

Appendix 2: Empirical evidence for KER 3349 decreased circulating testosterone leading to short AGD.

The table details the data sets considered reliable with or without restriction in the evaluation of methodological reliability.

For the effects on circulating testosterone and AGD, ↓* denotes a statistically significant reduction in the parameter at the given dose.

Abbreviations: GD=gestational day; Ns= not significant; PND=postnatal day

Study design				Upstream event (testosterone)						Downstream event (AGD)				Reference
Substance	Species	Exposure window	Doses (mg/kg bw/day)	Serum/plasma	Method	Timepoints	Effect (pg/mL)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Timepoint	Effect (AGDi)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	
2,3,7,8-Tetrachlorodibenzo-p-dioxin	Rat	GD15	0 1 µg/kg	Plasma	Radioimmunoassay	Daily from GD17-21	↓*	-	1	PND1, 3 & 5	↓* ¹	-	1	(Mably TA et al., 1992)
Dicyclohexyl phthalate	Rat	GD6-19	0 20 100 500	Plasma	Enzyme immunoassay	GD20	638 ±42.9 564 ±22.8 388 ±12.6* 373 ±15.7*	20	100	GD20	↓* ↓* ↓*	-	20	(Aydoğan Ahabab M & Barlas N, 2015)
Diethylhexyl phthalate	Rat	GD7-PND17	0 750	Serum	Fluoroimmunoassay	GD21	↓*	-	750	PND3	↓* ²	-	750	(Borch J et al., 2004)
Diethylhexyl phthalate + Diethylhydroxylamine	Rat	GD7-PND17	0 750 + 400	Serum	Fluoroimmunoassay	GD21	↓*	-	750 + 400	PND3	↓* ²	-	750 + 400	(Borch J et al., 2004)
Di-n-hexyl phthalate	Rat	GD6-19	0 20 100 500	Plasma	Enzyme immunoassay	GD20	638 ±42.9 450 ±22.6* 387 ±17.8* 352 ±24.4*	-	20	GD20	↓* ns ↓*	100	20	(Aydoğan Ahabab M & Barlas N, 2015)
Perfluorotridecanoic acid	Rat	GD14-21	0 1 5 10	Serum	Immunoassay	GD21	↓* ↓* ↓*	-	1	GD21	Ns ¹ Ns ↓*	5	10	(Li C et al., 2021)
Prochloraz	Rat	GD7-PND17	0 30	Serum	Fluoroimmunoassay	GD21	↓*	-	30	PND0	4.34 ±0.32 ¹ 4.43 ±0.29	30	-	(Vinggaard AM et al., 2005)

Prochloraz	Rat	GD7-PND16	0 50 150	Plasma	Fluoroimmunoassay	GD21	↓ ² ↓ ²	-	50 ²	PND1	11.6 ±0.4 10.9 ±0.6* 10.2 ±0.8*	-	50	(Laier P et al., 2006)
Zearalenone	Rat	GD14-21	0 2.5 5 10 20	Serum	Immunoassay	GD21	Ns Ns ↓* ↓*	5	10	GD21	0.84±0.02 ³ 0.78±0.02 0.73±0.01* 0.73±0.02* 0.75±0.02*	2.5	5	(Pan P et al., 2020)
Mixture (prochloraz, deltamethrin, methiocarb, simazine, tribenuron)	Rat	GD7-PND17	0 20	Serum	Fluoroimmunoassay	GD21	↓*	-	20	PND0	4.34 ±0.32 ¹ 4.43 ±0.29	20	-	(Vinggaard AM et al., 2005)

*statistically significant from control group
¹AGD (mm), not corrected for body weight in statistics
²AGD (mm), corrected for body weight in statistics.
³AGD/body weight