

3M MEDICAL DEPARTMENT
CORPORATE TOXICOLOGY

To: John Butenhoff
Andrew Seacat

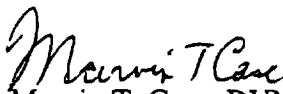
From: Marvin Case

Date: 5 April 2000

Subject: Liver Slide Review

I have completed my microscopic review of the liver sections of the 14-week sacrifice rats on the PFOS chronic study. My findings are listed, by group, on attached pages. My overall conclusions are:

- 1) Centrolobular hepatocyte hypertrophy is present in group 5 males and females. In the males, but not in the females, the hepatocyte hypertrophy is accompanied by increased number of cells with lipid type cytoplasmic vacuoles.
- 2) Centrolobular hepatocyte hypertrophy is present in group 4 males but there is no increase in cells with lipid type cytoplasmic vacuoles.
- 3) Centrolobular hepatocyte hypertrophy is not present in group 4 females.
- 4) Group 2 and 3 animals (male and female) were not different from controls.
- 5) The centrolobular hepatocyte hypertrophy is a compound-related change but is an adaptive change and not necessarily an adverse change. When increased number of cells with lipid type cytoplasmic vacuoles occur, I would consider that an adverse change. Thus, for liver histologic changes, my NOAEL is group 4, male & female; and my compound-related NOEL is group 3 males and group 4 females.


Marvin T. Case, DVM, PhD

Findings on Microscopic Review of Liver Sections
From 14-week Sacrifice of PFOS Rats
(review done by Marvin Case, March 2000)

Group 1 Males

<u>Histologic Finding</u>	<u>Animal Number</u>				
	C92509	C92511	C92521	C92528	C92532
Foci of mononuclear cells	1	1	1	1	1
Hepatocytes with cytoplasm vacuoles, appearance of hydrophilic droplets	1	2	1	1	-
Hepatocytes with cytoplasm vacuoles, appearance of lipid droplets	1	-	1	1	-

Grade key – 1 = minimal (< 10% involvement)
2 = mild (< 30% involvement)
3 = moderate (< 60% involvement)
4 = marked (> 60% involvement)
- = finding not observed

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Group 2 Males

<u>Histologic Finding</u>	<u>Animal Number</u>				
	C92593	C92600	C92616	C92621	C92627
Foci of mononuclear cells	1	-	1	-	1
Hepatocytes with cytoplasm vacuoles, appearance of hydrophilic droplets	1	1	1	-	-
Hepatocytes with cytoplasm vacuoles, appearance of lipid droplets	-	-	1	1	-

Grade key – 1 = minimal (< 10% involvement)
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**Findings on Microscopic Review of Liver Sections
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Group 3 Males

<u>Histologic Finding</u>	<u>Animal Number</u>				
	C92640	C92645	C92662	C92676	C92684
Foci of mononuclear cells	1	1	1	-	1
Hepatocytes with cytoplasm vacuoles, appearance of hydrophilic droplets	2	1	1	-	2
Hepatocytes with cytoplasm vacuoles, appearance of lipid droplets	-	-	-	-	-
No histologic findings				X	

Grade key – 1 = minimal (< 10% involvement)
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**Findings on Microscopic Review of Liver Sections
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Group 4 Males

<u>Histologic Finding</u>	<u>Animal Number</u>				
	C92713	C92714	C92719	C92722	C92728
Foci of mononuclear cells	1	1	1	1	1
Hepatocytes with cytoplasm vacuoles, appearance of hydrophilic droplets	-	-	2	-	-
Hepatocytes with cytoplasm vacuoles, appearance of lipid droplets	2	2	2	1	2
Hypertrophic hepatocytes, generally centrilobular	3	3	2	2	3

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Findings on Microscopic Review of Liver Sections
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Group 5 Males

<u>Histologic Finding</u>	<u>Animal Number</u>				
	C92765	C92777	C92789	C92799	C92812
Foci of mononuclear cells	1	1	1	1	1
Hepatocytes with cytoplasm vacuoles, appearance of hydrophilic droplets	2	-	-	-	-
Hepatocytes with cytoplasm vacuoles, appearance of lipid droplets	1	3	2	3	3
Hypertrophic hepatocytes, generally centrilobular	3	4	4	3	4

Grade key – 1 = minimal (< 10% involvement)
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3 = moderate (< 60% involvement)
4 = marked (> 60% involvement)
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**Findings on Microscopic Review of Liver Sections
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Group 1 Females

<u>Histologic Finding</u>	<u>Animal Number</u>				
	C92880	C92887	C92898	C92903	C92905
Foci of mononuclear cells	1	1	-	1	-
Hepatocytes with cytoplasm vacuoles, appearance of hydrophilic droplets	1	-	-	1	1
Hepatocytes with cytoplasm vacuoles, appearance of lipid droplets	1	1	1	1	-

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**Findings on Microscopic Review of Liver Sections
From 14-week Sacrifice of PFOS Rats
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Group 2 Females

<u>Histologic Finding</u>	<u>Animal Number</u>				
	C92944	C92962	C92967	C92978	C92987
Foci of mononuclear cells	-	-	-	1	1
Hepatocytes with cytoplasm vacuoles, appearance of hydrophilic droplets	-	1	-	1	-
Hepatocytes with cytoplasm vacuoles, appearance of lipid droplets	1	-	-	1	-
No histologic findings			X		

Grade key – 1 = minimal (< 10% involvement)
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 3 = moderate (< 60% involvement)
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 - = finding not observed

**Findings on Microscopic Review of Liver Sections
From 14-week Sacrifice of PFOS Rats
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Group 3 Females

<u>Histologic Finding</u>	<u>Animal Number</u>				
	C92993	C93000	C93018	C93023	C93035
Foci of mononuclear cells	-	-	1	-	***
Hepatocytes with cytoplasm vacuoles, appearance of hydrophilic droplets	-	-	1	1	
Hepatocytes with cytoplasm vacuoles, appearance of lipid droplets	-	-	-	-	-
No histologic findings	X	X			

*** no slide sent for review

Grade key – 1 = minimal (< 10% involvement)
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Group 4 Females

<u>Histologic Finding</u>	<u>Animal Number</u>				
	C93051	C93064	C93071	C93085	C93109
Foci of mononuclear cells	1	1	-	1	-
Hepatocytes with cytoplasm vacuoles, appearance of hydrophilic droplets	1	-	-	-	1
Hepatocytes with cytoplasm vacuoles, appearance of lipid droplets	-	-	-	1	-
No histologic findings			X		

Grade key – 1 = minimal (< 10% involvement)
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Group 5 Females

<u>Histologic Finding</u>	<u>Animal Number</u>				
	C93111	C93127	C93143	C93155	C93169
Foci of mononuclear cells	-	-	1	-	-
Hepatocytes with cytoplasm vacuoles, appearance of hydrophilic droplets	-	2	2	-	-
Hepatocytes with cytoplasm vacuoles, appearance of lipid droplets	-	-	1	-	1
Hypertrophic hepatocytes, generally centrilobular	3	4	3	2	3

Grade key – 1 = minimal (< 10% involvement)
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