

SUPPLEMENTARY MATERIAL to

**PULMONARY PHTHALATE EXPOSURE AND ASTHMA –
 IS PPAR A PLAUSIBLE MECHANISTIC LINK?**

Anette Kocbach Bølling^{1*}, Jørn A Holme¹, Carl Gustaf Bornehag², Unni C Nygaard¹,
 Randi J Bertelsen¹, Eewa Nånberg², Johanna Bodin¹, Amrit Kaur Sakhi¹, Cathrine Thomsen¹, Rune Becher¹

¹ Division of Environmental Medicine, Norwegian Institute of Public Health, PO Box 4404 Nydalen, N-0403 Oslo, Norway

² University of Karlstad, 651-88, Karlstad, Sweden

Phthlate-induced activation of PPARs in transfection studies – complete tables

Table A1-3. Phthlate-induced activation of PPARs in transfection studies. Summary of the reported EC₅₀ values, the range of concentrations that caused significant PPAR activation and the corresponding range of fold increase in PPAR activation for a selection of monophthalates. If references only reported lowest activation concentration or only the maximum fold increase, these values are listed. The shaded rows represent the summary of the ranges reported in the literature for each phthalate, whereas the other rows show data reported in the literature with the appropriate reference. The data in the shaded rows is equivalent to the data presented in Table 3 in the main manuscript.
 - : no activation observed for the highest tested concentration

Table A1: PPARα

Phthalate monoester	human PPARα			mouse PPARα		
	EC ₅₀ (μM)	Range/ Lowest act. conc. (μM)	Fold increase	EC ₅₀ (μM)	Range/ Lowest act. conc. (μM)	Fold increase
MMP	- ^b	No act.		- ^c	No act.	2 ^b
MEP	-	No act.		- ^c - ^g	No act.	
MsecBP	- ^b	No act.		63 ^b	10 10-300 ^b	1.5-3 ~1.5-3 ^b
MnBP	- ^b	10-200	0.5-2	- ^b	100	4
MBzP		10-100 ^d 200 ^g	~0.5-0.7 ^d 2.4 ^g		100 ^g	3.7 ^g
MEHP	3.2 ^b	30-300 30-300 ^b 200 ^g 3-100 5-20 ^a 4-50 ^b 125-750 ^{c*} 100 ^d	2-3 ~1.8-2.8 ^b 2.5 2-4 3.4-4.2 ^a ~1.8-2.2 ^b ~3 ^c ~1.5 ^d	21 ^b 125 ^c 0.6 ^b 40 ^c	10-100 10-400 ^b 100 ^g 0.5-40 5-20 ^a 0.5-20 ^b 63-750 ^{c*} 3.2-200 ^e 1-100 ^f 10 ^g	2-12 ~2-5 ^b 12.3 ^g 2-7 2.7-3.1 ^a ~1.9-2.2 ^b ~2-7 ^c ~2-3 ^e ~2-4 ^f 11.1 ^g
MnOP		30 ^g 10 10 ^g	4.8 ^g 8 8		10 ^g 10 10 ^g	32 32 ^g
MiNP		10 10 ^g	6 6 ^g		3 3 ^g	27 27 ^g
MiDP		30 30 ^g	4 4 ^g		3 3 ^g	27 27 ^g

Table A2: PPAR γ

Phthalate monoester	human PPAR γ			mouse PPAR γ		
	EC ₅₀ (μ M)	Range/ Lowest act. conc. (μ M)	Fold increase	EC ₅₀ (μ M)	Range/ Lowest act. conc. (μ M)	Fold increase
MMP	- ^b	No act.		- ^b - ^c	No act.	
MEP	- ^g	No act.		- ^c - ^g	No act.	
MsecBP	- ^b	No act.			300 300 ^b	2 ~2 ^b
MnBP	- ^b - ^d - ^g	No act.		- ^b - ^g	No act.	
MBzP	100 ^b	30-200 30-300 ^b	2-4 ~1.5-4 ^b	75 ^b 100 ^c	10-100 10-300 ^b	2-8 ~1.5-4 ^b
MEHP	6.2 ^b 4.9 ^d 30 ^e	200 ^g 0.1-10 1-100 ^a 5-60 63-750 ^{c*} 0.1-100 ^d 3.2-200 ^e	4.2 ^g 1.5-10 1.3-3.2 ^a ~2-3 ^b ~2-7 ^c ~2-10 ^d ~2-2.5 ^e	10.1 ^b 30 ^c	100 ^g 3-30 5-100 ^a 3-50 ^b 63-750 ^{c*} 3.2-200 ^e 25-250 ^t 30 ^g	7.8 ^g 1.5-7 1.8-3.7 ^a ~1.5-4 ^b ~2-7 ^c ~1.5-2 ^e ~3-4 ^t 2.5 ^g
MnOP		100 100 ^g	19 19 ^g		10 10 ^g	11 11 ^g
MiNP		30 30 ^g	9 9 ^g		3 3 ^g	14 14 ^g
MiDP		3 3 ^g	8 8 ^g		30 30 ^g	4 4 ^g

Table A3: PPAR δ/β

Phthalate monoester	human PPAR δ/β			mouse PPAR δ/β		
	EC ₅₀ (μ M)	Range/ Lowest act. conc. (μ M)	Fold increase	EC ₅₀ (μ M)	Range/ Lowest act. conc. (μ M)	Fold increase
MMP		No act.		No act.		
				- ^c		
MEP		No act.		No act.		
				- ^c		
	- ^g			- ^g		
MnBP		No act.			0.1-3	0.5-5
				125 ^c		
	- ^d				0.1-100 ^d	~0.8-0.5 ^d
	- ^g				3 ^g	4.7 ^g
MBzP		No act.			100	11
	- ^g				100 ^g	10.8 ^g
MEHP		60	3-6		0.1-200	0.6-17
		63-750 ^c	~3-6 ^c	200 ^c	250-750 ^c	~3 ^c
	- ^d				0.1-10 ^d	~0.9-0.6 ^d
					3.2-200 ^e	~ 1.5-4 ^e
					25-250 ^f	~ 3-4 ^f
	- ^g				200 ^g	16.8 ^g
MnOP		No act.			100	13
	- ^g				100 ^g	13 ^g
MiNP		No act.				3
	- ^g					3 ^g
MiDP		No act.			100	8
	- ^g				100 ^g	8 ^g

- ^a Maloney and Waxman (1999) (transfection of Cos-1 cells with PPAR expression plasmids and a PPRE-firefly luciferase reporter)
- ^b Hurst and Waxman (2003) Mouse/human PPAR (transfection of Cos-1 cells with PPAR expression plasmids and a PPRE-firefly luciferase reporter)
- ^c Lampen et al: (2003) (monophthalate esters activation of PPAR–ligand binding domain in transfected ovary reporter cells)
- ^d Gopisetty Venkata et al. (2006) (trans-activation of human PPARs in a transfected breast cell line MCF-7)
- ^e Feige et al: (2007) (transient transfection of Cos-7, C2C12 and HeLa cells with a PPRE-firefly luciferase reporter construct, a normalisation vector encoding Renilla luciferase and an expression vector coding for various PPARs/empty)
- ^f Lapinskas et al. (2005) (trans-activation of mouse PPARs in a transfected liver cell line HepG2)
- ^g Bility et al. (2004) (trans-activation of mouse and human PPARs in a transfected mouse fibroblast cell line 3T3-L1)
- * These lowest activation range data were excluded from the summary range presented in the table in the main manuscript. For the mouse PPARs the range of concentrations was higher than the EC50 level reported in the same study, whereas for the human PPARs, the range of concentrations did not include sufficiently low concentrations.