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Dose-response relationships of indicator-PCBs in orally exposed piglets: assessment of linearity and concentrations in individual tissues

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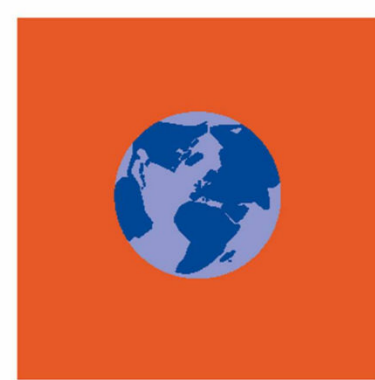
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ADEME



Agence de l'Environnement
et de la Maîtrise de l'Energie

INTRODUCTION

Because of their hand-to-mouth activity, children (1-3 yrs) are particularly exposed to PCBs through soil ingestion. Since piglets are considered as valuable model for children, this animal specie has been used to establish linearity of dose-responses I-PCBs (USEPA 2006).

The aim of the study was to assess both linearity and levels of I-PCBs in 4 tissues: liver, subcutaneous fat, muscle and cerebral.

MATERIAL & METHODS



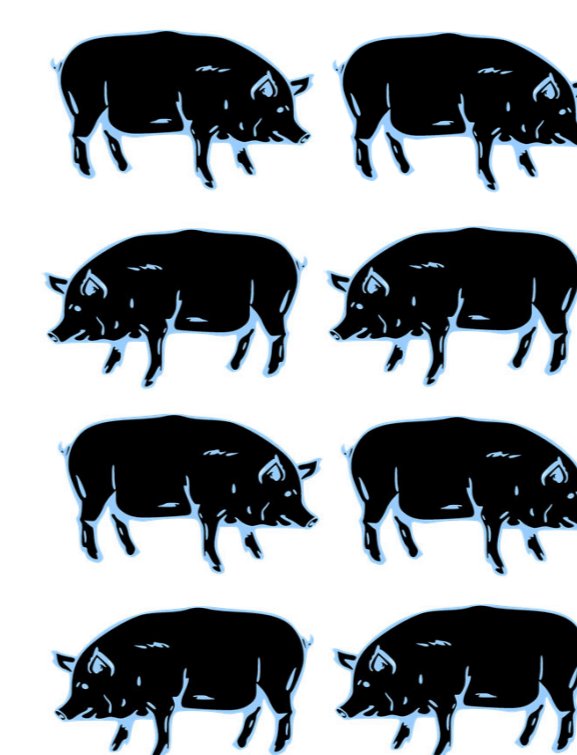
Once a day :

1xD = 190 ng I-PCB.Kg⁻¹

3xD = 560 ng I-PCB.Kg⁻¹

5xD = 940 ng I-PCB.Kg⁻¹

7xD = 1 310 ng I-PCB.Kg⁻¹



GC-MS Analysis of
liver, muscle, adipose
and brain tissues

Corn oil was spiked with Aroclor 1254 to obtain 4 increasing doses | 4x2 male piglets were exposed to one of the 4 experimental mixtures during 10 days

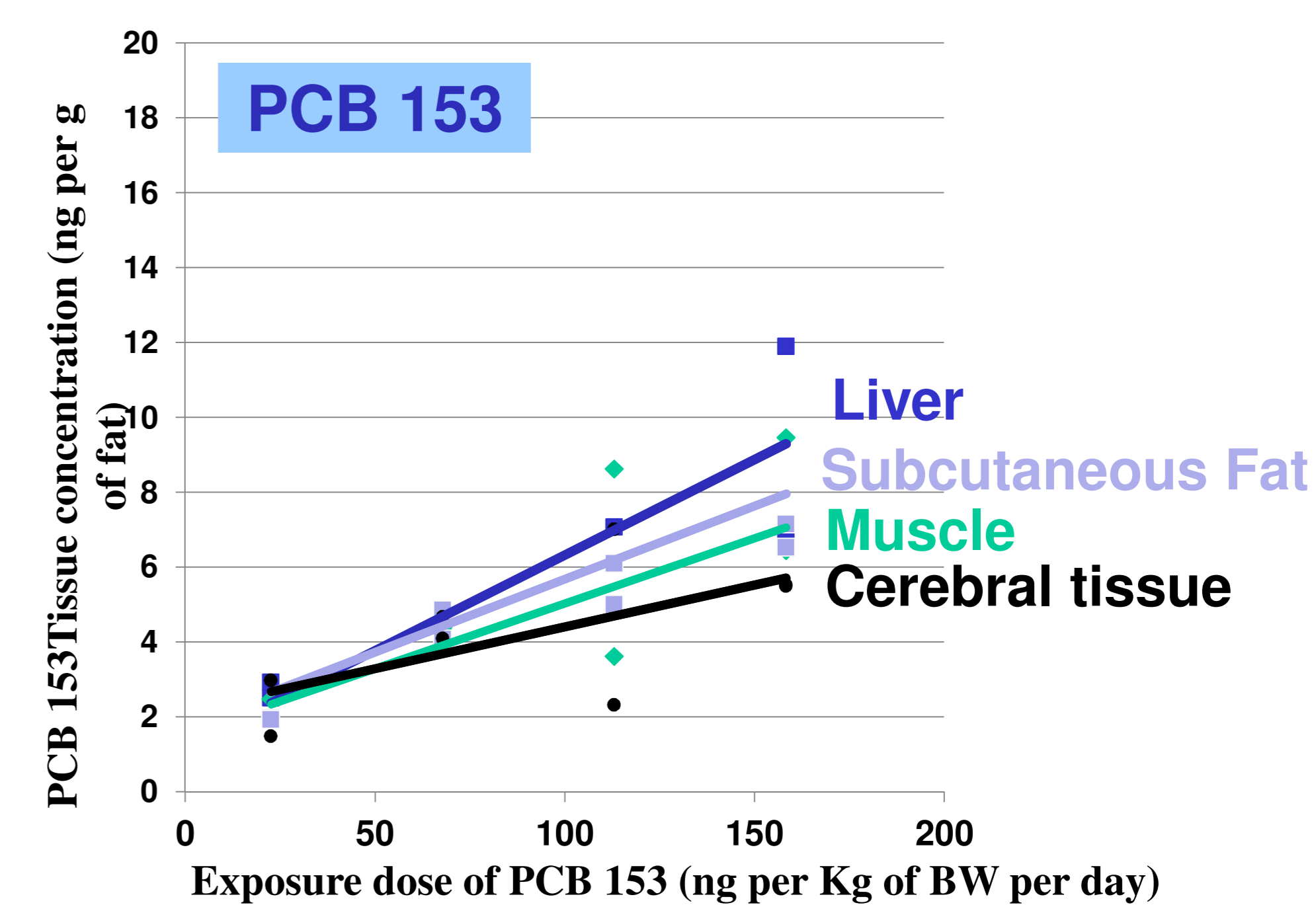
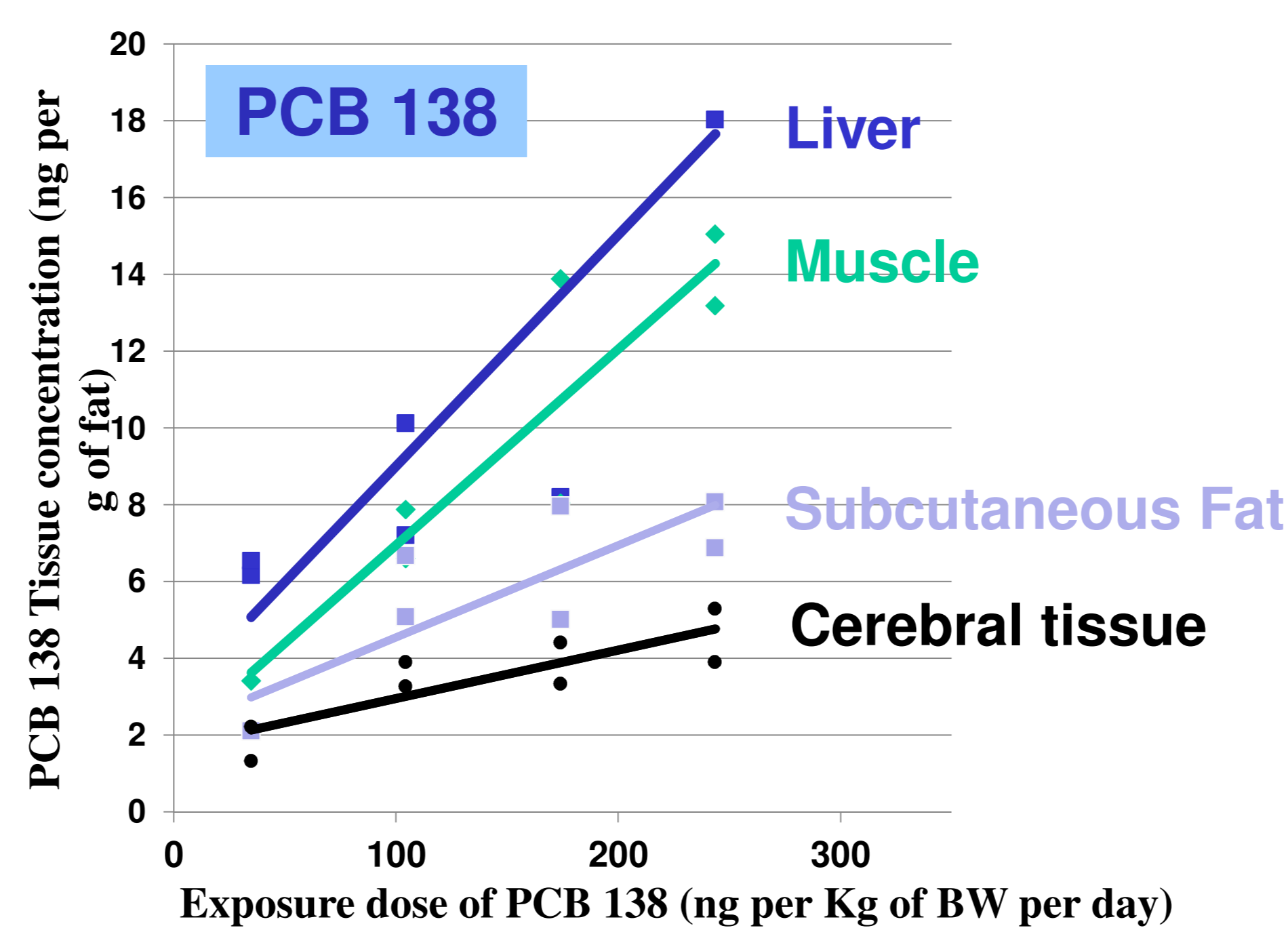
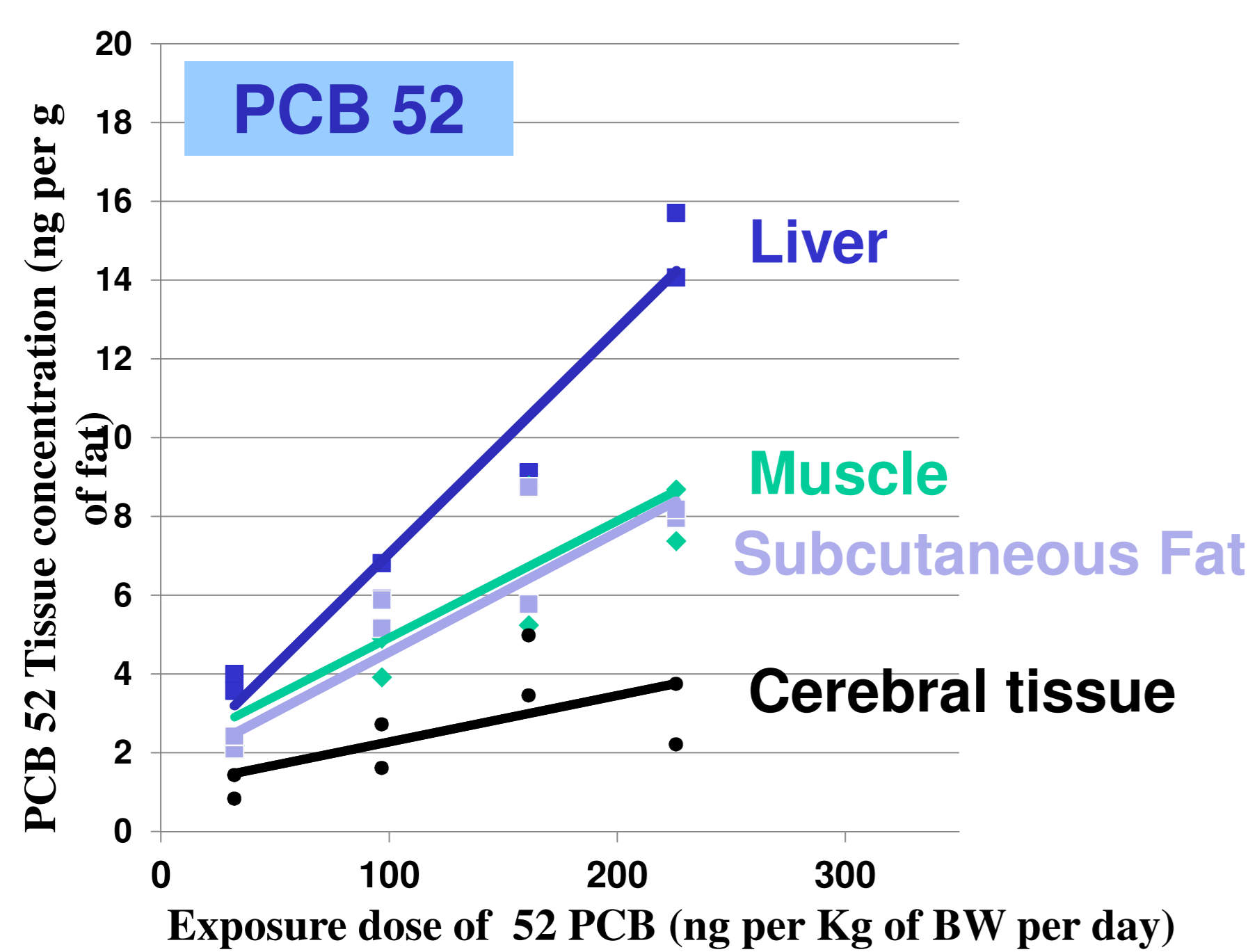
Statistical analysis was performed using R. A second-order polynomial model was evaluate in first. Linear regression was assessed through the R² and p-value

RESULTS AND DISCUSSION

1- Dose-response curves

Dose response curves were obtained by linear regression. Three I-PCBs were chosen for their representativeness of I-PCBs to illustrate dose-response relationships.

Levels of responses (ng I-PCB / g fat) to increasing doses in the four target organs



- The different I-PCBs congeners were found to **show similar responses**
- Linear model significantly fit data** for liver, muscle and adipose samples.
- In general liver tissues exhibit higher responses than other target tissues
- In cerebral tissue I-PCBs are not really linear

Dose-response relationship appeared to be linear in all studied tissues except the cerebral one.

2- Statistical Analysis of linear regression

In order to assess linearity regression, a statistical analysis was performed to evaluate regression coefficients and correlation of the model to data.

		PCB 28	PCB 52	PCB 101	PCB 118	PCB 138	PCB 153	PCB 180
Liver	slope (y/x .10 ²)	-54,4	57,0	43,8	28,1	51,0	60,3	71,0
	R ²	0,17	0,96	0,92	0,95	0,78	0,80	0,86
	p	N.S.	0,001	0,001	0,000	0,001	0,009	N.S.
Subcutaneous fat	slope(y/x .10 ²)	13,0	29,7	1,9	27,6	24,0	34,9	-10,2
	R ²	0,12	0,83	0,87	0,78	0,83	0,91	0,77
	p	N.S.	0,002	0,001	0,004	0,001	0,000	0,004
Muscle	slope(y/x .10 ²)	90,4	30,5	32,2	28,1	39,1	51,1	28,1
	R ²	0,52	0,76	0,81	0,78	0,71	0,92	0,43
	p	N.S.	0,010	0,006	0,009	0,005	0,049	N.S.
Cerebral Tissue	slope(y/x .10 ²)	19,56	1,18	16,6	0,72	1,26	51,1	28,1
	R ²	0,04	0,43	0,56	0,02	0,71	0,43	0,00
	p	N.S.	N.S.	0,032	N.S.	0,009	N.S.	N.S.

N.S. : p<0,05

- Regression analysis for PCB 52,101, 118,138 and 153 **demonstrated significant linear relationships** between the administrated doses and the levels measured in adipose tissue (R²>0.77), liver (R²>0.77) and muscle (R²>0.71).
- Cerebral tissue shows no evidence of linear or quadratic relation.** This suggest that transfer of I-PCBs to the brain is not linear, however further research has to be carry out to clarify the transfer to brain.
- Weak concentrations of PCB28 in Aroclor 1254 could explain very low levels in tissues (ASTDR 2000)
- Liver samples exhibit higher slope than other organs suggesting a heavy bound of this contaminant to hepatic macromolecules like enzymes.

CONCLUSION

- Liver, subcutaneous fat and muscle **exhibit significant linear responses to increasing doses of I-PCBs in a range of 190 ng to 1310 ng of Aroclor 1254 I-PCB per Kg of Body Weight**.
- Cerebral tissues **show no evidence of linear or quadratic dose-response relationships, however this result needs to be confirmed by further experiments.**
- These results have to be considered as an important step for further relative bioavailability studies involving complex matrices.