

Table 5. Metofluthrin Dose-Response and Time Concordance – Male Wistar Rats:

Key Events / Associative Events	Dose Levels (ppm) Metofluthrin and Effects			
	200	900	1800	3600 ^c
MIE: CAR Activation (Day 7)				
via KE1 – <i>Cyp2b1/2</i> mRNA ^a	-	+ (2.9)	+ (6.2)	+ (10.5)
via KE1 – <i>Cyp3a1</i> mRNA ^a	-	-	+ (1.7)	+ (2.4)
via AE1 – PROD activity (Day 7) ^a	ND	ND	ND	+
via AE1 – CYP2B protein levels (Day 7) ^a	-	+ (1.5)	+ (1.8)	+ (2.4)
via AE2 – Hepatocellular hypertrophy (Day 7) ^a	-	-	1/5	2/7
via AE3 – Relative Liver wt. (Day 7) ^a	-	+ (1.06)	+ (1.13)	+(1.06)
KE2: increased cell proliferation, BrdU (7 Days) ^a	-	+ (2.0)	+ (2.2)	-(0.5) ^c
KE3: clonal expansion, increased altered foci (2 years) ^a	-	+ ^d	+ ^d	ND
AO: Liver adenomas, carcinomas (2 yrs) ^b	-	+ 8/50	+ 12/50	ND

Legend (comparative effects vs. untreated controls): + Positive; - Negative; ± Equivocal, based on treatment effects determined by the authors (Deguchi et al., 2009; Yamada et al., 2009). ND = Not determined. Values in parenthesis are fold-change vs. controls.

^aData from Deguchi et al. (2009), including supplementary data Tables 1-5

^bData from Yamada et al. (2009). Control group tumor incidence was 1/50.

^cDeaths and significant clinical signs occurred at 3600 ppm, indicating 3600 ppm was in excess of MTD.

^dAt 2 years, increased mixed foci were observed at 900 ppm (p<0.01) and increased eosinophilic foci were observed at 1800 ppm (p<0.01). (Deguchi et al., 2009 suppl data).