and thyroid)
- Apoptotic indices analysed using the TUNEL assay (liver and thyroid)
- BrdU incorporation analysed as a measure of cell proliferation (liver and thyroid)
- The DNA content of liver was measured using the diphenylamine reaction
- Acyl CoA oxidase activity was determined in liver heavy pellets as CN^--insensitive palmitoyl CoA oxidation
- Total P450 content was determined in liver microsomes
- Lauric acid hydroxylation (LAH, CYP4A) was determined in liver microsomes
- Pentoxyresorufin-*O*-dependentylation (PROD, CYP2B) was determined in liver microsomes
- Testosterone hydroxylation (CYP 3A) was determined in liver microsomes

2. ANIMALS (Scientific Procedures) ACT 1986 COMPLIANCE

The in-life procedures undertaken during the course of this Study were subject to the provisions of the United Kingdom Animals (Scientific Procedures) Act 1986. The Act, administered by the UK Home Office, regulates all scientific procedures in living animals which may cause pain, suffering, distress or lasting harm and provides for the designation of

establishments where procedures may be undertaken, the licensing of trained individuals who perform the practical techniques, and the issue of project licences for specified programmes of work.

This Study complied with all applicable sections of the Act and the associated Codes of Practice for the Housing and Care of Animals used in Scientific Procedures and the Humane Killing of Animals under Schedule 1 to the Act, issued under section 21 of the Act.

2.1 Licensee Responsibilities

The procedure performed was PD1 as detailed in the PD project licence (60/3005).
The severity limit for this procedure is MODERATE. Mr F Simeons returned the animals at the start of the study under the PD project licence.

3. MATERIALS AND METHODS

3.1 Test Substances

Perfluorooctane sulfonate potassium salt (PFOS K^+, Lot no. 217, purity 87.6%), supplied by 3M Company, St. Paul Minnesota, USA, was a white powder.
It was handled, and its identity verified, according to CXR Biosciences SOP 0010. This SOP describes routine procedures for the receipt, identification, labelling, handling, sampling and storage of Test and Reference Items. These procedures are implemented to ensure that:

- Test and Reference Items used are those Items specified in Study Protocols.
- Handling and storage of Test and Reference Items preserves their identity and integrity during use.

3.2 Safety Precautions

The normal safety precautions as detailed in the relevant Sop's and COSHH assessments were applied, no additional precautions were considered necessary.

3.3 Diet

RM1 powdered diet (Special Diet Services Ltd., Stepfield, Witham, Essex, UK) was used; Biological Sciences Resource Unit (BSRU) hold the specification of the diet.
The Sponsor requested the dietary route of administration.
The test diets, containing 20ppm PFOS or 100ppm PFOS, were prepared by CXR Biosciences (Laboratory Method Sheet [LMS] TSC-002) and samples were retained for analysis by the Sponsor.
Rats were fed RM1 powdered diet or test diets *ad libitum* throughout the study.

3.4 Animals

A sufficient number of male 6-7 week old Charles River Sprague Dawley (CD) rats were obtained from Charles River, UK. On arrival in the BSRU the rats were housed 2 per cage on sawdust in solid -bottom, polypropylene cages. The rats were acclimatised for a period of at

least 5 days before use. No animals were excluded from the study. Environmental enhancing additions were not used in the cages prior to the start of the Study.

The Sprague Dawley (CD) rat was the test system of choice for this study because previous work on PFOS has been undertaken using this strain. In addition, CXR Biosciences has extensive experience in the use of this strain of rat, and the strain is well accepted by the regulatory authorities.

3.5 Animal Accommodation and Husbandry

The environment was controlled in the animal room to provide conditions suitable for the Sprague Dawley (CD) strain of rat. The temperature was maintained within a range of 19-23°C and relative humidity within a range of 40-70%. There were a nominal 14-15 air changes per hour. Twelve-hour periods of light were cycled with twelve-hour periods of darkness.

Drinking water was taken from the local supply and provided in bottles. Drinking water was provided *ad libitum* prior to and throughout the study.

Prior to the start of the study the rats were allowed powdered RM1 diet *ad libitum*.

4. EXPERIMENTAL DESIGN

The animals were uniquely numbered by ear-punch and randomly allocated to groups up to one week after arrival. An experimental card was placed on each cage and showed the project licence code, treatment group, study number, sex and individual numbers of the rats within, and identified the Home Office Licensee. In addition, these cards were colour coded to correlate with the coding for the treatment group on the diet boxes and jars.

The study consisted of one control and two test groups, each containing 40 male animals. Control animals received powdered RM1 diet *ad libitum* for the duration of the study. The test groups of animals were administered either 20ppm or 100ppm PFOS in the diet *ad libitum* for 7 days. On Day 8 the test diets were withdrawn and all animals were administered powdered RM1 diet *ad libitum* for the remainder of the study. The dietary concentrations of PFOS were prepared with purity correction. The corresponding PFOS concentrations in the powdered RM1 diet will be analyzed by the Sponsor. Ten animals from each group were sacrificed on days 8, 36, 64 and 92.

Animals were implanted with osmotic pumps (Alzet 2ML1) containing bromodeoxyuridine (BrdU, 15mg/mL in phosphate buffered saline [PBS], pH7.4) 5 days before termination, whilst still receiving the treatment regimen (Table 1).

TABLE 1
EXPERIMENTAL DESIGN

Group	Colour code	Animal No	Treatment	Dates			
				Arrival	Start	Implant	Kill
1	Blue	1 – 10	Control	21/11/06	29/11/06	01/12/06	06/12/06
		11 – 20				29/12/06	03/01/07
		21 – 30				26/01/07	31/01/07
		31 – 40				23/02/07	28/02/07
2	Green	41 – 50	PFOS 20ppm	21/11/06	29/11/06	01/12/06	06/12/06
		51 – 60				29/12/06	03/01/07
		61 – 70				26/01/07	31/01/07
		71 – 80				23/02/07	28/02/07
3	Yellow	81 – 90	PFOS 100ppm	21/11/06	29/11/06	01/12/06	06/12/06
		91 – 100				29/12/06	03/01/07
		101 – 110				26/01/07	31/01/07
		111 – 120				23/02/07	28/02/07

5. EXPERIMENTAL PROCEDURES

5.1 Bodyweight

The bodyweight of each rat was recorded at the start of the study. The animals were weighed weekly on the same day of the week. All animals were weighed prior to termination. Bodyweights were recorded electronically and records of the weights were stored in the Study File.

5.2 Clinical Observations

Prior to the start of the study, all rats were observed to ensure that they were physically normal and that they exhibited normal activity. Each rat was observed at least once daily during the study. Clinical abnormalities of individual animals were recorded in the Study Diary. This was kept in the BSRU until completion of the in life phase of the study and then transferred to the Study File for retention and archiving.

5.3 Food Consumption

Food consumption was measured every time the diet jars were changed / refilled, and when the animals were sacrificed, for the first week of the study so that food consumption could be recorded. Following reversion to control diet on Day 8, food consumption was not recorded.

5.4 Intercurrent Deaths

There were no rats requiring euthanasia during the study, nor were there any intercurrent deaths.

5.5 Terminal Procedures

On the day of termination the rats were weighed and transferred to the post mortem room. The rats were killed by exposure to a rising concentration of CO_2.

- Approximately 6 to 10 mL of venous blood was taken by cardiac puncture and dispensed at equal volume into uncoated tubes (to obtain serum) and lithium/heparin-coated tubes (to obtain plasma). The tubes were mixed on a roller for 10 min then cooled on ice. Serum and plasma were prepared by centrifugation (2,000 rpm for 10 min at 8 - 10°C) then stored at approximately -70°C pending analysis. The pellet was discarded.

- The liver was removed from each animal and weighed.
- 2 samples of liver, approximately 2mm strips, were taken, one from the Left lobe and one from the Median lobe. These were placed in 10% neutral buffered formaldehyde (NBF), for approximately 48hours, for BrdU immunohistochemistry and analysis of the apoptotic index.
- 2 samples of liver, approximately 2mm strips, were taken, one from the Left lobe and one from the Median lobe. These were placed in NBF, for at least 1 week, for H&E histopathology.
- 1 sample of liver, of approximately 0.25g, was weighed and then flash frozen in liquid nitrogen then stored at approximately -70°C for DNA determination.
- 2 samples of liver, of approximately 1g each, were flash frozen in liquid nitrogen then stored at approximately -70°C prior to dispatch, on dry ice, to the Sponsor for further analytical determination under a separate protocol
- The remainder of the liver was weighed and scissor-minced in ice-cold 1.15% (w/v) KCl prior to subcellular fractionation according to Laboratory Method Sheet (LMS) Cent-001. Samples of homogenate, heavy pellet and microsomes were stored at approximately -70°C prior to analysis. Samples of cytosol were stored at approximately -70°C prior to dispatch, on dry ice, to the Sponsor for further analytical determination under a separate protocol.

- 1 sample of duodenal small intestine, of approximately 1cm, was taken and placed in NBF, for approximately 48 hours, as a positive control for BrdU immunohistochemistry.

- The thyroid was removed from each animal, including the parathyroid gland together with trachea and oesophagus. This tissue was placed in NBF, for approximately 48 hours, for BrdU immunohistochemistry, analysis of the apoptotic index and H&E histology.

6. BIOCHEMICAL MEASUREMENTS

6.1 Clinical Chemistry

Plasma samples, prepared as described above, were assayed for ALT, AST, cholesterol,

glucose and triglycerides using a Roche Integra 400 automated analyser according to the manufacturer's instructions. System control samples and calibration standards were those supplied by the manufacturer. Results were maintained in the Study File.

6.2 Peroxisome Proliferation

CN^- -insensitive acyl CoA oxidation was determined spectrophotometrically in liver heavy pellet, using palmitoyl CoA as a substrate, according to LMS Spec003. Results were expressed as nmol NAD^+ reduced/min/mg protein. Results were maintained in the Study File.

6.3 DNA Content of Liver

The DNA content of liver was measured spectrophotometrically in whole tissue using the diphenylamine reaction, according to LMS Spec005. Results were expressed as µg DNA/g liver and mg DNA/whole liver. Results were maintained in the Study File.

6.4 Total Cytochrome P450

The total cytochrome P450 content of liver microsomes was determined by measuring the carbon monoxide difference spectrum of ferrocytochrome P450 according to LMS Spec002. Results were expressed as nmol total P450/mg protein. Results were maintained in the Study File.

6.5 Lauric Acid 12-Hydroxylation (LAH)

The activity of CYP4A in liver microsomes was determined using lauric acid and LC-MS-MS. Results were expressed as nmols 12-OH lauric acid formed/10minutes/mg protein. Results were maintained in the Study File.

6.6 Pentoxyresorufin-*O*-dependentylation (PROD)

The activity of CYP2B in liver microsomes was determined spectrofluorometrically by the formation of resorufin from pentoxyresorufin, according to LMS Fluor-002. Results were expressed as pmols resorufin formed/minute/mg protein. Results were maintained in the Study File.

6.7 Testosterone 6β-Hydroxylation

The activity of CYP3A in liver microsomes was determined by HPLC followed by UV detection, according to LMS HPLC-006. Results were expressed as nmols hydroxytestosterone formed/minute/mg protein. Results were maintained in the Study File.

6.8 Protein Determination

The protein concentration of tissue heavy pellets and microsomes was determined in aqueous solutions using a modification of the method of Lowry *et al.*, (1951) and bovine serum albumin standards, according to LMS Spec001. Results were maintained in the Study File.

6.9 Statistical Analysis

Statistical comparisons between treated and control groups have been undertaken for all numerical data sets. The statistical analyses performed are documented with the results.

6.10 Additional Analyses

The Sponsor has requested no additional analyses.

7. HISTOPATHOLOGY

Following fixation, all fixed liver and thyroid samples were processed, embedded and 5 µM sections cut according to LMS Pat-005, Pat-006 and Pat-007.

Sections were:

- Stained using H&E, according to LMS Pat-010, Pat-011 and Pat-012.
- Analysed for *in situ* cell death. The method used was an indirect TUNEL labelling assay, according to LMS Pat-014.
- Analysed for BrdU incorporation as a measure of cell proliferation. The method used was an indirect BrdU labelling assay, according to LMS Pat-008.

H&E sections were evaluated by Dr. med. vet. Ortwin Vogel, Goethestraße 26, 24116 Kiel, Schleswig-Holstein, Deutschland. The histopathology report was maintained in the Study File and as an appendix to the Study Report.

8. SPECIMEN SHIPMENT

The powdered RM1 diets, cytosol, serum, and the liver samples designated for further analytical determination by the Sponsor were shipped on dry ice and sent to:
Dave Ehresman
3M Company
3M Center
Building 236-C148
St. Paul, MN 55144

9. PROTOCOL AMENDMENTS

There were no changes to the protocol, and no Protocol Amendments have been signed by the Study Director.

10. RESULTS

10.1 Bodyweights, Food Consumption and Liver Weights.

10.1.1 Bodyweights.

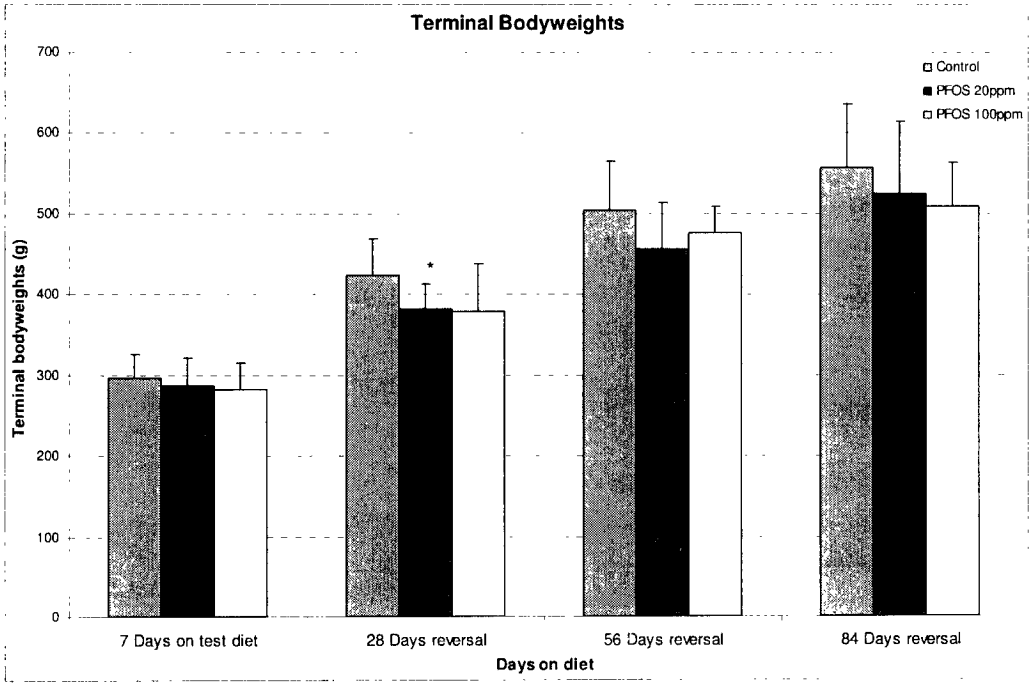
Administration of dietary PFOS (20ppm) to rats for 7 days followed by 28 days on control

diet lead to decreased body weights (Table 2). This effect was not deemed toxicologically significant. No adverse clinical observations accompanied the decreased body weights.

Table 2. Terminal Bodyweights

Days on diet/reversal	Bodyweight (g)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	296.4 ± 30.1[a] (100 ± 10.2)	286.5 ± 34.1 (96.7 ± 11.5)	282.0 ± 32.5 (95.1 ± 11.0)
7/28	423.3 ± 46.0 (100 ± 10.9)	382.2 ± 30.8* (90.3 ± 7.3)	378.2 ± 59.9 (89.4 ± 14.1)
7/56	504.3 ± 61.4 (100 ± 12.2)	456.1 ± 57.8 (90.5 ± 11.5)	476.6 ± 32.8 (94.5 ± 6.5)
7/84	557.8 ± 78.7 (100 ± 14.1)	524.3 ± 89.5 (94.0 ± 16.1)	509.8 ± 54.1 (91.4 ± 9.7)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.



10.1.2 Food consumption.

The food consumption of the PFOS 20ppm and PFOS 100ppm-treated rats were essentially the same as control values throughout the experimental period (Table 3.).
When diet consumption was calculated per unit body weight, the PFOS 20ppm and PFOS 100ppm-treated rats were essentially the same as control values throughout the experimental period.

Table 3. Food Consumption

Days on diet	0ppm	PFOS 20ppm	PFOS 100ppm
	Diet consumed (g) / Rat / Week		
7	194.1 ± 12.7 (100 ± 6.5)	191.7 ± 15.1 (98.7 ± 7.8)	188.8 ± 23.1 (97.3 ± 11.9)
	Diet consumed (g) / Kg Bwt / Day		
7	94.2 ± 3.6 (100 ± 3.78)	96.7 ± 4.4 (102.6 ± 4.7)	96.5 ± 8.0 (102.5 ± 8.5)
	Test Item Consumption: mg Test Item / Kg Bwt / Day		
7	0 ± 0	1.93 ± 0.01	9.65 ± 0.08

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; ** $p<0.01$; *** $p<0.001$.

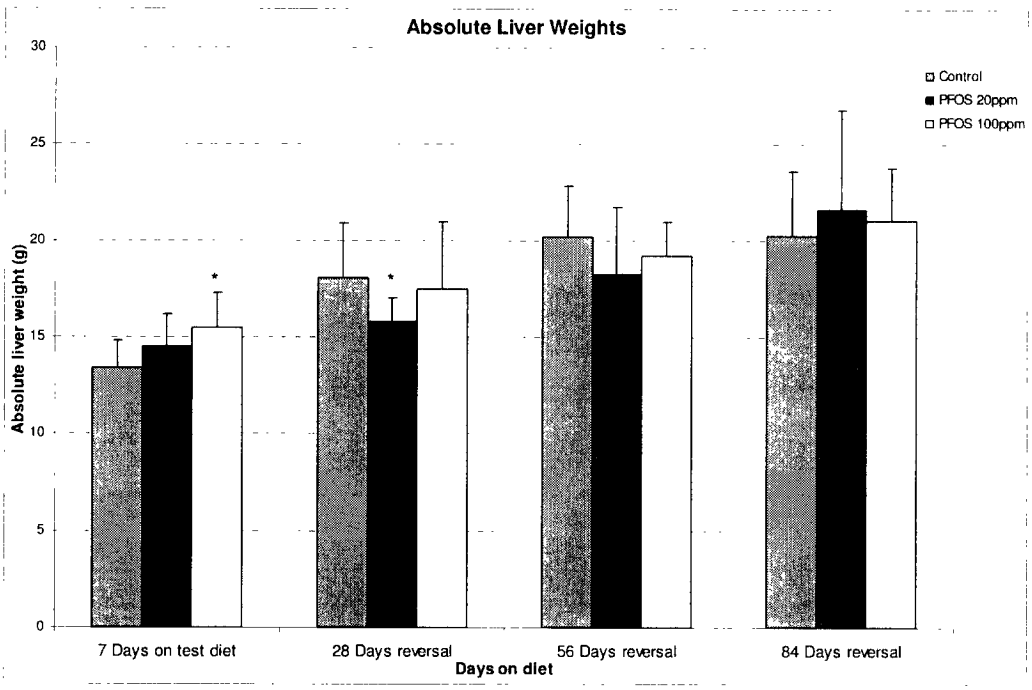
10.1.3 Liver weights.

Absolute liver weights were increased following exposure to PFOS 100ppm for 7 days, reaching 115% of control values (Table 4). After 28 days on control diet, following exposure to PFOS 20ppm for 7 days, absolute liver weights were decreased to 87% of control values.

Table 4. Absolute Liver Weights

Days on diet/reversal	Liver weight (g)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	13.40 ± 1.38[a] (100 ± 10.31)	14.45 ± 1.71 (107.86 ± 12.78)	15.42 ± 1.85* (115.08 ± 13.80)
7/28	18.04 ± 2.88 (100 ± 15.95)	15.76 ± 1.24* (87.36 ± 6.86)	17.46 ± 3.46 (96.80 ± 19.18)
7/56	20.19 ± 2.61 (100 ± 12.92)	18.23 ± 3.48 (90.30 ± 17.23)	19.19 ± 1.76 (95.07 ± 8.73)
7/84	20.23 ± 3.40 (100 ± 16.79)	21.56 ± 5.20 (106.58 ± 25.72)	21.03 ± 2.74 (103.95 ± 13.55)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.

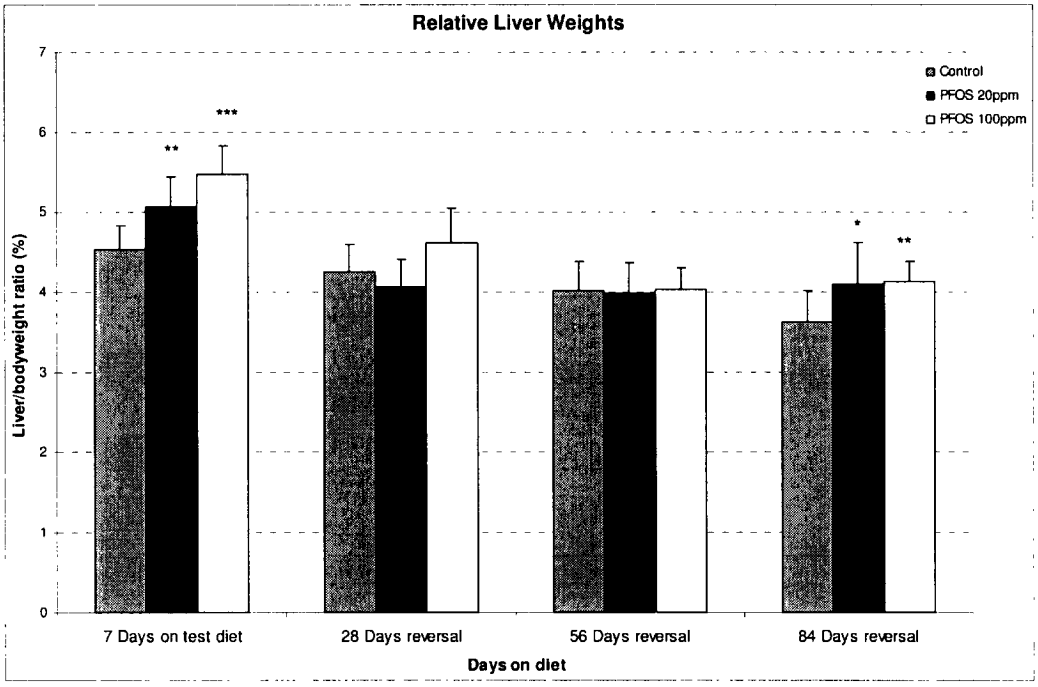


After normalisation with respect to bodyweight, relative liver weights were increased following exposure to both PFOS 20ppm and PFOS 100ppm for 7 days to approximately 112% and 120% of control values, respectively (Table 5). After 84 days on control diet, following exposure to both dietary concentrations of PFOS, relative liver weights were again increased, to approximately 113% of control values.

Table 5. Liver/bodyweight ratio (%)

Days on diet/reversal	Liver/bodyweight ratio (%)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	4.53 ± 0.29[a] (100 ± 6.46)	5.06 ± 0.38** (111.73 ± 8.40)	5.48 ± 0.36*** (120.91 ± 7.86)
7/28	4.25 ± 0.34 (100 ± 8.12)	4.07 ± 0.34 (95.71 ± 8.02)	4.61 ± 0.44 (108.50 ± 10.27)
7/56	4.02 ± 0.36 (100 ± 9.05)	3.98 ± 0.38 (99.03 ± 9.58)	4.03 ± 0.27 (100.27 ± 6.68)
7/84	3.63 ± 0.39 (100 ± 10.62)	4.09 ± 0.51* (112.78 ± 14.03)	4.12 ± 0.25** (113.58 ± 7.01)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.


Relative Liver Weights
Liver/bodyweight ratio (%)
0
1
2
3
4
5
6
7
**
***
*
**
Control
PFOS 20ppm
PFOS 100ppm
7 Days on test diet
28 Days reversal
56 Days reversal
84 Days reversal
Days on diet

10.2 Clinical Chemistry

The lack of overt hepatotoxicity was indicated by the absence of toxicologically significant increases in plasma ALT and AST (Tables 6 and 7).

Table 6. Plasma Alanine Aminotransferase Activity

Days on diet/reversal	ALT (U/L)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	110.60 ± 18.64[a] (100 ± 16.86)	93.97 ± 10.47* (84.96 ± 9.47)	90.04 ± 16.66* (81.41 ± 15.06)
7/28	110.32 ± 17.16 (100 ± 15.56)	117.56 ± 54.52 (106.56 ± 49.42)	102.78 ± 22.45 (93.17 ± 20.35)
7/56	90.54 ± 15.55 (100 ± 17.18)	89.07 ± 22.47 (98.38 ± 24.82)	103.85 ± 29.44 (114.70 ± 32.52)
7/84	84.15 ± 16.68 (100 ± 19.83)	84.82 ± 18.03 (100.80 ± 21.42)	99.36 ± 36.44 (118.07 ± 43.31)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.

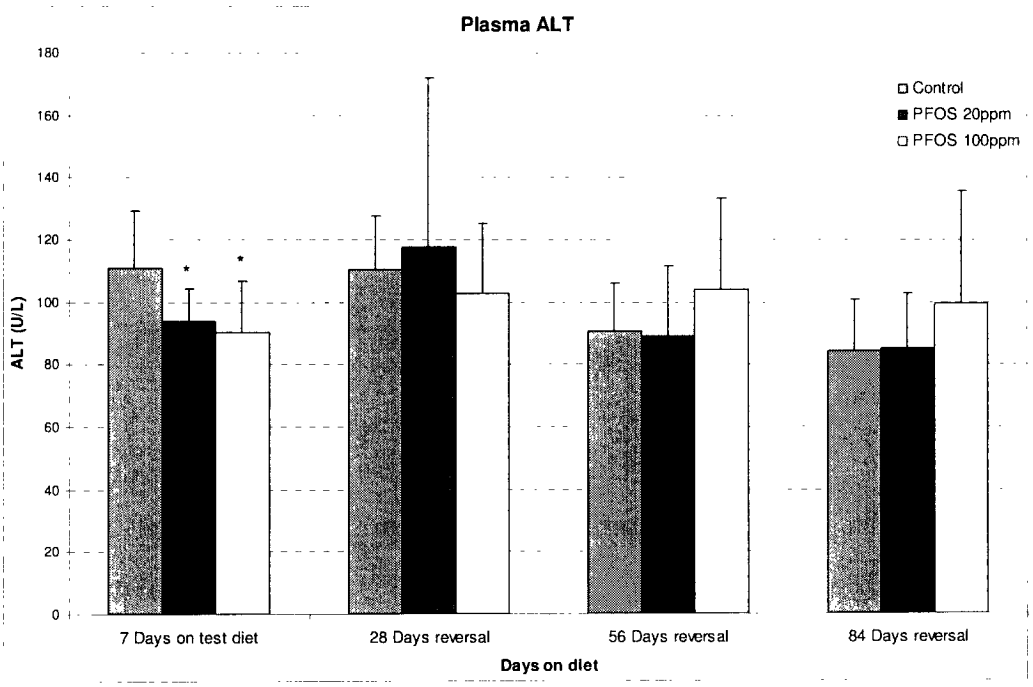
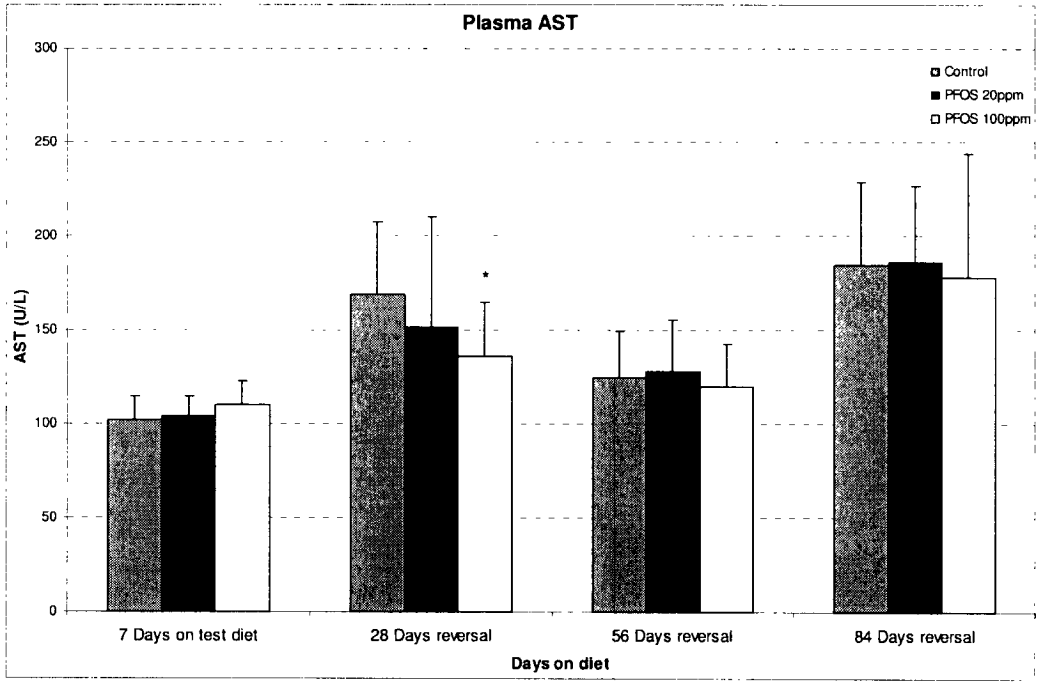


Table 7. Plasma Aspartate Transaminase Activity

Days on diet/reversal	AST (U/L)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	102.25 ± 12.09[a] (100 ± 11.83)	103.94 ± 10.47 (101.65 ± 10.24)	109.97 ± 12.75 (107.55 ± 12.47)
7/28	168.98 ± 38.11 (100 ± 22.55)	151.51 ± 58.79 (89.66 ± 34.79)	136.02 ± 28.85* (80.49 ± 17.07)
7/56	124.75 ± 24.75 (100 ± 19.84)	128.30 ± 26.87 (102.85 ± 21.54)	120.31 ± 22.49 (96.44 ± 18.03)
7/84	184.34 ± 44.30 (100 ± 24.03)	186.13 ± 40.44 (100.97 ± 21.94)	177.97 ± 66.32 (96.54 ± 35.98)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.

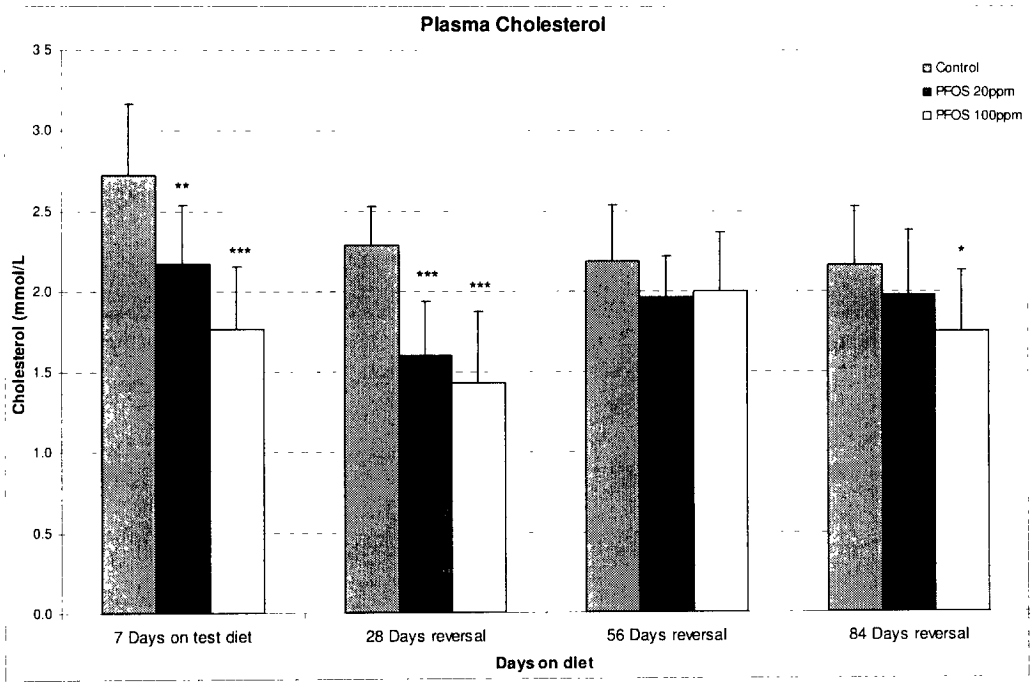


Mean plasma cholesterol concentrations were decreased, in a dose dependant manner, by PFOS 20ppm and PFOS 100ppm after 7 days of treatment (Table 8). Following a return to control diet for 28 days, plasma cholesterol concentrations were still decreased in a dose dependant manner. After 56 days reversal, cholesterol concentrations were recovered to near control levels in animals administered both concentrations of PFOS; however this recovery was not present after 84 days reversal in animals treated with PFOS 100ppm.

Table 8. Plasma Total Cholesterol Concentration

Days on diet/reversal	Total Cholesterol (mmol/L)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	2.73 ± 0.44[a] (100 ± 16.16)	2.17 ± 0.37** (79.63 ± 13.49)	1.77 ± 0.39*** (64.84 ± 14.15)
7/28	2.29 ± 0.24 (100 ± 10.49)	1.61 ± 0.33*** (70.19 ± 14.30)	1.43 ± 0.44*** (62.59 ± 19.26)
7/56	2.19 ± 0.35 (100 ± 15.93)	1.96 ± 0.26 (89.44 ± 11.77)	2.00 ± 0.37 (91.36 ± 16.87)
7/84	2.17 ± 0.36 (100 ± 16.68)	1.98 ± 0.40 (91.37 ± 18.49)	1.75 ± 0.38* (80.70 ± 17.63)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.

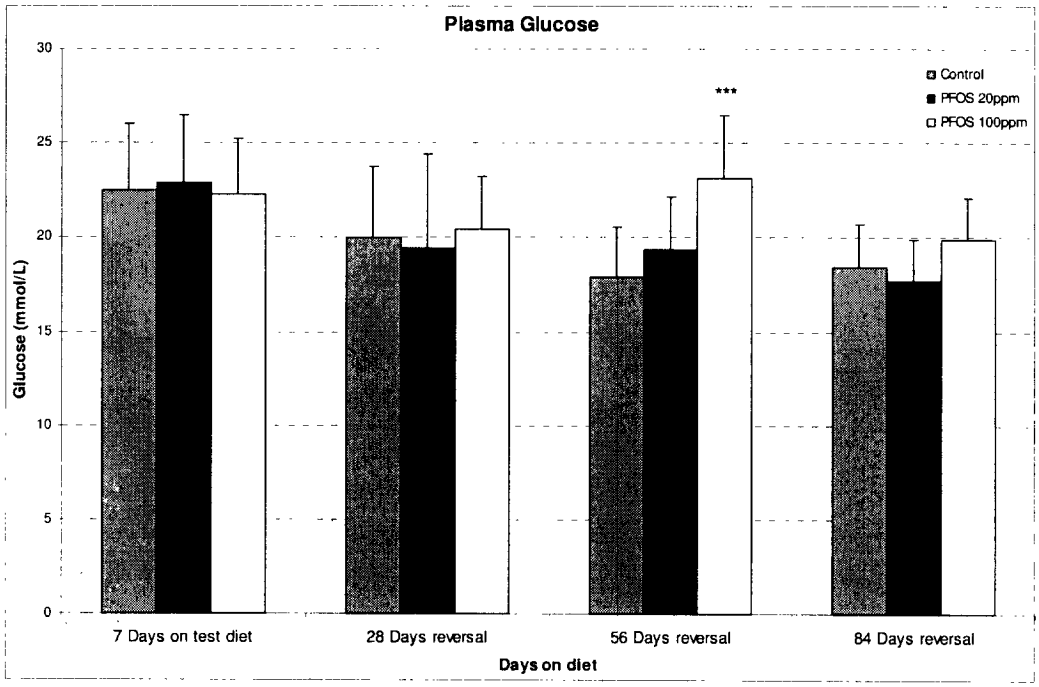


Mean plasma glucose concentrations showed only one significantly different value after 56 days reversal following 7 days of PFOS at 100ppm (Table 9). This is not considered to be biologically significant.

Table 9. Plasma Glucose Concentration

Days on diet/reversal	Glucose (mmol/L)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	22.51 ± 3.47[a] (100 ± 15.44)	22.92 ± 3.58 (101.82 ± 15.90)	22.26 ± 2.93 (98.92 ± 13.02)
7/28	19.98 ± 3.75 (100 ± 18.76)	19.43 ± 4.98 (97.28 ± 24.94)	20.40 ± 2.81 (102.12 ± 14.06)
7/56	17.87 ± 2.67 (100 ± 14.96)	19.34 ± 2.82 (108.24 ± 15.77)	23.18 ± 3.29*** (129.71 ± 18.44)
7/84	18.43 ± 2.24 (100 ± 12.17)	17.70 ± 2.20 (96.02 ± 11.92)	19.86 ± 2.21 (107.76 ± 11.97)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.

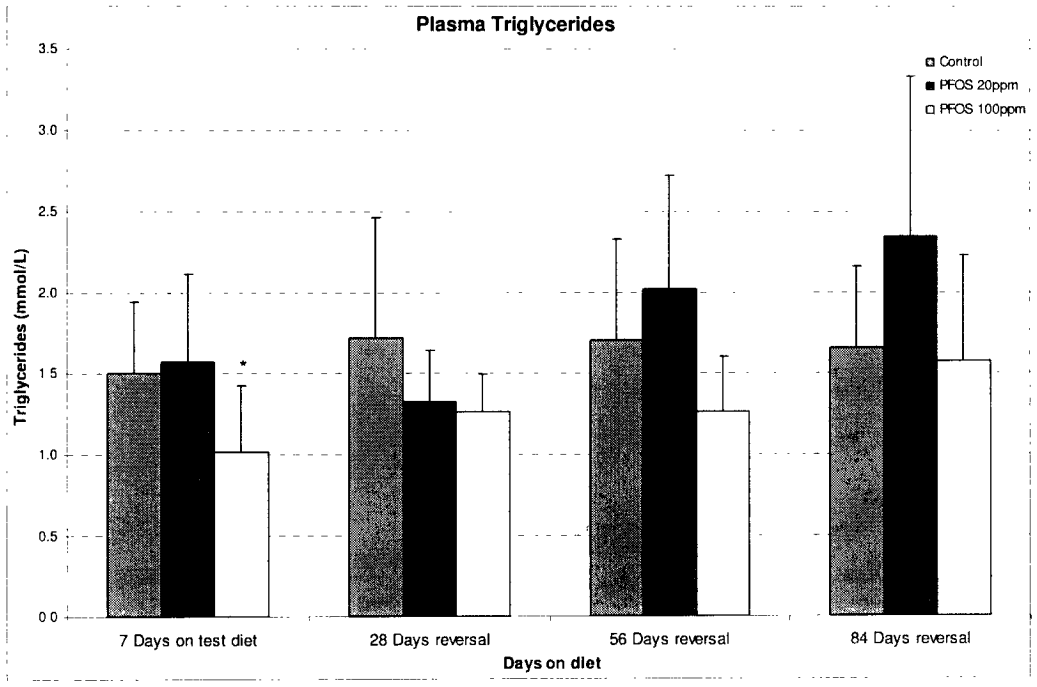


After 7 days on diet there was a marked reduction in mean plasma triglyceride levels following administration of 100ppm PPFOS. The mean plasma triglyceride concentrations recovered to near control levels upon reversal to control diet (Table 10).

Table 10. Plasma Triglyceride Concentration

Days on diet/reversal	Triglycerides (mmol/L)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	1.51 ± 0.44[a] (100 ± 28.92)	1.58 ± 0.53 (104.65 ± 35.48)	1.02 ± 0.41* (67.44 ± 27.17)
7/28	1.72 ± 0.74 (100 ± 43.17)	1.32 ± 0.32 (76.92 ± 18.60)	1.26 ± 0.24 (73.31 ± 13.84)
7/56	1.70 ± 0.63 (100 ± 36.74)	2.02 ± 0.70 (118.81 ± 41.38)	1.26 ± 0.34 (74.25 ± 19.80)
7/84	1.66 ± 0.50 (100 ± 30.09)	2.35 ± 0.99 (141.35 ± 59.47)	1.58 ± 0.65 (95.02 ± 39.18)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.



10.3 Liver Biochemistry

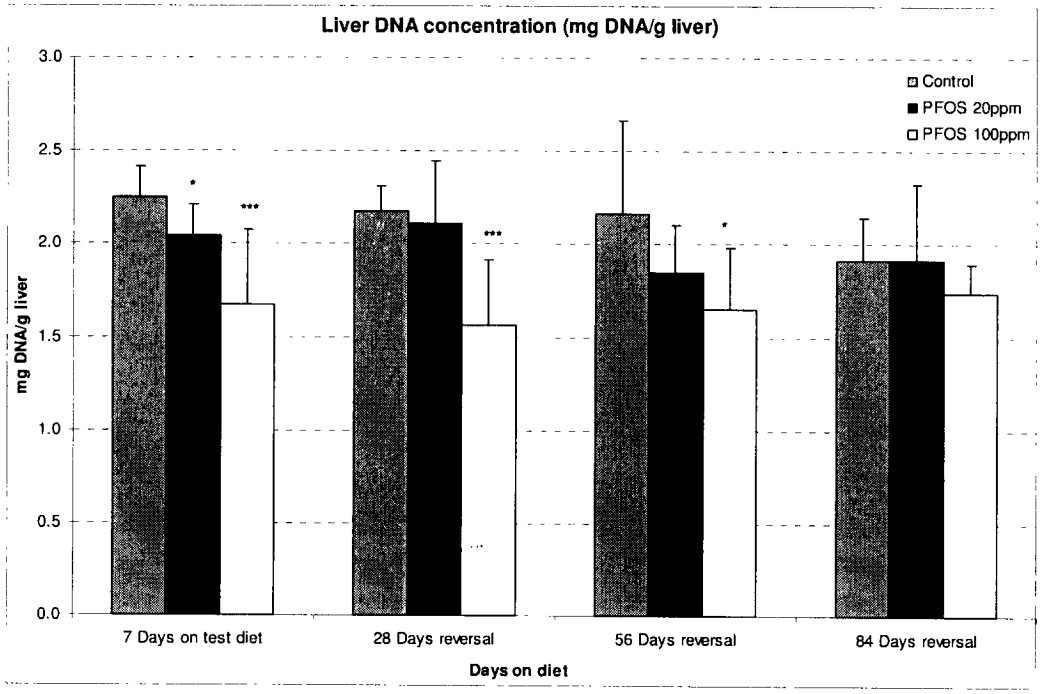
10.3.1 DNA content of liver

The mean hepatic concentration of DNA was decreased by PFOS 20ppm and PFOS 100ppm treatments after 7 days on diet. Upon reversal to control diet, PFOS 20ppm treated animals recovered to near control levels after 28 days, whilst PFOS 100ppm treated animals did not recover to this level until 84 days (Table 11).

Table 11. Liver DNA Concentration (mg DNA/g liver)

Days on diet/reversal	Liver DNA (mg/g liver)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	2.253 ± 0.163[a] (100 ± 7.23)	2.043 ± 0.165* (90.65 ± 7.34)	1.669 ± 0.406*** (74.07 ± 18.04)
7/28	2.179 ± 0.132 (100 ± 6.04)	2.109 ± 0.339 (96.77 ± 15.56)	1.562 ± 0.355*** (71.69 ± 16.28)
7/56	2.162 ± 0.504 (100 ± 23.30)	1.844 ± 0.259 (85.28 ± 11.96)	1.655 ± 0.325* (76.52 ± 15.03)
7/84	1.915 ± 0.226 (100 ± 11.78)	1.918 ± 0.408 (100.12 ± 21.28)	1.740 ± 0.153 (90.87 ± 7.97)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.

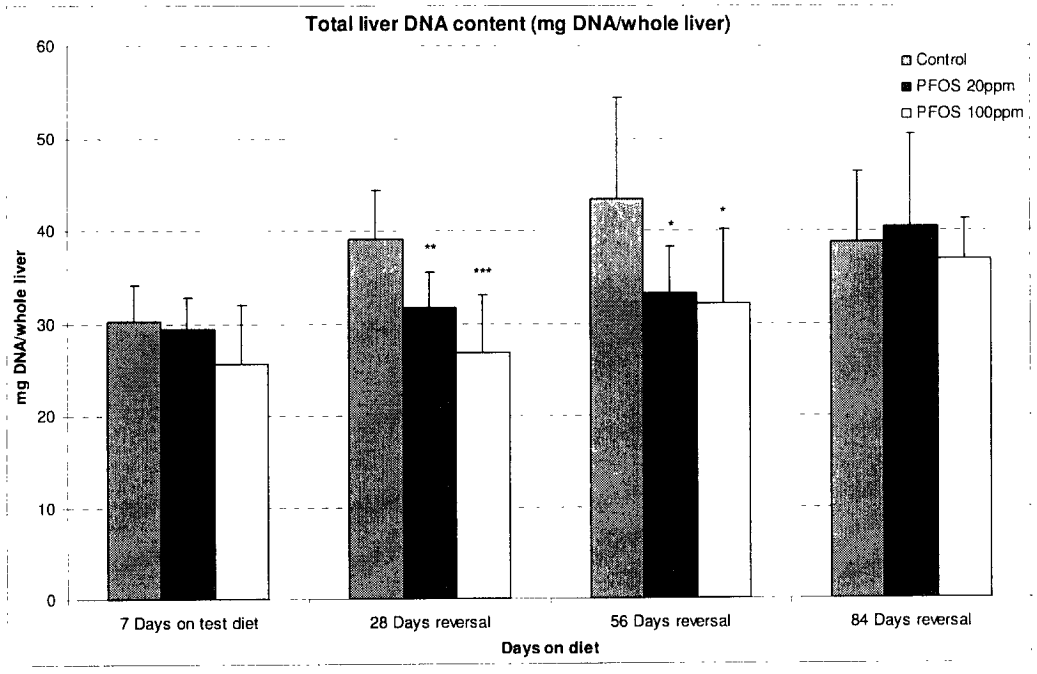


Although neither PFOS administration at 20ppm nor 100ppm decreased the total liver content of DNA after 7 days on diet, upon reversal to control diet they both decreased the total liver content of DNA after 28 and 56 days of reversal. A return to control levels was seen after 84 days on control diet for both dose levels (Table 12).

Table 12. Total Liver DNA Content (mg DNA/whole liver)

Days on diet/reversal	Liver DNA (mg/whole liver)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	30.21 ± 3.95[a] (100 ± 13.08)	29.43 ± 3.33 (97.43 ± 11.02)	25.59 ± 6.37 (84.72 ± 21.09)
7/28	39.10 ± 5.30 (100 ± 13.56)	31.71 ± 3.74** (81.09 ± 9.57)	26.83 ± 6.27*** (68.61 ± 16.03)
7/56	43.45 ± 10.91 (100 ± 25.10)	33.14 ± 5.09* (76.26 ± 11.72)	32.10 ± 8.08* (73.87 ± 18.59)
7/84	38.80 ± 7.55 (100 ± 19.45)	40.44 ± 9.99 (104.22 ± 25.74)	36.91 ± 4.37 (95.12 ± 11.25)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.



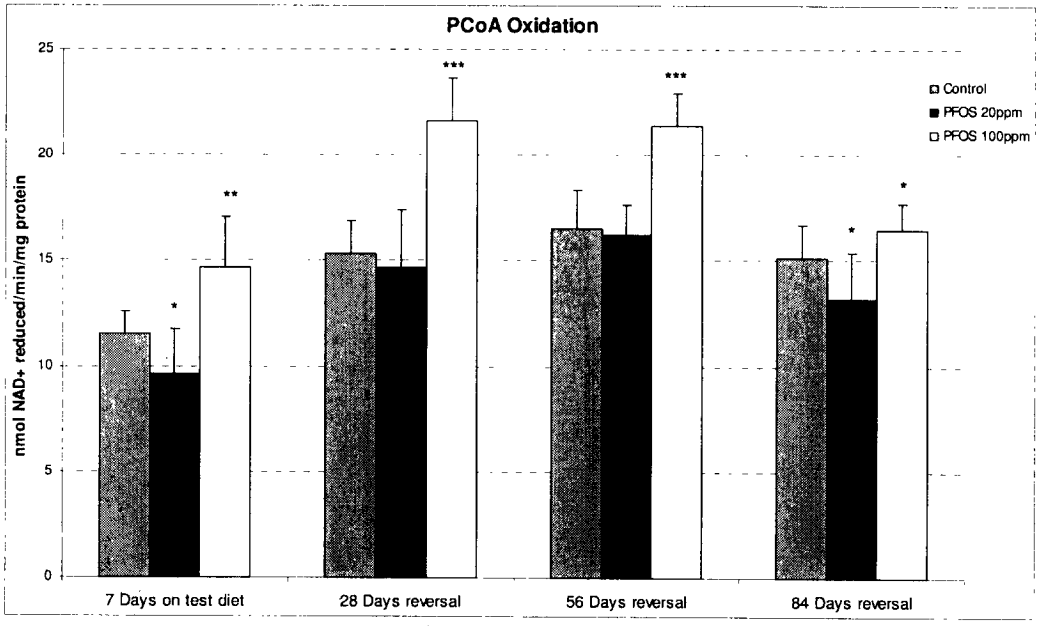
10.3.2 Peroxisome proliferation

Administration of PFOS 100ppm to rats for 7 days followed by up to 84 days reversal on control diet resulted in marked increases in hepatic peroxisomal β-oxidation, as determined by measurement of CN-insensitive palmitoyl CoA (PCO) oxidation, at all time points studied. Administration of PFOS 20ppm, however, had no effect or a slight decrease in PCO (Table 13).

Table 13. Hepatic Cyanide-insensitive Palmitoyl CoA Oxidation (PCO)

Days on diet/reversal	PCO (nmol NAD^+ reduced/minute/mg protein)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	11.51 ± 1.10[a] (100 ± 9.59)	9.64 ± 2.09* (83.73 ± 18.15)	14.66 ± 2.37** (127.31 ± 20.57)
7/28	15.31 ± 1.57 (100 ± 10.25)	14.67 ± 2.71 (95.77 ± 17.67)	21.63 ± 2.01*** (141.24 ± 13.16)
7/56	16.49 ± 1.87 (100 ± 11.34)	16.23 ± 1.40 (98.44 ± 8.48)	21.40 ± 1.53*** (129.80 ± 9.28)
7/84	15.17 ± 1.51 (100 ± 9.97)	13.20 ± 2.18* (86.99 ± 14.36)	16.47 ± 1.21* (108.59 ± 7.99)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.



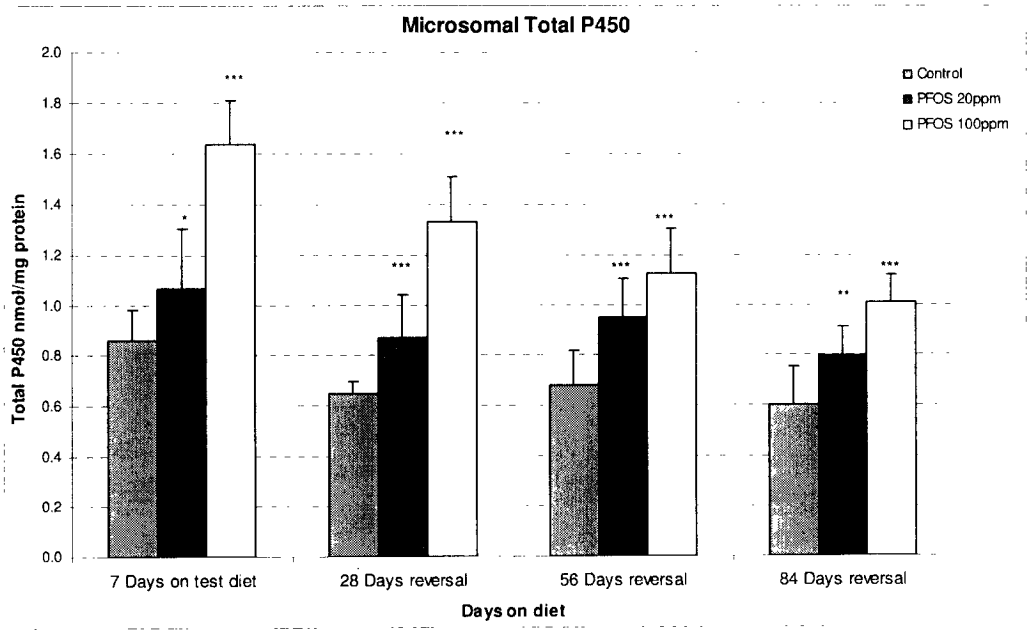
10.3.3 Total cytochrome P450 content of liver

Administration of PFOS 20ppm and PFOS 100ppm to rats resulted in marked increases in hepatic total P450. Administration of PFOS increased total P450 in a dose dependent manner. Reversal to control diet for up to 84 days had no effect on hepatic total P450 content (Table 14).

Table 14. Hepatic Total P450 Content

Days on diet/reversal	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	0.86 ± 0.12[a] (100 ± 13.90)	1.07 ± 0.24* (123.53 ± 27.82)	1.63 ± 0.17*** (189.47 ± 20.09)
7/28	0.65 ± 0.05 (100 ± 7.70)	0.87 ± 0.17*** (134.16 ± 26.38)	1.33 ± 0.18*** (205.06 ± 28.35)
7/56	0.68 ± 0.14 (100 ± 20.27)	0.95 ± 0.16*** (139.08 ± 22.86)	1.12 ± 0.18*** (164.68 ± 26.70)
7/84	0.60 ± 0.15 (100 ± 25.40)	0.80 ± 0.12** (132.12 ± 19.85)	1.01 ± 0.11*** (167.27 ± 18.81)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.



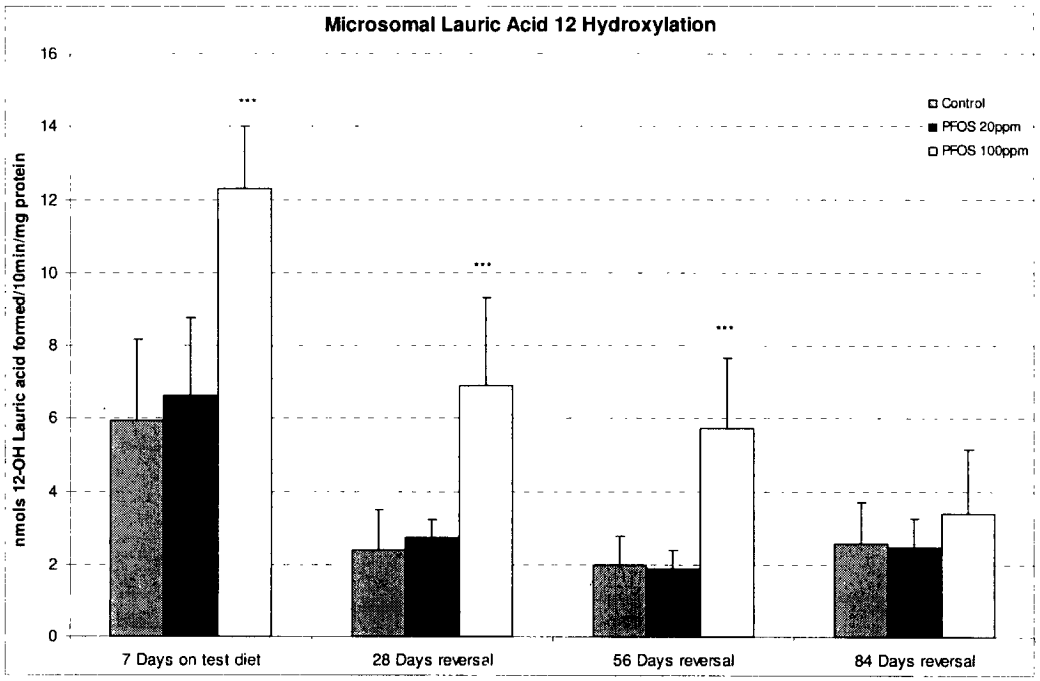
10.3.4 Lauric acid hydroxylation

Lauric acid 12-hydroxylation (12-OH LAH) is used as a marker for cytochrome P450 4A activity. PFOS administration at 20ppm had no effect on 12-OH LAH after 7 days on diet, whilst administration at 100ppm increased the 12-OH LAH by approximately 2-fold after 7 days on diet, and 3-fold after 28 and 56 days on control diet (Table 15). After 84 days on control diet, however, 12-OH LAH activity had returned to control values.

Table 15. Lauric Acid 12-Hydroxylation

Days on diet/reversal	Lauric Acid 12 Hydroxylation (nmol/10minutes/mg protein)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	5.95 ± 2.24[a] (100 ± 37.62)	6.62 ± 2.12 (111.34 ± 35.65)	12.28 ± 1.73*** (206.35 ± 29.09)
7/28	2.40 ± 1.09 (100 ± 45.65)	2.75 ± 0.48 (114.96 ± 19.92)	6.91 ± 2.40*** (288.53 ± 100.13)
7/56	2.01 ± 0.76 (100 ± 38.10)	1.89 ± 0.53 (94.18 ± 26.23)	5.72 ± 1.92*** (285.20 ± 95.70)
7/84	2.56 ± 1.16 (100 ± 45.436)	2.48 ± 0.79 (97.05 ± 31.04)	3.41 ± 1.73 (133.23 ± 67.75)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.



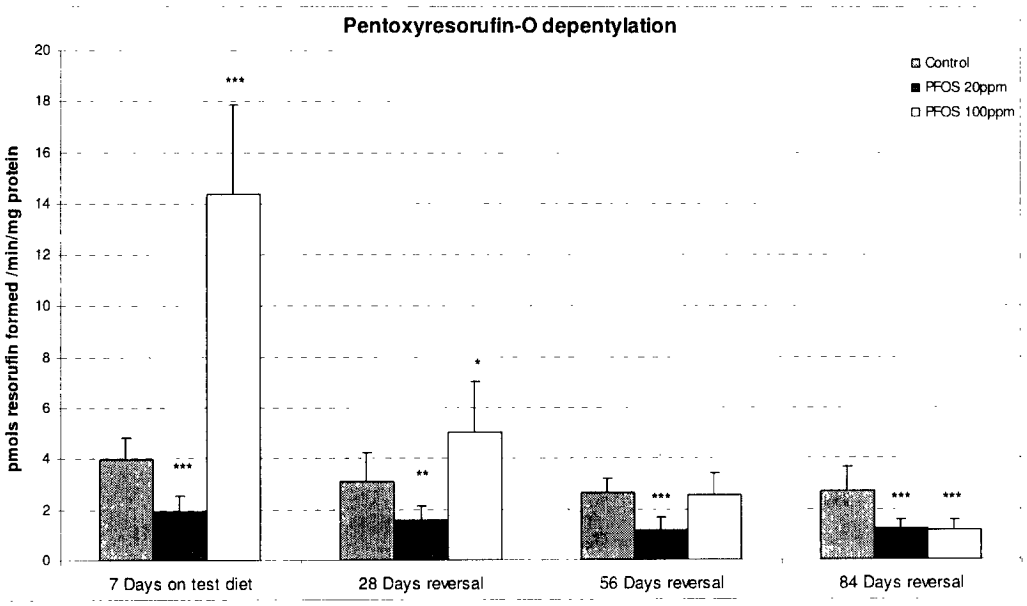
10.3.5 Pentoxyresorufin-*O*-dependentylation

Pentoxyresorufin-*O*-dependentylation (PROD) is used as a marker for cytochrome P450 2B activity. PFOS administration at 20ppm initially decreased the PROD activity by approximately half the control value after 7 days on diet. Reversal to control diet for up to 84 days had no effect, and the decrease in activity was maintained throughout (Table 16). PFOS administration at 100ppm increased the PROD activity by approximately 3.5-fold after 7 days on diet. Reversal to control diet resulted in an increase in activity of approximately 1.5-fold after 28 days; a return to control values after 56 days; and a decrease of approximately half the control value after 84 days.

Table 16. Pentoxyresorufin-O-dependentylation

Days on diet/reversal	PROD (pmols resorufin formed/minute/mg protein)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	3.97 ± 0.84[a] (100 ± 21.22)	1.95 ± 0.61*** (49.19 ± 15.48)	14.36 ± 3.51*** (361.52 ± 88.35)
7/28	3.12 ± 1.12 (100 ± 35.97)	1.57 ± 0.58** (50.16 ± 18.44)	5.06 ± 1.95* (161.99 ± 62.37)
7/56	2.66 ± 0.54 (100 ± 20.32)	1.17 ± 0.49*** (43.99 ± 18.55)	2.56 ± 0.86 (95.91 ± 32.30)
7/84	2.71 ± 0.97 (100 ± 35.86)	1.20 ± 0.37*** (44.37 ± 13.77)	1.18 ± 0.38*** (43.73 ± 14.05)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.



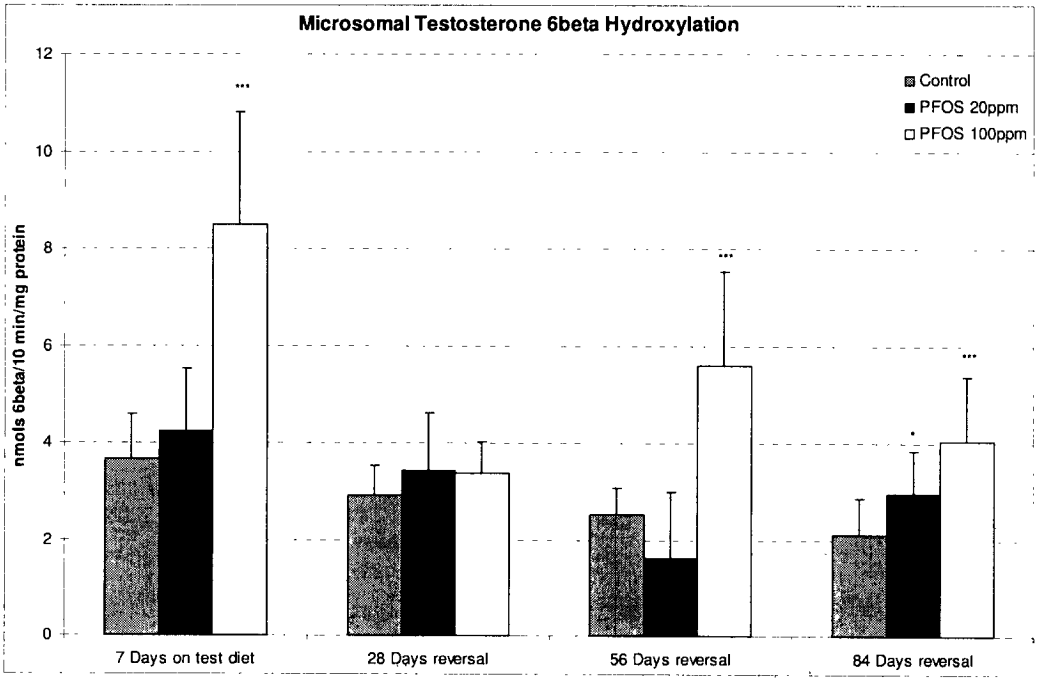
10.3.6 Testosterone hydroxylation

Testosterone 6β-hydroxylation (Test-6β-OH) is used as a marker for cytochrome P450 3A activity. PFOS administration at 20ppm had no effect on the Test-6β-OH activity until after 84 days on control diet. This is not considered to be biologically significant (Table 17). PFOS administration at 100ppm initially increased the Test-6β-OH activity by 2.3-fold after 7 days on diet. Reversal to control diet resulted in a return to control values after 28 days followed by an increase in activity of approximately 2.2- and 1.9-fold after 56 days and 84 days, respectively.

Table 17. Testosterone 6β hydroxylation

Days on diet/reversal	Test-6β-OH (nmols 6β-OH formed/minute/mg protein		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	3.66 ± 0.93[a] (100 ± 25.45)	4.24 ± 1.27 (115.88 ± 34.87)	8.48 ± 2.34*** (231.87 ± 64.06)
7/28	2.92 ± 0.63 (100 ± 21.63)	3.43 ± 1.20 (117.51 ± 41.17)	3.39 ± 0.63 (116.10 ± 21.48)
7/56	2.54 ± 0.54 (100 ± 21.29)	1.63 ± 1.35 (64.34 ± 53.22)	5.60 ± 1.93*** (220.67 ± 75.84)
7/84	2.12 ± 0.74 (100 ± 34.66)	2.97 ± 0.89* (139.72 ± 41.84)	4.06 ± 1.31*** (191.09 ± 61.70)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.



10.4 Histopathology

10.4.1 Liver H&E

Microscopically, treatment related findings were recorded in the liver. When compared with the control animals, a slight decrease in the usual glycogen induced hepatocellular vacuolation was noted in the animals of the 20ppm and 100ppm PFOS groups at each sacrifice period.

Additionally, a minimal to moderate, centrilobular hepatocellular hypertrophy was noted, dose related in severity, in the animals of the 20ppm PFOS and 100ppm PFOS after 7 days of treatment. This finding was still present after a 4-, 8- or 12-week treatment-free recovery period. An unequivocal difference in the severity and incidence of this finding between the various recovery periods was not observed, indicating an incomplete reversibility during the various recovery periods used.

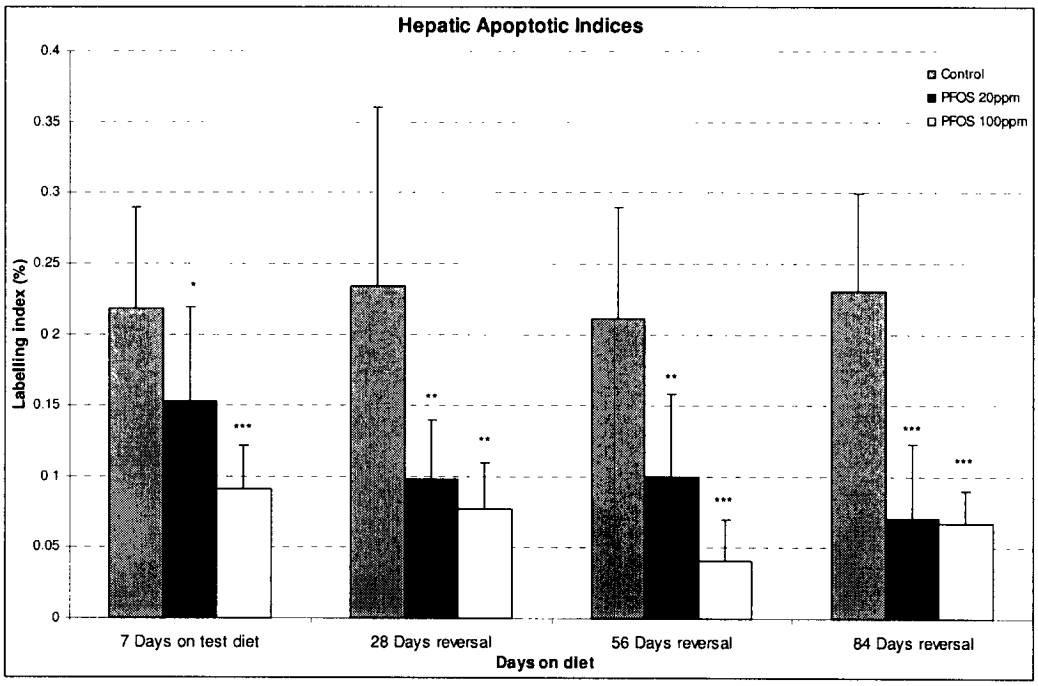
10.4.2 Hepatic Apoptosis

Administration of PFOS 20ppm and PFOS 100ppm for 7 days decreased the hepatic apoptotic index to approximately 70% and 40% of control values, respectively. Reverting to control diet did not reverse this decrease in hepatic apoptotic index, and the decrease continued, reaching a minimum of 30% of control values after 84 days for PFOS 20ppm treated animals, and 20% of control values after 56 days for PFOS 100ppm treated animals (Table 18).

Table 18. Hepatic Apoptotic Indices

Days on diet/reversal	Apoptotic Index (%)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	0.22 ± 0.07[a] (100 ± 32.73)	0.15 ± 0.07* (69.92 ± 30.44)	0.09 ± 0.03*** (41.76 ± 13.93)
7/28	0.23 ± 0.13 (100 ± 53.68)	0.10 ± 0.04** (41.79 ± 17.86)	0.08 ± 0.03** (32.68 ± 14.03)
7/56	0.21 ± 0.08 (100 ± 36.82)	0.10 ± 0.06** (47.26 ± 27.49)	0.04 ± 0.03*** (19.17 ± 13.62)
7/84	0.23 ± 0.07 (100 ± 29.79)	0.07 ± 0.05*** (30.70 ± 22.55)	0.07 ± 0.02*** (29.24 ± 9.73)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.



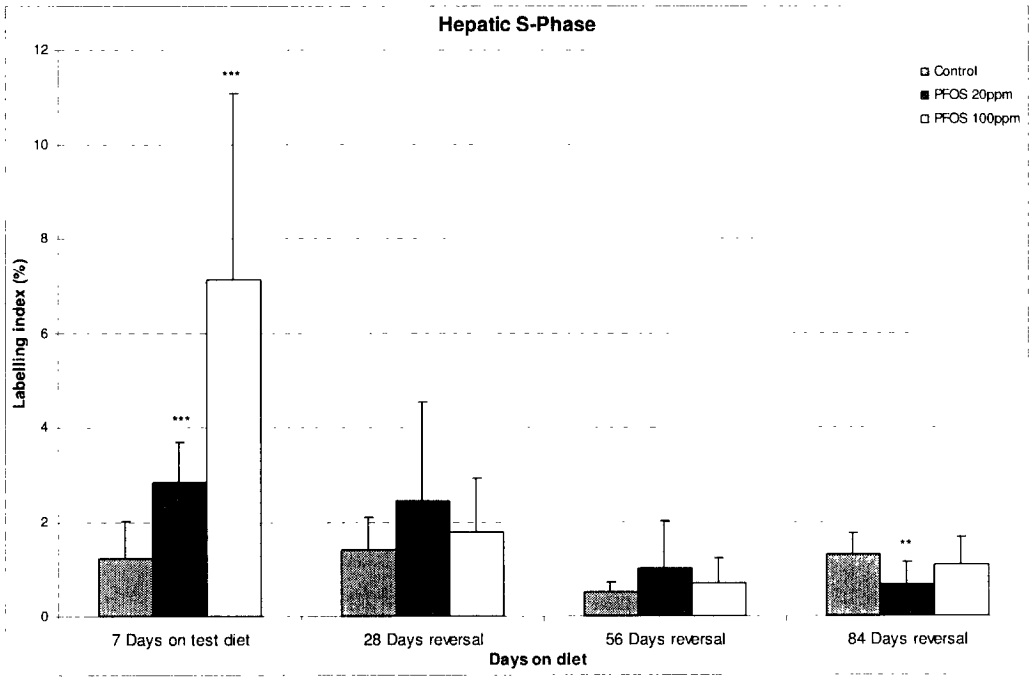
10.4.3 Cell proliferation in liver

PFOS 20ppm and PFOS 100ppm administration for 7 days both increased the hepatocellular labelling index (S-phase) by 2.5- and 5.9-fold, respectively (Table 19). Reversal to control diet resulted in a return to control values after 28 days.

Table 19. Hepatic S-phase Labelling Indices

Days on diet/reversal	Labelling Index (%)		
	0ppm	PFOS 20ppm	PFOS 100ppm
7/0	1.22 ± 0.80[a] (100 ± 65.77)	2.83 ± 0.85*** (231.97 ± 69.58)	7.14 ± 3.93*** (585.99 ± 322.37)
7/28	1.41 ± 0.68 (100 ± 48.23)	2.44 ± 2.09 (173.23 ± 148.40)	1.77 ± 1.13 (126.01 ± 80.52)
7/56	0.50 ± 0.22 (100 ± 43.81)	1.00 ± 1.00 (200.05 ± 200.63)	0.68 ± 0.54 (136.91 ± 107.27)
7/84	1.30 ± 0.44 (100 ± 34.16)	0.67 ± 0.46** (51.43 ± 35.53)	1.08 ± 0.60 (83.07 ± 46.08)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD. n = 10 per group. A Student's t-test (2-sided) was performed on the results; *statistically different from control $p<0.05$; **$p<0.01$; *** $p<0.001$.



10.4.4 Thyroid H&E

In the thyroid gland, no microscopic findings considered to be related to the treatment with the test items were recorded.

10.4.5 Thyroid *in situ* cell death

The level of apoptosis found in both treatment groups, at all time points, was minimal. It was usual to find either no cells, or just one cell per thyroid, staining in the TUNEL assay as apoptotic, regardless of treatment.

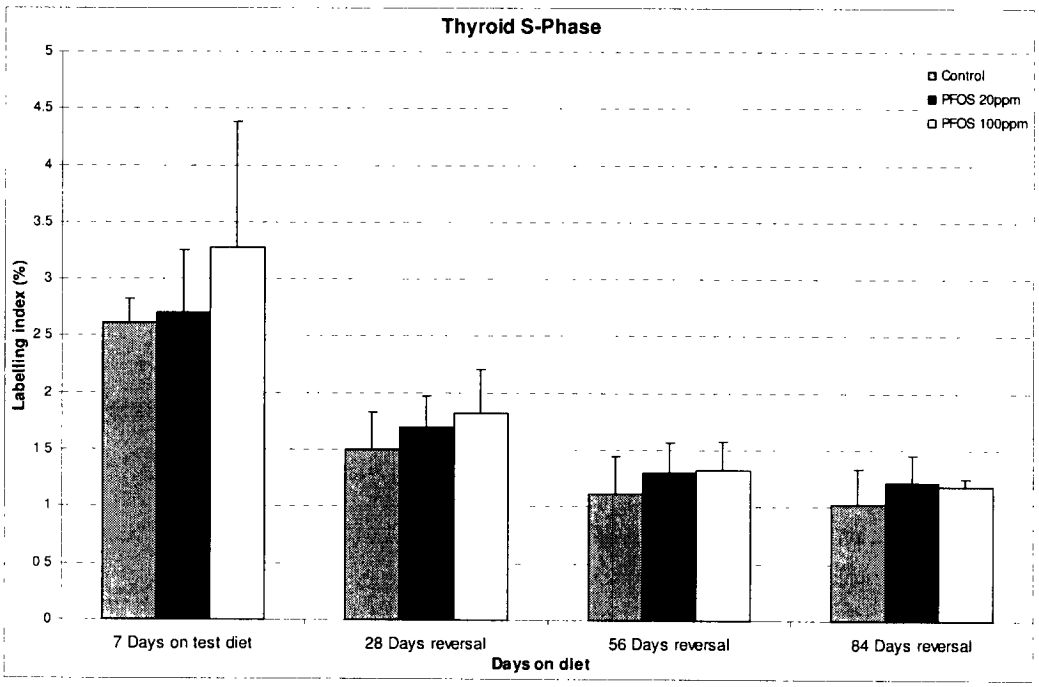
10.4.6 Cell proliferation in thyroid

PFOS 20ppm and PFOS 100ppm treatment had no effect on S-phase at any time point studied (Table 20).

Table 20. Thyroid S-phase Labelling Indices

Days on diet/reversal	Labelling Index (%)		
	0ppm	PFOS[1] 20ppm	PFOS[1] 100ppm
7/0	2.62 ± 0.21[a] (100 ± 8.14)	2.70 ± 0.56 (103.16 ± 21.38)	3.28 ± 1.10 (125.34 ± 42.08)
7/28	1.50 ± 0.33 (100 ± 21.81)	1.70 ± 0.27 (113.49 ± 18.00)	1.82 ± 0.38 (121.56 ± 25.44)
7/56	1.12 ± 0.33 (100 ± 29.70)	1.30 ± 0.26 (116.27 ± 23.60)	1.32 ± 0.25 (118.41 ± 22.55)
7/84	1.02 ± 0.31 (100 ± 30.58)	1.21 ± 0.24 (118.61 ± 23.52)	1.18 ± 0.07 (115.03 ± 6.57)

[a] Values are Mean ± SD. Values in parenthesis are mean % control ± SD.
n = 10 per group; [1] n = 5 per group.
A Student's t-test (2-sided) was performed on the results; *statistically different from control p<0.05; **p<0.01; *** p<0.001.



11. DISCUSSION

In this study, PFOS appeared to exhibit the combined hepatic effects of a peroxisome proliferator and "phenobarbital-like" enzyme inducer. Thus, PFOS administration for 7 days generally reflected the results obtained in a previous study, CXR0481. As in the earlier study no effects of PFOS on the thyroid were observed.

Both histopathologically and biochemically, reversibility was not complete after 7 days of PFOS treatment followed by up to an 84 day treatment-free recovery period. Hepatic apoptosis, particularly, was still severely inhibited after this reversal time. Likewise the induced microsomal cytochrome P450 content and representative monoxygenase activities were maintained throughout the treatment-free recovery period. This latter observation was reflected by the maintenance of hepatocellular hypertrophy.

12. DATA STORAGE AND ARCHIVING

The data has been held in a Study File according to CXR Biosciences SOPs 0003 and 0005. On completion of the study, the following items will be retained in the CXR Archive:

- Study protocol and possible amendments
- Study Report and possible amendments
- Study File (including Study Diary)
- Relevant correspondence

All items will be kept for two years from the date of signing the Study Report unless, in the opinion of CXR Biosciences, the quality of the specimens no longer allows evaluation. At the end of the two-year period, the Study Sponsor will be contacted and the items either sent to the Study Sponsor or retained by CXR Biosciences under a separate agreement.

13. REPORT

The Study Report has been prepared as described in CXR Biosciences SOP 0004.

14. QUALITY ASSURANCE

Study activities at the Test Facility (CXR Biosciences Ltd and BSRU) have been conducted according to relevant SOPs.
There were no deviations from this protocol.

No claim of GLP compliance has been made for this study.

15. STUDY DIRECTORS STATEMENT

Final Report signature by the Study Director indicates acceptance of responsibility for the validity and integrity of the Study data.

APPENDIX 1. PATHOLOGY REPORT

PATHOLOGY REPORT		CXR : 0486s
TEST ITEM	: Perfluorooctane Sulfonate (PFOS)	PATHOL. NO.: 07059 VOO
TEST SYSTEM	: RAT, 13 weeks, feeding	DATE : 19-MAR-08
SPONSOR	: CXR Biosciences Ltd.	PathData®System V6.2d1

PREPARED BY: Dr. med. vet. Ortwin Vogel
Veterinary Pathologist

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TEST ITEM : Perfluorooctane Sulfonate (PFOS) | PATHOL. NO.: 07059 VOO
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AUTHENTICATION

The undersigned hereby declares that the histopathology data in this report were compiled by him, and that they reflect accurately the raw data records.

Dr. med. vet. Ortwin Vogel
Veterinary Pathologist

TPC
Toxicologic Pathology Consultancy
Goethestr. 26
D-24116 Kiel

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

SUMMARY

To investigate the reversibility of Perfluorooctane Sulfonate (PFOS)-induced effects, pathomorphological examinations were performed on 120 male Sprague Dawley rats. The rats were allocated to 3 dose groups each consisting of 40 males and received the test item via the feed at dose levels of 20 ppm "PFOS" or, 100 ppm "PFOS" (groups 02 and 03, respectively) for a treatment period of 7 days. The rats of group 01 received the same diet without any test item and served as control animals. Ten rats of each group were assigned for the sacrifice at the end of the treatment period (test day 8) and ten animals each were assigned to the sacrifices after a 4-week (R1), 8-week (R2) and 12-week (R3) recovery period. At the end of the treatment/recovery periods, the rats were sacrificed and detailed necropsies performed. Histopathological examination was performed on the liver and thyroid from all animals of all groups.

Microscopically, treatment related findings were recorded in the liver. When compared with the control animals, a slight decrease in the usual glycogen induced hepatocellular vacuolation was noted in the animals of groups 02 (20 ppm PFOS) and 03 (100 ppm PFOS) on each sacrifice period.

In addition, a minimal to moderate, centrilobular hepatocellular hypertrophy was noted, dose related in severity, in the animals of groups 02 (20 ppm PFOS) and 03 (100 ppm PFOS) after 7 days of treatment. This finding was still present in animals of groups 02 and 03 sacrificed after a 4-, 8- or 12-week treatment-free recovery period. An unequivocal difference in the severity and incidence of this finding between the various recovery periods was not observed indicating an incomplete reversibility during the various recovery periods used in this study.

In the thyroid gland, no microscopic finding was recorded, that is considered to be related to the treatment with the test items.

All other microscopic findings recorded did not distinguish significantly treated rats from vehicle control rats or the differences noted were regarded as random events. All these findings are considered to be spontaneous in nature and within the normal background pathology commonly seen in rats of these strains and age.

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SPONSOR	: CXR Biosciences Ltd.	PathData®System	V6.2d1

SUMMARY

Under the conditions of this study, the repeated administration of 20 or 100 ppm "PFOS" via the feed to rats of the Sprague Dawley strain for a treatment period of 7 days produced a centrilobular hepatocellular hypertrophy, that was not completely reversible during a 4-, 8- or 12-week treatment-free recovery period.

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SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

METHODS

Group Design for Pathological Evaluation

Dose Group	Pathdata Group	Test item+	Number of Rats* Males	Animal numbers Males
01	01	0 (Control)	10**	1 - 10
			10***	11 - 20
			10****	21 - 30
			10*****	31 - 40
02	02	20 ppm PFOS	10**	41 - 50
			10***	51 - 60
			10****	61 - 70
			10*****	71 - 80
03	03	100 ppm PFOS	10**	81 - 90
			10***	91 - 100
			10****	101 - 110
			10*****	111 - 120

\+ Perfluorooctane sulfonate potassium salt (PFOS K+), 3M Company, St. Paul, Minnesota, USA.
* strain: Sprague Dawley (CD), (Breeder: Charles River, UK);
** These animals are listed in the tables under necropsy status K0.
*** These animals are listed in the tables under necropsy status R1.
**** These animals are listed in the tables under necropsy status R2.
***** These animals are listed in the tables under necropsy status R3.

Administration of the Test Item

The in-life part of the study was performed at CXR Biosciences Ltd., James Lindsay Place, Dundee DD1 5JJ, UK. The animals were administered 20 ppm PFOS (group 02) or 100 ppm PFOS (group 03) in the diet ad libitum for 7 days. The animals of group 01 received the same diet without the test item and served as control animals.

Necropsy and Histopathology

At the end of the assigned study periods (test days 8, (sacrifice group K0), 36 (sacrifice group R1), 64 (sacrifice group R2) and 92 (sacrifice

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METHODS

group R3), the rats were killed by exposure to a rising concentration of CO2. Two samples of the liver (one from the left lobe, one from the median lobe) and the thyroid including parathyroid gland together with trachea and oesophagus were taken and preserved in 10% neutral buffered formaldehyde (NBF).

Histotechnique was performed at Progenix Research UK Ltd., Suite 1 Forth House, Burnside Business Court, Inverkeithing, Fife, KY11 1NZ, Scotland. The preserved liver and thyroid samples of all rats of all groups were trimmed, processed, embedded in paraffin wax and sectioned at a nominal thickness of about 5 µm. All sections were stained with haematoxylin and eosin. One section of each organ sample was examined by the undersigned pathologist by light microscope.

Data compilation

The animal heading data recorded by CXR at postmortem examination were taken from the post-mortem records and entered manually into the PathData Computer system, current version, under Pathology No. 07059 (PathData is a registered trademark of Pathology Data Systems, Inc.). Microscopic findings are recorded by the undersigned pathologist during histopathological examination using on-line data input into the pathology computer system.

All microscopic observations are presented for each rat in the "Table of Individual Microscopic Findings" as well as in full descriptive terms in the "Individual Animal Data - Text of Gross and Microscopic Findings". The incidence of microscopic findings is also presented in tabular form. Incidence tables were created by the Pathdata software. Histologic alterations were described, wherever possible, according to their distribution, severity and morphologic character. Severity scores were assigned as given under "Explanation of Codes and Symbols".

The slides were evaluated on December 19/20, 2007.

Archive

For archiving purposes, the raw data including a CD-ROM containing the electronic study data and the microscopic slides will be returned to CXR Biosciences Ltd., James Lindsay Place, Dundee DD1 5JJ, UK.

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
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RESULTS

Microscopic findings

At histopathologic examination, few microscopic findings were recorded. These findings are described in detail in the "Individual Animal Data Text of Gross and Microscopic Findings".

THYROID:
There were no microscopic findings recorded that are considered to be related to the treatment with any test items in either sacrifice group.

LIVER:

Sacrifice at the end of the treatment period (sacrifice K0):
.....
A minimal to moderate, periportal hepatocellular vacuolation that is considered to be due to an intracytoplasmic glycogen accumulation was prominent in the control animals of group 01. Hepatocellular vacuolation was also present, similar in incidence and severity, in the animals of group 02 (20 ppm PFOS) and, with a slight decreased mean severity (mean 2.0) when compared with the control animals (mean 2.5), of group 03 (100 ppm PFOS)

Centrilobular hepatocellular hypertrophy was noted, minimal to slight in degree, in treated rats only. This finding occurred in 8 animals of group 02 (20 ppm PFOS, mean severity 1.0) and all animals of group 03 (100 ppm PFOS, mean severity 1.8).

Sacrifice after a 4-week treatment-free recovery period (sacrifice R1):
.....
Hepatocellular vacuolation similar to the finding noted in the animals of the K0-sacrifice was recorded also in all control animals of this sacrifice group. A slight decrease in incidence and severity of this finding was noted in groups 02 (20 ppm PFOS, 7 animals affected, mean severity 1.9) and 03 (100 ppm PFOS, 6 animals affected, mean severity 1.8) when compared with the control group (all ten animals affected, mean severity 2.0).

A minimal to moderate hepatocellular hypertrophy was noted in treated animals only occurring in 5 rats of group 02 (20 ppm PFOS, mean severity 1.2) and all ten rats of group 03 (PFOS 100 ppm, mean severity 2.1).

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RESULTS

Sacrifice after a 8-week treatment-free recovery period (sacrifice R2):

A similar hepatocellular vacuolation as recorded in the liver of the animals sacrificed at the end of the treatment period (K0-sacrifice) was also noted, minimal to moderate in degree, in all control rats of groups 01 and almost all treated animals of groups 02 and 03. A slight decrease in incidence and severity of this finding was noted in groups 02 (20 ppm PFOS, 9 animals affected, mean severity 2.1) and 03 (100 ppm PFOS, 9 animals affected, mean severity 1.7) when compared with the control group (mean severity 2.4).

Hepatocellular hypertrophy occurred only in treated animals. This finding was noted, minimal in degree, in 4 animals of group 02 (20 ppm PFOS, mean severity 1,0) and, slight to moderate in degree, in all ten animals of group 03 (100 PFOS, mean severity 2.1).

Sacrifice after a 12-week treatment-free recovery period (sacrifice R3):

Hepatocellular vacuolation similar to the finding noted in the animals of the K0-sacrifice was recorded also in all control animals. A slight decrease in the incidence and/or severity of this finding was noted in groups 02 (20 ppm PFOS, 10 animals affected, mean severity 2.0) and 03 (100 ppm PFOS, 7 animals affected, mean severity 1.7) when compared with the control group (all 10 animals affected, mean severity 2.6).

Hepatocellular hypertrophy occurred in treated animals only. This finding was recorded, minimal in degree, in 5 males of group 02 (20 ppm PFOS, mean severity 1.0) and in all 10 males of group 03 (100 pph PFOS, mean severity 1.7).

The type, incidence and severity of all other microscopic alterations recorded did not indicate a relationship to the treatment with the test item or the differences noted were regarded as random events. These findings were regarded to be spontaneous in nature and within the normal background pathology commonly seen in rats of these strains and age.

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SPONSOR	: CXR Biosciences Ltd.	PathData®System V6.2d1

CONCLUSIONS

In this 13-week toxicity study of the test item "PFOS" administered with the feed to Sprague Dawley rats at dose levels of 0 ppm (control), 20 ppm PFOS or 100 ppm PFOS, a hepatocellular vacuolation occurred in rats of all groups and sacrifice periods. The severity of this finding appeared to be decreased in treated groups when compared with the control group in all sacrifice periods. This kind of vacuolation is considered to be due to the intracytoplasmic presence of glycogen and is quite commonly observed in well-fed, untreated rodents. The difference between control and treated animals noted in this study at different sacrifice periods is considered to be related to the treatment with the test items.

A minimal to slight centrilobular hepatocellular hypertrophy was noted, dose related in severity, in the animals of groups 02 and 03 sacrificed at the end of the 7-day treatment period (K0). In the absence of any hepatocellular hypertrophy in the control animals, this alteration is considered to be related to the treatment with the test item. A large number of medicinal agents with different chemical structures and therapeutic activities produce liver enlargement when given in high doses to species used in toxicity studies (Greaves, 1990). This enlargement that may be characterized morphologically by hepatocyte hypertrophy, hepatocyte hyperplasia or both may be accompanied by an increase in activity of the hepatic microsomal drug metabolizing enzymes in the absence of any morphogical evidence of hepatocellular damage. The changes are typically reversible on cessation of treatment. In this study, however, hepatocellular hypertrophy was also present, similar in incidence and severity, in both treated groups sacrificed after a 4-, 8- or 12-week treatment-free observation period. An unequivocal difference in the severity and incidence of this finding between the various recovery periods was not observed. This indicates, that a complete recovery did not occur during the recovery periods used in this study.

In the thyroid gland, there were no microscopic findings recorded that are considered to be related to the treatment with any test items in either sacrifice group.

All other microscopic findings recorded did not distinguish significantly treated rats from vehicle control rats or the differences noted were regarded as random effects. All these findings are considered to be spontaneous in nature and within the normal background pathology commonly seen in rats of these strains and age.

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

CONCLUSIONS

Under the conditions of this study, the repeated administration of 20 or 100 ppm "PFOS" via the feed to rats of the Sprague Dawley strain for a treatment period of 7 days produced a centrilobular hepatocellular hypertrophy, that was not completely reversible during a 4-, 8- or 12-week treatment-free recovery period.

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REFERENCES

Greaves P. (1990): Histopathology of Preclinical Toxicity Studies: Interpretation and Relevance in Drug Safety Evaluation. Digestive System I, 278-392.
Elsevier, Amsterdam New York Oxford

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EXPLANATION OF CODES AND SYMBOLS

CODES AND SYMBOLS USED AT ANIMAL LEVEL:

M = Male animal
K0 = Terminal sacrifice group
R1...R9 = Recovery / post-treatment group 1...9

CODES AND SYMBOLS USED AT ORGAN LEVEL:

0 = Tissue not present for histologic examination
' = Histologic examination not required
+ = Organ examined, findings present
- = Organ examined, no pathologic findings noted (AOFT only)
(= Only one of paired organs examined/present

CODES AND SYMBOLS USED AT FINDING LEVEL:

GRADE 1 = Minimal / very few / very small
GRADE 2 = Slight / few / small
GRADE 3 = Moderate / moderate number / moderate size
P = Finding present, severity not scored
(= Finding unilateral in paired organs

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SPONSOR : CXR Biosciences Ltd. | PathData®System V6.2d1

SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
Necropsy Status: TERMINAL SACRIFICE GROUP (K0)

Sex		Males			Females		
Dose Group		01	02	03	01	02	03
No. Animals per Dose Group		10	10	10	-	-	-
LIVER	No.Examined	10	10	10	-	-	-
- mononuclear cell infiltrate(s)	GRADE 1	5	3	3	-	-	-
	TOTAL AFFECTED	5	3	3	-	-	-
	MEAN GRADE/TISS.AFFECTED	1.0	1.0	1.0	-	-	-
- (mixed) inflammatory cell infiltration	GRADE 1	7	8	6	-	-	-
	TOTAL AFFECTED	7	8	6	-	-	-
	MEAN GRADE/TISS.AFFECTED	1.0	1.0	1.0	-	-	-
- vacuolation	GRADE 1	1	-	1	-	-	-
	GRADE 2	3	2	8	-	-	-
	GRADE 3	6	8	1	-	-	-
	TOTAL AFFECTED	10	10	10	-	-	-
	MEAN GRADE/TISS.AFFECTED	2.5	2.8	2.0	-	-	-
- hepatocellular hypertrophy	GRADE 1	-	8	2	-	-	-
	GRADE 2	-	-	8	-	-	-
	TOTAL AFFECTED	-	8	10	-	-	-
	MEAN GRADE/TISS.AFFECTED	-	1.0	1.8	-	-	-
- mitotic figures	GRADE 1	7	7	8	-	-	-
	TOTAL AFFECTED	7	7	8	-	-	-
	MEAN GRADE/TISS.AFFECTED	1.0	1.0	1.0	-	-	-
THYROID GLAND	No.Examined	9	9	4	-	-	-
- branchiogenic cyst	GRADE 1	-	1	-	-	-	-
	TOTAL AFFECTED	-	1	-	-	-	-
	MEAN GRADE/TISS.AFFECTED	-	1.0	-	-	-	-

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SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
Necropsy Status: RECOVERY / POST-TREATMENT GROUP (R1)

Sex		Males			Females		
Dose Group		01	02	03	01	02	03
No. Animals per Dose Group		10	10	10	-	-	-
LIVER	No.Examined	10	10	10	-	-	-
- congestion	GRADE 1	-	1	-	-	-	-
	GRADE 2	-	1	-	-	-	-
	TOTAL AFFECTED	-	2	-	-	-	-
	MEAN GRADE/TISS.AFFECTED	-	1.5	-	-	-	-
- mononuclear cell infiltrate(s)	GRADE 1	6	5	3	-	-	-
	TOTAL AFFECTED	6	5	3	-	-	-
	MEAN GRADE/TISS.AFFECTED	1.0	1.0	1.0	-	-	-
- (mixed) inflammatory cell infiltration	GRADE 1	9	6	9	-	-	-
	TOTAL AFFECTED	9	6	9	-	-	-
	MEAN GRADE/TISS.AFFECTED	1.0	1.0	1.0	-	-	-
- vacuolation	GRADE 1	1	1	1	-	-	-
	GRADE 2	8	6	5	-	-	-
	GRADE 3	1	-	-	-	-	-
	TOTAL AFFECTED	10	7	6	-	-	-
	MEAN GRADE/TISS.AFFECTED	2.0	1.9	1.8	-	-	-
- hepatocellular hypertrophy	GRADE 1	-	4	-	-	-	-
	GRADE 2	-	1	9	-	-	-
	GRADE 3	-	-	1	-	-	-
	TOTAL AFFECTED	-	5	10	-	-	-
	MEAN GRADE/TISS.AFFECTED	-	1.2	2.1	-	-	-
- mitotic figures	GRADE 1	4	8	6	-	-	-
	TOTAL AFFECTED	4	8	6	-	-	-
	MEAN GRADE/TISS.AFFECTED	1.0	1.0	1.0	-	-	-
THYROID GLAND	No.Examined	8	10	10	-	-	-
- branchiogenic cyst	GRADE 1	-	-	2	-	-	-
	TOTAL AFFECTED	-	-	2	-	-	-
	MEAN GRADE/TISS.AFFECTED	-	-	1.0	-	-	-

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SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
Necropsy Status: RECOVERY / POST-TREATMENT GROUP (R2)

Sex		Males			Females		
Dose Group		01	02	03	01	02	03
No. Animals per Dose Group		10	10	10	-	-	-
LIVER	No.Examined	10	10	10	-	-	-
- congestion	GRADE 1	-	1	-	-	-	-
	TOTAL AFFECTED	-	1	-	-	-	-
	MEAN GRADE/TISS.AFFECTED	-	1.0	-	-	-	-
- mononuclear cell infiltrate(s)	GRADE 1	5	-	3	-	-	-
	TOTAL AFFECTED	5	-	3	-	-	-
	MEAN GRADE/TISS.AFFECTED	1.0	-	1.0	-	-	-
- (mixed) inflammatory cell infiltration	GRADE 1	8	9	10	-	-	-
	TOTAL AFFECTED	8	9	10	-	-	-
	MEAN GRADE/TISS.AFFECTED	1.0	1.0	1.0	-	-	-
- vacuolation	GRADE 1	1	2	3	-	-	-
	GRADE 2	4	4	6	-	-	-
	GRADE 3	5	3	-	-	-	-
	TOTAL AFFECTED	10	9	9	-	-	-
	MEAN GRADE/TISS.AFFECTED	2.4	2.1	1.7	-	-	-
- hepatocellular hypertrophy	GRADE 1	-	4	-	-	-	-
	GRADE 2	-	-	9	-	-	-
	GRADE 3	-	-	1	-	-	-
	TOTAL AFFECTED	-	4	10	-	-	-
	MEAN GRADE/TISS.AFFECTED	-	1.0	2.1	-	-	-
- mitotic figures	GRADE 1	1	3	2	-	-	-
	TOTAL AFFECTED	1	3	2	-	-	-
	MEAN GRADE/TISS.AFFECTED	1.0	1.0	1.0	-	-	-

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SUMMARY TABLES

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SUMMARY INCIDENCE OF GRADINGS BY ORGAN/GROUP/SEX
Necropsy Status: RECOVERY / POST-TREATMENT GROUP (R3)

Sex		Males			Females		
Dose Group		01	02	03	01	02	03
No. Animals per Dose Group		10	10	10	-	-	-
LIVER	No.Examined	10	10	10	-	-	-
- mononuclear cell infiltrate(s)	GRADE 1	6	7	4	-	-	-
	TOTAL AFFECTED	6	7	4	-	-	-
	MEAN GRADE/TISS.AFFECTED	1.0	1.0	1.0	-	-	-
- (mixed) inflammatory cell infiltration	GRADE 1	10	6	8	-	-	-
	TOTAL AFFECTED	10	6	8	-	-	-
	MEAN GRADE/TISS.AFFECTED	1.0	1.0	1.0	-	-	-
- vacuolation	GRADE 1	-	3	1	-	-	-
	GRADE 2	4	4	6	-	-	-
	GRADE 3	6	3	-	-	-	-
	TOTAL AFFECTED	10	10	7	-	-	-
	MEAN GRADE/TISS.AFFECTED	2.6	2.0	1.9	-	-	-
- hepatocellular hypertrophy	GRADE 1	-	5	3	-	-	-
	GRADE 2	-	-	7	-	-	-
	TOTAL AFFECTED	-	5	10	-	-	-
	MEAN GRADE/TISS.AFFECTED	-	1.0	1.7	-	-	-
- mitotic figures	GRADE 1	-	1	2	-	-	-
	TOTAL AFFECTED	-	1	2	-	-	-
	MEAN GRADE/TISS.AFFECTED	-	1.0	1.0	-	-	-

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INDIVIDUAL ANIMAL DATA — CXR : 0486s

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SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, Control

ANIMAL NUMBER :	1 MK0	2 MK0	3 MK0	4 MK0	5 MK0	6 MK0	7 MK0	8 MK0	9 MK0	10 MK0
LIVER	+	+	+	+	+	+	+	+	+	+
- mononuclear infilt.	.	1.	1.	1.	1.	.	.	.	1.	.
- inflammatory cell	1.	.	1.	.	.	1.	1.	1.	1.	1.
- vacuolation, hepat.	3.	3.	2.	2.	3.	2.	3.	1.	3.	3.
- mitotic figures	.	1.	.	1.	1.	1.	1.	1.	.	1.
THYROID GLAND	(-	-	-	(-	0	-	-	-	-	-

PATHOLOGY REPORT — PAGE : 17/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, Control

ANIMAL NUMBER :	11 MR1	12 MR1	13 MR1	14 MR1	15 MR1	16 MR1	17 MR1	18 MR1	19 MR1	20 MR1
LIVER	+	+	+	+	+	+	+	+	+	+
- mononuclear infilt.	1.	.	.	.	1.	1.	1.	1.	1.	.
- inflammatory cell	1.	1.	1.	.	1.	1.	1.	1.	1.	1.
- vacuolation, hepat.	2.	2.	1.	2.	2.	2.	3.	2.	2.	2.
- mitotic figures	.	.	.	1.	.	1.	.	1.	.	1.
THYROID GLAND	-	-	-	-	-	-	-	0	0	(-

PATHOLOGY REPORT — PAGE : 18/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, Control

ANIMAL NUMBER :	21 MR2	22 MR2	23 MR2	24 MR2	25 MR2	26 MR2	27 MR2	28 MR2	29 MR2	30 MR2
LIVER	+	+	+	+	+	+	+	+	+	+
- mononuclear infilt.	.	.	1.	1.	.	1.	1.	.	.	1.
- inflammatory cell	.	1.	1.	1.	1.	1.	.	1.	1.	1.
- vacuolation, hepat.	3.	3.	3.	2.	3.	2.	1.	2.	3.	2.
- mitotic figures	.	.	.	.	.	.	.	1.	.	.
THYROID GLAND	-	-	-	(-	(-	-	-	-	-	-

PATHOLOGY REPORT — PAGE : 19/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, Control

ANIMAL NUMBER :	31 MR3	32 MR3	33 MR3	34 MR3	35 MR3	36 MR3	37 MR3	38 MR3	39 MR3	40 MR3
LIVER	+	+	+	+	+	+	+	+	+	+
- mononuclear infilt.	1.	.	1.	.	.	.	1.	1.	1.	1.
- inflammatory cell	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
- vacuolation, hepat.	3.	2.	3.	3.	3.	2.	3.	3.	2.	2.
THYROID GLAND	-	-	-	-	-	-	-	-	-	(-

PATHOLOGY REPORT — PAGE : 20/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 02, PFOS 20 ppm

ANIMAL NUMBER :	41 MK0	42 MK0	43 MK0	44 MK0	45 MK0	46 MK0	47 MK0	48 MK0	49 MK0	50 MK0
LIVER	+	+	+	+	+	+	+	+	+	+
- mononuclear infilt.	.	.	1.	.	.	1.	.	1.	.	.
- inflammatory cell	1.	1.	1.	1.	1.	1.	.	.	1.	1.
- vacuolation, hepat.	3.	3.	3.	3.	3.	2.	2.	3.	3.	3.
- hypertrophy, hepat.	1.	1.	1.	1.	1.	.	1.	.	1.	1.
- mitotic figures	1.	1.	1.	.	.	1.	1.	.	1.	1.
THYROID GLAND	(-	(-	(-	0	-	+	-	(-	(-	+
- ectopic thymus	.	.	.	.	.	(P.	.	.	.	.
- branchiogenic cyst	.	.	.	.	.	.	.	.	.	(1.

PATHOLOGY REPORT — PAGE : 21/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 02, PFOS 20 ppm

ANIMAL NUMBER :	51 MR1	52 MR1	53 MR1	54 MR1	55 MR1	56 MR1	57 MR1	58 MR1	59 MR1	60 MR1
LIVER	+	+	+	+	+	+	+	+	+	+
- congestion	.	.	.	.	2.	1.	.	.	.	.
- mononuclear infilt.	.	1.	.	.	1.	1.	1.	.	1.	.
- inflammatory cell	1.	1.	.	1.	.	.	1.	1.	.	1.
- vacuolation, hepat.	2.	.	2.	.	.	2.	1.	2.	2.	2.
- hypertrophy, hepat.	1.	.	.	2.	.	.	.	1.	1.	1.
- mitotic figures	1.	1.	1.	.	.	1.	1.	1.	1.	1.
THYROID GLAND	-	-	-	-	-	-	-	-	-	-

PATHOLOGY REPORT — PAGE : 22/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 02, PFOS 20 ppm

ANIMAL NUMBER :	61 MR2	62 MR2	63 MR2	64 MR2	65 MR2	66 MR2	67 MR2	68 MR2	69 MR2	70 MR2
LIVER	+	+	+	+	+	+	+	+	+	+
- congestion	.	.	.	.	.	.	.	1.	.	.
- inflammatory cell	1.	1.	1.	1.	1.	1.	1.	1.	.	1.
- vacuolation, hepat.	3.	3.	1.	2.	2.	1.	2.	.	2.	3.
- hypertrophy, hepat.	1.	1.	.	.	.	.	1.	.	.	1.
- mitotic figures	.	1.	.	.	.	.	1.	.	.	1.
THYROID GLAND	(-	-	-	(-	0	-	-	-	-	-

PATHOLOGY REPORT — PAGE : 23/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 02, PFOS 20 ppm

ANIMAL NUMBER :	71 MR3	72 MR3	73 MR3	74 MR3	75 MR3	76 MR3	77 MR3	78 MR3	79 MR3	80 MR3
LIVER	+	+	+	+	+	+	+	+	+	+
- mononuclear infilt.	1.	.	1.	1.	1.	1.	1.	.	1.	.
- inflammatory cell	1.	1.	.	.	.	1.	1.	1.	.	1.
- vacuolation, hepat.	3.	2.	1.	1.	2.	1.	2.	3.	2.	3.
- hypertrophy, hepat.	.	.	1.	1.	1.	.	1.	.	.	1.
- mitotic figures	.	.	.	.	1.	.	.	.	.	.
THYROID GLAND	-	-	0	(-	-	-	-	-	-	-

PATHOLOGY REPORT — PAGE : 24/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 03, PFOS 100 ppm

ANIMAL NUMBER :	81 MK0	82 MK0	83 MK0	84 MK0	85 MK0	86 MK0	87 MK0	88 MK0	89 MK0	90 MK0
LIVER	+	+	+	+	+	+	+	+	+	+
- mononuclear infilt.	1.	1.	1.	.	.	.	.	.	.	.
- inflammatory cell	1.	.	.	1.	1.	1.	.	1.	.	1.
- vacuolation, hepat.	2.	1.	2.	3.	2.	2.	2.	2.	2.	2.
- hypertrophy, hepat.	2.	1.	1.	2.	2.	2.	2.	2.	2.	2.
- mitotic figures	.	1.	1.	1.	1.	.	1.	1.	1.	1.
THYROID GLAND	0	0	0	0	0	-	-	-	0	(-

PATHOLOGY REPORT — PAGE : 25/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 03, PFOS 100 ppm

ANIMAL NUMBER :	91 MR1	92 MR1	93 MR1	94 MR1	95 MR1	96 MR1	97 MR1	98 MR1	99 MR1	100 MR1
LIVER	+	+	+	+	+	+	+	+	+	+
- mononuclear infilt.	.	.	.	.	.	1.	.	.	1.	1.
- inflammatory cell	1.	1.	.	1.	1.	1.	1.	1.	1.	1.
- vacuolation, hepat.	2.	2.	2.	2.	.	1.	2.	.	.	.
- hypertrophy, hepat.	3.	2.	2.	2.	2.	2.	2.	2.	2.	2.
- mitotic figures	1.	1.	1.	.	.	1.	1.	.	.	1.
THYROID GLAND	-	-	-	-	-	-	-	+	-	+
- branchiogenic cyst	.	.	.	.	.	.	.	(1.	.	(1.

PATHOLOGY REPORT — PAGE : 26/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 03, PFOS 100 ppm

ANIMAL NUMBER :	101 MR2	102 MR2	103 MR2	104 MR2	105 MR2	106 MR2	107 MR2	108 MR2	109 MR2	110 MR2
LIVER	+	+	+	+	+	+	+	+	+	+
- mononuclear infilt.	.	.	1.	.	.	.	1.	.	1.	.
- inflammatory cell	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
- vacuolation, hepat.	2.	1.	2.	2.	2.	2.	2.	.	1.	1.
- hypertrophy, hepat.	3.	2.	2.	2.	2.	2.	2.	2.	2.	2.
- mitotic figures	1.	.	1.	.	.	.	.	.	.	.
THYROID GLAND	-	-	(-	-	(-	-	-	-	-	-

PATHOLOGY REPORT — PAGE : 27/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 03, PFOS 100 ppm

ANIMAL NUMBER :	111 MR3	112 MR3	113 MR3	114 MR3	115 MR3	116 MR3	117 MR3	118 MR3	119 MR3	120 MR3
LIVER	+	+	+	+	+	+	+	+	+	+
- mononuclear infilt.	.	1.	.	1.	1.	.	.	.	1.	.
- inflammatory cell	1.	1.	1.	1.	.	1.	1.	1.	1.	.
- vacuolation, hepat.	2.	2.	1.	.	2.	2.	.	2.	2.	.
- hypertrophy, hepat.	1.	2.	2.	2.	1.	2.	2.	1.	2.	2.
- mitotic figures	.	.	.	.	.	.	1.	.	.	1.
THYROID GLAND	-	(-	(-	-	-	-	-	-	-	-

PATHOLOGY REPORT PAGE : 28/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

ANIMAL HEADING DATA
DOSE GROUP : 01, Control

ANIMAL NUMBER	SEX M/F	DEFINED STATE OF NECROPSY	FINAL STATE OF NECROPSY	TEST DAYS	FIRST DAY UNDER TEST	LAST DAY UNDER TEST	DATE OF NECROPSY
1	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
2	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
3	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
4	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
5	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
6	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
7	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
8	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
9	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
10	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
11	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
12	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
13	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
14	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
15	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
16	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
17	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
18	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
19	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
20	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
21	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
22	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
23	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
24	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
25	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
26	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
27	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
28	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
29	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
30	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
31	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
32	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
33	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
34	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
35	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
36	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
37	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
38	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
39	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
40	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07

PATHOLOGY REPORT — PAGE : 29/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 1

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 2

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 30/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 — * ANIMAL NO. : 3

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 — * ANIMAL NO. : 4

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 31/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 5

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Tissue not present for histologic examination

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 6

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 32/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 7

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 8

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 33/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 9

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

---

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 10

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT PAGE : 34/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 11

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

---

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 12

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 35/ 90
CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS)
TEST SYSTEM : RAT, 13 weeks, feeding
SPONSOR : CXR Biosciences Ltd.

PATHOL. NO.: 07059 VOO
DATE : 19-MAR-08
PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control

MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 13

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 14

* MICROSCOPIC FINDINGS

LIVER:
-vacuolation, hepatocellular, periportal, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 36/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control — MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 — * ANIMAL NO. : 15

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R1
DAYS ON TEST : 36 — * ANIMAL NO. : 16

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 37/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control — MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 — * ANIMAL NO. : 17

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R1
DAYS ON TEST : 36 — * ANIMAL NO. : 18

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Tissue not present for histologic examination

PATHOLOGY REPORT — PAGE : 38/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control — MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 — * ANIMAL NO. : 19

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 2
THYROID GLAND (BOTH LOBES):
Tissue not present for histologic examination

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* STATE AT NECROPSY: R1
DAYS ON TEST : 36 — * ANIMAL NO. : 20

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 39/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control — MALE

* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 21

* MICROSCOPIC FINDINGS

LIVER:
-vacuolation, hepatocellular, periportal, grade 3
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 22

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 3
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 23

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3

PATHOLOGY REPORT | PAGE : 40/ 90
INDIVIDUAL ANIMAL DATA | CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) | PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding | DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. | PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control MALE

CONT./FF. ANIMAL NO. : 23

THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 24

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 25

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 41/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control — MALE

* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 26

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 27

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-vacuolation, hepatocellular, periportal, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT PAGE : 42/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control MALE

* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 28

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 29

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 43/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control — MALE

* STATE AT NECROPSY: R2
DAYS ON TEST : 64 — * ANIMAL NO. : 30

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 31

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT PAGE : 44/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 32

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 33

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 3
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 45/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control — MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 34

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 3
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 35

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 3
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 46/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control — MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 36

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 37

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 3
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT PAGE : 47/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 38

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 39

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 48/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 01, Control — MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 40

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 49/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

ANIMAL HEADING DATA
DOSE GROUP : 02, PFOS 20 ppm

ANIMAL NUMBER	SEX M/F	DEFINED STATE OF NECROPSY	FINAL STATE OF NECROPSY	TEST DAYS	FIRST DAY UNDER TEST	LAST DAY UNDER TEST	DATE OF NECROPSY
41	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
42	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
43	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
44	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
45	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
46	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
47	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
48	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
49	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
50	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
51	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
52	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
53	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
54	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
55	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
56	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
57	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
58	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
59	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
60	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
61	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
62	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
63	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
64	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
65	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
66	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
67	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
68	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
69	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
70	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
71	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
72	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
73	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
74	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
75	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
76	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
77	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
78	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
79	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
80	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07

PATHOLOGY REPORT PAGE : 50/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 41

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 42

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 51/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 — * ANIMAL NO. : 43

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: K0
DAYS ON TEST : 8 — * ANIMAL NO. : 44

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-hepatocellular hypertrophy, centrilobular, grade 1
THYROID GLAND (BOTH LOBES):
Tissue not present for histologic examination

PATHOLOGY REPORT — PAGE : 52/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 — * ANIMAL NO. : 45

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-hepatocellular hypertrophy, hepatocellular, centrilobular, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: K0
DAYS ON TEST : 8 — * ANIMAL NO. : 46

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
-ectopic thymus, unilateral

PATHOLOGY REPORT — PAGE : 53/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 47

* MICROSCOPIC FINDINGS

LIVER:
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 48

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-vacuolation, hepatocellular, diffuse, grade 3
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 54/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 49

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 50

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
-branchiogenic cyst, unilateral, grade 1

PATHOLOGY REPORT — PAGE : 55/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 51

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 52

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT PAGE : 56/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 53

* MICROSCOPIC FINDINGS

LIVER:
-vacuolation, hepatocellular, periportal, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 54

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 57/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 55

* MICROSCOPIC FINDINGS

LIVER:
-congestion, grade 2
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 56

* MICROSCOPIC FINDINGS

LIVER:
-congestion, grade 1
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT PAGE : 58/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 57

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 58

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 59/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 — * ANIMAL NO. : 59

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R1
DAYS ON TEST : 36 — * ANIMAL NO. : 60

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT PAGE : 60/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm MALE

* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 61

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-hepatocellular hypertrophy, centrilobular, grade 1
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 62

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 61/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: R2
DAYS ON TEST : 64 — * ANIMAL NO. : 63

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 — * ANIMAL NO. : 64

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 62/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: R2
DAYS ON TEST : 64 — * ANIMAL NO. : 65

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 2
THYROID GLAND (BOTH LOBES):
Tissue not present for histologic examination

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 — * ANIMAL NO. : 66

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 63/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: R2
DAYS ON TEST : 64 — * ANIMAL NO. : 67

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, diffuse, grade 2
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 — * ANIMAL NO. : 68

* MICROSCOPIC FINDINGS

LIVER:
-congestion, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 64/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 69

* MICROSCOPIC FINDINGS

LIVER:
-vacuolation, hepatocellular, periportal, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 70

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 65/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 71

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 72

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 66/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 73

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-vacuolation, hepatocellular, diffuse, grade 1
-hepatocellular hypertrophy, centrilobular, grade 1
THYROID GLAND (BOTH LOBES):
Tissue not present for histologic examination

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 74

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-vacuolation, hepatocellular, periportal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 1
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 67/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 75

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 76

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT PAGE : 68/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 77

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 78

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 69/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 02, PFOS 20 ppm — MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 79

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-vacuolation, hepatocellular, periportal, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 80

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-hepatocellular hypertrophy, centrilobular, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 70/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

ANIMAL HEADING DATA
DOSE GROUP : 03, PFOS 100 ppm

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY		TEST DAYS	FIRST AND LAST DAY UNDER TEST		DATE OF NECROPSY
81	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
82	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
83	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
84	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
85	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
86	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
87	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
88	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
89	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
90	M	K0	K0	8	29-NOV-06	06-DEC-06	06-DEC-06
91	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
92	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
93	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
94	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
95	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
96	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
97	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
98	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
99	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
100	M	R1	R1	36	29-NOV-06	03-JAN-07	03-JAN-07
101	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
102	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
103	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
104	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
105	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
106	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
107	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
108	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
109	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
110	M	R2	R2	64	29-NOV-06	31-JAN-07	31-JAN-07
111	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
112	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
113	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
114	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
115	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
116	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
117	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
118	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
119	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07
120	M	R3	R3	92	29-NOV-06	28-FEB-07	28-FEB-07

PATHOLOGY REPORT — PAGE : 71/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 — * ANIMAL NO. : 81

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Tissue not present for histologic examination

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* STATE AT NECROPSY: K0
DAYS ON TEST : 8 — * ANIMAL NO. : 82

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-vacuolation, hepatocellular, periportal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Tissue not present for histologic examination

PATHOLOGY REPORT PAGE : 72/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 83

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 1
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Tissue not present for histologic examination

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* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 84

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 3
-hepatocellular hypertrophy, centrilobular, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Tissue not present for histologic examination

PATHOLOGY REPORT — PAGE : 73/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 — * ANIMAL NO. : 85

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Tissue not present for histologic examination

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* STATE AT NECROPSY: K0
DAYS ON TEST : 8 — * ANIMAL NO. : 86

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 74/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 87

* MICROSCOPIC FINDINGS

LIVER:
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: K0
DAYS ON TEST : 8 * ANIMAL NO. : 88

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 75/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 8 — * ANIMAL NO. : 89

* MICROSCOPIC FINDINGS

LIVER:
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Tissue not present for histologic examination

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* STATE AT NECROPSY: K0
DAYS ON TEST : 8 — * ANIMAL NO. : 90

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

PATHOLOGY REPORT PAGE : 76/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 91

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 3
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 92

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 77/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm — MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 — * ANIMAL NO. : 93

* MICROSCOPIC FINDINGS

LIVER:
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

---

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 — * ANIMAL NO. : 94

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT PAGE : 78/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 95

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 96

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 79/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm — MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 — * ANIMAL NO. : 97

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R1
DAYS ON TEST : 36 — * ANIMAL NO. : 98

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
-branchiogenic cyst, unilateral, grade 1

PATHOLOGY REPORT PAGE : 80/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm MALE

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 99

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

---

* STATE AT NECROPSY: R1
DAYS ON TEST : 36 * ANIMAL NO. : 100

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
-branchiogenic cyst, unilateral, grade 1

PATHOLOGY REPORT — PAGE : 81/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm — MALE

* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 101

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 3
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 102

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 82/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm — MALE

* STATE AT NECROPSY: R2
DAYS ON TEST : 64 — * ANIMAL NO. : 103

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 — * ANIMAL NO. : 104

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 83/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm — MALE

* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 105

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 106

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 84/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm — MALE

* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 107

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 * ANIMAL NO. : 108

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 85/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
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TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm — MALE

* STATE AT NECROPSY: R2
DAYS ON TEST : 64 — * ANIMAL NO. : 109

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R2
DAYS ON TEST : 64 — * ANIMAL NO. : 110

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT PAGE : 86/ 90
INDIVIDUAL ANIMAL DATA CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 111

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 112

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

PATHOLOGY REPORT
INDIVIDUAL ANIMAL DATA

PAGE : 87/ 90
CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS)
TEST SYSTEM : RAT, 13 weeks, feeding
SPONSOR : CXR Biosciences Ltd.

PATHOL. NO.: 07059 VOO
DATE : 19-MAR-08
PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm

MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 113

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Only one of paired organs examined/present
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 * ANIMAL NO. : 114

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 88/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm — MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 115

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 116

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 89/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm — MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 117

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-hepatocellular hypertrophy, centrilobular, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 118

* MICROSCOPIC FINDINGS

LIVER:
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

PATHOLOGY REPORT — PAGE : 90/ 90
INDIVIDUAL ANIMAL DATA — CXR : 0486s

TEST ITEM : Perfluorooctane Sulfonate (PFOS) — PATHOL. NO.: 07059 VOO
TEST SYSTEM : RAT, 13 weeks, feeding — DATE : 19-MAR-08
SPONSOR : CXR Biosciences Ltd. — PathData®System V6.2d1

TEXT OF MICROSCOPIC FINDINGS
DOSE GROUP : 03, PFOS 100 ppm — MALE

* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 119

* MICROSCOPIC FINDINGS

LIVER:
-mononuclear cell infiltrate(s), periportal-/biliar, grade 1
-(mixed) inflammatory cell infiltration, focal, grade 1
-vacuolation, hepatocellular, periportal, grade 2
-hepatocellular hypertrophy, centrilobular, grade 2
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

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* STATE AT NECROPSY: R3
DAYS ON TEST : 92 — * ANIMAL NO. : 120

* MICROSCOPIC FINDINGS

LIVER:
-hepatocellular hypertrophy, centrilobular, grade 2
-mitotic figures, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted

ECOA
ETHICS & COMPLIANCE OFFICER ASSOCIATION

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AGENDA

Updated 8/11/08

[Tuesday - Pre-conference workshops] [Wednesday] [Thursday] [Friday]

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Tuesday, September 23, 2008

Pre-conference workshops
9:00 a.m. - 4:00 p.m.
This year's pre-conference workshops are scheduled for Tuesday, September 23, 2008. Full-day workshop times are 9:00 a.m. to 4:00 p.m. Half-day workshop times are 9:00 a.m. to 12:00 p.m. and 1:00 p.m. to 4:00 p.m. **Pre-registration is required.** Pre-conference workshops include continental breakfast, coffee breaks, and lunch.

Please use the registration code to the left of the workshop title to register for the workshop you would like to attend. As they become available, you can click on the registration code to read a description of the workshop. When registering for two sessions (one half-day AM and one half-day PM) use the appropriate combination code in the second list below. **If you have previously registered for the conference, please call the ECOA at 1.781.647.9333 to register by phone for your pre-conference workshops.**

Single pre-conference workshops:

Code	Session Titles

PC-BEECP	Building an Effective Ethics & Compliance Program [9 am-4 pm]
PC-TYPTNL	Taking Your Program to the Next Level [9 am-4 pm] Click on the registration code to view a description.
PC-TATM	Shaping the Middle: How to Create and Drive the Tone Down to All Levels of Management [9 am-12 pm] Click on the registration code to view a description.
PC-AEECP	Assessing the Effectiveness of Your Ethics & Compliance Program [9 am-12 pm]
PC-CII	Conducting Internal Investigations [1-4 pm]
(PC-CECB)	Creative Engagement and Communication 101/Director's Showcase [1-4 pm] Click on the registration code to view a description.

AM/PM Combinations

Combination Code	Session Titles
PC-TATM/CII	Shaping the Middle: How to Create and Drive the Tone Down to All Levels of Management [9 am-12 pm] Conducting Internal Investigations [1-4 pm]
PC-TATM/CECB	Shaping the Middle: How to Create and Drive the Tone Down to All Levels of Management [9 am-12 pm] Creative Engagement and Communication 101/Director's Showcase [1-4 pm]
PC-AEECP/CECB	Assessing the Effectiveness of Your Ethics and Compliance Program [9 am-12 pm] Creative Engagement and Communication 101/Director's Showcase [1-4 pm]
PC-AEECP/CII	Assessing the Effectiveness of Your Ethics and Compliance Program [9 am-12 pm] Conducting Internal Investigations [1-4 pm]

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New Conference Attendee Orientation
4:30 p.m. - 5:30 p.m.

Created especially for first-time attendees. Since many new ECOA members attend the annual conference, and there are a number of first-time conference participants, we invite you to a special orientation session to learn more about the Ethics & Compliance Officer Association and our largest conference of the year. This is a perfect time to: (1) begin networking with other ECOA members; (2) learn more about ECOA programs, services, and benefits, and; (3) learn how to navigate the conference so that it maximally meets your interests and needs. It's also a good time to meet members of the ECOA staff and board. We look forward to meeting you!

Retail & Consumer Products Industry Group Meeting
* Time to be determined.

Wednesday, September 24, 2008
Registration & Networking Breakfast
Vendor Exhibit Area Opens
7:00 - 9:00 a.m.

An opportunity to visit with providers of ethics and compliance products and services in the vendor exhibit area.

Welcome
9:00 - 9:45 a.m.

- Keith Darcy, Executive Director, Ethics & Compliance Officer Association

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Plenary Session

10:00 - 11:45 a.m.

***The Ethics & Compliance Handbook*: An Analysis in Relation to the U.S. Sentencing Guidelines**

- Honorable Ruben Castillo (U.S. Sentencing Commission)
- Beryl Howell (U.S. Sentencing Commission)
- Andrew Weissmann (Jenner & Block LLP)
- Andrea Bonime-Blanc (Daylight Forensic & Advisory LLP; Chair, Global Strategy Committee, ECOA Board of Directors)
- MODERATOR: Keith Darcy (Ethics and Compliance Officer Association)

Lunch & Keynote Speaker
12:15 - 1:45 p.m.

Frank Bucaro (Frank C. Bucaro and Associates)
Taking the High Road: How to Succeed Ethically When Others Bend the Rules

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Concurrent Sessions
2:00 - 3:15 p.m.

- **The Role of the Ethics Officer in Creating Culture in the Corporation**
  Charles Chadwick (BAE Systems)
- **Evaluating Next-Generation Employee Training and Communication Tools**
  Jeremy Wilson (Cisco Systems Inc.)
- **Benchmarking Hotline Data: How Does Your Hotline Measure Up?**
  Carrie Penman (Ethical Leadership Group, a Global Compliance company)
- **Global Privacy and Data Protection**
  Lisa Sotto (Hunton & Williams)
  Isabelle Theisen (First Advantage)
  Rebecca Herold (Rebecca Herold & Associates, LLC)
- **Managing Ethics and Compliance Crises**
  William Senhauser (Fannie Mae)
- **Engaging Senior Management**

Karen Moore (Philip Morris International)

- **How to Work with and Not Work with the GC's Office**
  Biz Scott (Patton Boggs LLP)
- **Societe Generale: Anatomy of an Ethics and Compliance Failure**
  Gary Brown (Baker, Donelson, Bearman, Caldwell & Berkowitz LLP)

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Concurrent Sessions
3:30 - 4:45 p.m.

- **DPAs and Corporate Monitors: What Are the Ethical Upsides and Downsides?**
  Ryan McConnell (Office of the U.S. Attorney)
  Larry Finder (Haynes Boone LLP)
- **Creating High-Impact Annual Reports**
  Joan Dubinsky (International Monetary Fund)
- **Compliance Programs under Cross Examination**
  Scott Avelino (KPMG LLP)
- **Dangerous Silence: What Employees Won't Tell You, Why, and What You Can Do about It**
  Gary Edwards (Ethos International)
- **Cyclic Training: Integrating Multiple Forms of E-Learning Training and Communications**
  Tina Wyder (Accenture)
- **Re-Imagining the Third Iteration of Your Risk Assessment**
  John Stoxen (3M)
- **The State of Corporate Social Responsibility (CSR) in Korea**
  Young-Chan Nam (SK telecom)
- **Justin Tegrity Trains the Board - An Interactive Mock Board Training** *
  Donna Boehme (Principal, Compliance Strategists LLC)
  Steve Grubb (Diageo)
  Jo Pease (former Chief Ethics and Compliance Officer, Shell Oil Company)
  Win Swenson (Compliance Systems Legal Group)

  ** extended session until 5:30 p.m.*

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Networking Reception

6:00 - 7:00 p.m.

Annual Conference Dinner
7:00 - 9:00 p.m.
After a full day of conference activities, this will be an opportunity to meet new ECOA members and network with colleagues. Guests are welcome to attend at no additional fee.

Thursday, September 25, 2008
Networking Breakfast & Vendor Exhibit Area Opens
Registration Open
7:00 - 8:00 a.m.

ECOA MEMBER MEETING
8:00 - 9:00 a.m.
Members are invited to the association's annual meeting.

Plenary Session
9:00 - 10:45 a.m.

The Great Debate: Righting the Balance
If Sarbanes-Oxley Is Ruled Unconstitutional, What Should Replace It: Improved Legislation (emphasis on rules and compliance) or Something Global and Principles-based (emphasis on ethics and CSR)?

- Debaters TBA

Concurrent Sessions
11:00 a.m. - 12:15 p.m.

- **Investigations 101 for the Non-Investigator**
  Meric Bloch (Adecco Group North America)
- **The Latest on the Recent Changes to the Federal Acquisition Regulations (FAR)**
  David Laufman (Kelley Drye & Warren LLP)
- **Cross-Cultural Issues in Business Ethics**
  Simon Webley (Institute of Business Ethics)
- **Surveys, Ratings, and Metrics: Ethical Issues in Data Collection and Analysis**
  Brad Agle (University of Pittsburgh)
- **Analysis of DOJ Convictions against CEOs**
  Greg Riggs (Compliance Systems Legal Group)
- **Fine Tuning Your Code of Conduct When It's Up for Revision**
  Randall Peterson (Sempra Energy)
- **Difficult but Not Impossible: Developing and Measuring an Ethical Corporate Culture**
  Len Brooks (University of Toronto)
- **Integrating the ECOA's *Ethics on Trial* DVD into Your Organization's Training**
  David Schmidt (OMI, an IDNA company)

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Lunch and Keynote Speaker
12:30 - 1:45 p.m.

Lynn E. Turner
Member, Advisory Committee on the Auditing Profession, U.S. Treasury Department
Member, Standards Advisory Group, PCAOB
Member, FASB Investor Technical Advisory Committee
Former Chief Accountant, U.S. Securities and Exchange Commission

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Concurrent Sessions
2:00 - 3:15 p.m.

- **Culture Matters: FCPA and Anti-Corruption Initiatives in Europe**
  Laurence Harris (Edwards Angell Palmer & Dodge UK LLP)
  Sam Yoon (Textron Industrial Segment)
- **Optimizing Corporate Ethics and Compliance Programs in the Federal Government**
  Michael Korwin (FDIC)

Emil Moschella (formerly with the FBI)

- **Using Crisis Communications to Manage Your Company's Reputation through Tough Times**
  Lee Essrig
- **Data Mining to Detect Fraud, Waste, and Abuse**
  Mia Okinaga (Kaiser Permanente)
- **"Reporting on Responsibility: The New Ethics Challenge"**
  Anita Baker (University of Maryland University College)
  Santiago Reich (Ethical Leadership Group, A Global Compliance Company)
- **A Principles-Based Approach to Integrating Governance, Risk, and Compliance**
  Bobby Kipp (PricewaterhouseCoopers)
- **How Effective Is Your Employee Training?**
  Leslie Altizer (Ethics Resource Center)
  Kevin Caffrey (Ethics Resource Center)
- **On the Road Again: Cultural Considerations in Developing Effective Ethics and Compliance Programs**
  Win Swenson (Compliance Systems Legal Group)

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Concurrent Sessions
3:30 - 4:45 p.m.

- **The Latest Research on Ethical Decision-Making and Culture**
  Jerry Goldstein (Washington State University at Vancouver)
  Francesca Gino (University of North Carolina at Chapel Hill)
  MODERATOR: Gretchen Winter (University of Illinois at Urbana-Champaign)
- **Rock and a Hard Place: Maintaining an Ethics Program in Times of Transition**
  Maria Conner (USA Space Operations)
  Brian Sears (Lockheed Martin Company)
  Lani de Benedictis (NASA Jet Propulsion Laboratory)
  Charles Giesting (Rolls-Royce)
- **Organizing and Maintaining a Regional Ethics and Compliance Network**
  Danna Walton (South Texas College of Law)
  Linda Lipps (CenterPoint Energy, Inc.)
- **Ethics and Compliance Issues in Latin America**
  Zeke Barrios (Kraft Foods Global, Inc.)
- **Using Outcome Data to Demonstrate the Effectiveness of an Ethics and Compliance Program**

Art Weiss (Tamko)

- **Ethics Education through an Engaging Series of Custom Video Vignettes**
  David LaJoie (Raytheon)
- **Conducting Third Party FCPA Due Diligence**
  Scott Moritz (Daylight Forensic & Advisory LLC)
  Jay Perlman (Daylight Forensic & Advisory LLC)
- **Compliance and Ethics Moot Court**
  Jeff Kaplan (Kaplan & Walker LLP)
  Rebecca Walker (Kaplan & Walker LLP) *

** extended session until 5:15 p.m.*

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Thursday Evening Reception & Dinner
6:00 - 9:00 p.m.
Conference attendees, speakers and exhibitors will enjoy an evening of entertainment and activities. Guests & children are welcome to attend but require separate registration.

Guest Fees:
$50 for 1 guest
$80 for 2 or more guests

Friday, September 26, 2008
Networking Breakfast
7:00 - 8:00 a.m.

Plenary Session
8:00 - 9:45 a.m.

Measuring the Divide between HR and Ethics

- Patricia Harned, Ph.D. (Ethics Resource Center)

- Deborah Keary (Society for Human Resources and Management)
- Keith Darcy (Ethics and Compliance Officer Association)

Concurrent Sessions
10:00 - 11:15 a.m.

- **Can They Sue Me, Too? Personal Liability Issues for Chief Ethics and Compliance Officers**
  Ian Roffman (Nutter McClennen & Fish LLP)
  Jonathan Kotlier (Nutter McClennen & Fish LLP)
- **Making the Business Case for Anti-Corruption Initiatives**
  Michael Pedersen (World Economic Forum)
  Mark Snyderman (Coca-Cola)
  Glenn T. Ware (PricewaterhouseCoopers LLP)
- **College Bowls: Leveraging the Relationship between Business Schools and Organizational Ethics and Compliance Programs**
  Tom White (Loyola Marymount University)
  Debbie Asirvatham (McGill University)
  Cecile Dupin (McGill University)
  Tiffany Uman (McGill University)
- **Completing the Circle: What Corporate Ethics Managers Can Learn from the Public Sector**
  Deni Elliott (Metropolitan Water District of Southern California)
  Carla Miller (City of Jacksonville)
- **Stark Lessons in Conflict of Interest from the 2007 U.S. Student Loan Scandal**
  Leigh-Anne Walker (Ethical Leadership Group, A Global Compliance Company)
- **The Latest Labor-Related Gotchas You Need to Know**
  Mindy Chapman (Mindy Chapman & Associates LLP)
  Alice Peterson (Syrus Global)

Industry Group Meetings

11:30 a.m. - 12:30 p.m.

- Cross-Industry Group
- Financial Services Industry Group
- Healthcare Industry Group
- Utility Industry Group

12:30 p.m. CONFERENCE ENDS

A boxed lunch will be provided to go.

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Agenda subject to change. *Check this page often for updates!*

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