

Appendix A: Supplemental Material

Table A-1. Comparison of Liver Effects and Associated Effect Levels from Repeated-Dose Animal Studies for Non-Cancer Oral Toxicity for <i>p,p'</i>-DDD and Analogues^a			
<i>p,p'</i>-DDD	<i>p,p'</i>-DDT	<i>p,p'</i>-DDE	Methoxychlor
<ul style="list-style-type: none"> • No effects on liver histopathology in rats at a NOAEL of 231 mg/kg-day and in mice at a NOAEL of 142 mg/kg-day after exposure for 78 weeks but study was limited in design as a cancer bioassay (NCI, 1978) 	<ul style="list-style-type: none"> • Increased liver weight in rats and mice at LOAELs of 6.25-40 mg/kg-day for 12-28 days (Gupta et al., 1989; DeWaziers and Azais 1987; Kostka et al. 2000; Orberg and Lundberg, 1974) and in hamsters at a LOAEL of 67 mg/kg-day after lifetime exposure (Graillot et al., 1975) • Liver histopathology (ranging from hypertrophy, fatty degeneration and necrosis) in rats, mice, hamsters and dogs at LOAELs of 0.25-160 mg/kg-day after subchronic and chronic exposure (Cabral et al., 1982a; Deichmann et al., 1967; Fitzhugh and Nelson 1947; Jonsson et al., 1981; Laug et al., 1950; Lehman, 1965; NCI, 1978; Ortega, 1956) • Hepatocyte vacuolation, proliferation of bile duct cells, clear hepatocyte foci and necrosis in rhesus and cynomolgus monkeys at a LOAEL of 6.4 mg/kg-day after exposure for 130 months (Takayama et al., 1999) but no effects on liver histopathology in rhesus monkeys at a lower dose (NOAEL of 3.9 mg/kg-day) after exposure for 3.5-7.5 years (Durham et al., 1963) 	<ul style="list-style-type: none"> • Increased liver weight in rats and mice at LOAELs of 5-50 mg/kg-day after exposure for 1-6 weeks (Banerjee et al., 1996; Pash 1981) or after in utero and postnatal exposure (Patrick et al., 2016; Yamasaki et al., 2009) • Liver histopathology (fatty degeneration and necrosis) in rats and hamsters at LOAELs of 31-48 mg/kg-day after subchronic and chronic exposure (NCI, 1978; Patrick et al., 2016; Rossi et al., 1983) • No effects on liver histopathology in mice at a NOAEL of 49 mg/kg-day after exposure for 78 weeks (NCI, 1978) 	<ul style="list-style-type: none"> • Changes in liver weight (both increase and decrease) in rats at a LOAELs of 150-1,200 mg/kg-day after subchronic exposure (Chapin et al., 1997; Davidson and Cox, 1976; Gray et al., 1999) • Decreased serum albumin in rats at a LOAEL of 20 mg/kg-day after exposure for 28 days (Okazaki et al., 2001) • Gross liver lesions (pale/molting appearance) in rabbits at a LOAEL of 35.5 mg/kg-day after in utero exposure (GD 7-19) but no effects on liver histopathology in rats at NOAELs of 77-917 mg/kg-day (Deichmann et al., 1967; NCI, 1978; Hagg et al., 1950) and in mice at a NOAEL of 599 mg/kg-day (NCI, 1978) after chronic exposure

^aData show liver effects and associated effect levels (no-observed-adverse-effect levels [NOAEL] and lowest-observed-adverse-effect levels [LOAEL]) from repeated-dose animal toxicity studies via oral administration reported by ATSDR (2002a, b) and U.S. EPA (2017 b, c). Studies for DDT, DDD, and methoxychlor include technical grade and analytical formulations of the *p,p'* isomers.

Table A-2. Comparison of Reproductive Effects and Associated Effect Levels from Repeated-Dose Animal Studies for Non-Cancer Oral Toxicity for *p,p'*-DDD and Analogues^a

<i>p,p'</i> -DDD	<i>p,p'</i> -DDT	<i>p,p'</i> -DDE	Methoxychlor
Fertility and Pregnancy Outcomes			
Not Available	<ul style="list-style-type: none"> • Decreased fertility and/or infertility in female rats at a LOAEL of 12 mg/kg-day for 36-weeks (Jonsson et al., 1976) and in male and female in mice at a LOAEL of 51.4 mg/kg-day for 60-90 days (Bernard and Gaertner 1964) or a LOAEL of 20 mg/kg-day for 3 generations (Keplinger et al., 1970) • Adverse pregnancy outcomes, including increased resorptions in rabbits at LOAELs of 10-50 mg/kg-day after in utero exposure (gestational day [GD] 7-9) (Hart et al., 1971, 1972) and decreased corpora lutea, implants and implanted ova in mice at a LOAEL of 1.67 mg/kg-day after exposure for 4-12 weeks (Lundberg 1974). • No effects on fertility and/or pregnancy outcomes generally at lower exposure doses: NOAELs of 1.3-6.25 mg/kg-day in mice exposed for 4-64 weeks (Ledoux et al., 1977; Orberg and Lundberg 1974; Ware and Good, 1967; Wolfe et al., 1979); NOAELs of 0.75-10 mg/kg-day in rats in multigenerational/chronic studies (Duby et al., 1971; Ottoboni 1969, 1972; Treon et al., 1954); a NOAEL of 10 mg/kg-day in a 2-generation study in dogs (Ottoboni et al., 1977) 	<ul style="list-style-type: none"> • Decreased fertility in male and female rat offspring at LOAELs of 50-100 mg/kg-day after in utero and/or post-natal exposure (Song et al., 2014; Yamasaki et al., 2009) but no effects on fertility and pregnancy outcomes in parental rat dams at a LOAEL of 10 mg/kg-day after exposure for 5 weeks pre-mating through post-natal day (PND) 8 or 19 (Kornbrust et al., 1986) 	<ul style="list-style-type: none"> • Decreased fertility and/or infertility in male and female rats at LOAELs of 50-200 mg/kg-day after subchronic exposure (Bal, 1984; Chapin et al., 1997; Gray et al., 1989, 1999; Harris et al., 1974) and at a LOAEL of 92 mg/kg-day after chronic/multigenerational exposure (Haskell Laboratories, 1966) • Adverse pregnancy outcomes (including, pre- and post- implantation loss, accelerated embryo transport into the uterus, increased resorptions and abortions and decreased number of live pups per litter) in rats and rabbits at LOAELs of 50-250 mg/kg-day after in utero only exposure (Culik and Kaplan 1976; Cummings and Laskey 1993; Cummings and Perreault 1990; Khera et al., 1978; Kincaid Enterprises 1986) or after short-term and subchronic exposures (Chapin et al., 1997; Cummings and Gray 1989; Gray et al. 1989)
Male-Specific Effects			
Not Available	<ul style="list-style-type: none"> • Decreased testes weight in juvenile rats at a LOAEL of 200 mg/kg-day 	<ul style="list-style-type: none"> • Decreased anogenital distance, nipple retention, delayed puberty 	<ul style="list-style-type: none"> • Delayed puberty (delayed preputial separation) in rats at a LOAEL of 100

	<p>after postnatal exposure (PND 4 and 5 or PND 4-23) (Krause et al., 1975) and decreased testicular testosterone in adult rats at a LOAEL of 100 mg/kg-day after 3-week exposure (Krause, 1977)</p>	<p>(delayed preputial separation), decreased weights of male reproductive organs (testis, ventral and dorsolateral prostate, seminal vesicle, glans penis, cauda epididymis and levator ani/bulbocavernosus muscles), altered sperm parameters and histopathology of the prostate and testes in prenatal and juvenile rats at LOAELs of 10-100 mg/kg-day after in utero and/or postnatal exposure (Gray et al., 1999; Kelce et al., 1995; Loeffler and Peterson, 1999; Patrick et al., 2016; Song et al., 2014; Yamasaki et al., 2009; You et al., 1998)</p> <ul style="list-style-type: none"> • Decreased seminal vesicle and ventral prostate weight in adult rats at a LOAEL of 200 mg/kg-day after short-term exposure (4-5 days) (Kelce et al., 1995) • No effects on serum hormones (LH, FSH and testosterone), sperm counts and male reproductive organ weights and histopathology (testes, epididymides, prostate and seminal vesicles) at a NOAEL of 10 mg/kg-day in rats exposed from GD 1- PND 21 (Makita and Omura, 2006) or from PNDs 42-84 (Makita et al., 2005) 	<p>mg/kg-day after exposure for 309 days (Gray et al., 1999)</p> <ul style="list-style-type: none"> • Decreased sperm counts in rats at LOAELs of 100-200 mg/kg-day after exposure for 28-309 days (Gray et al., 1989, 1999; Okazaki et al., 2001) • Gross and histopathological changes in male reproductive organs (including decreased testes weight and atrophy/degeneration of the testes, epididymis and mammary acinus) in rats at LOAELs of 100-1,400 mg/kg-day after exposure for 28-309 days (Bal 1984, Gray et al. 1999; Hodge et al. 1950; Okasaki et al., 2001) • Increased hormone levels in the pituitary (prolactin, FSH, TSH) in rats at LOAELs of 25-100 mg/kg-day after exposure for 56-99 days (Gray et al. 1989; Goldman et al., 1986) • Altered mating behavior including decreased mating frequency in rats at LOAELs of 60-200 mg/kg-day after exposure for 42-309 days (Gray et al., 1999; Harris et al., 1974)
Female-Specific Effects			
	<ul style="list-style-type: none"> • Prolongation of estrus cycle in mice at a LOAEL of 1.67 mg/kg-day (Lundberg 1974) and reduced ovulation rate and decreased circulating progesterone post-insimulation in rabbits at a LOAEL of 3 mg/kg-day after a 12-week exposure (Lindenau et al., 1994) 	<ul style="list-style-type: none"> • Precocious puberty (early vaginal opening) in rats at a LOAEL of 50 mg/kg-day after exposure from GD 6- PND 20 (Yamasaki et al., 2009) • No effects on serum hormones (LH, FSH, 17beta-estradiol and thyroxine) female reproductive organ weights and histopathology, 	<ul style="list-style-type: none"> • Precocious puberty (early vaginal opening) in rats at LOAELs of 5-60 mg/kg-day after short-term and subchronic exposures (Chaplin et al., 1997; Gray et al., 1989; Harris et al., 1974; Laws et al., 2000) • Abnormal estrous cycle, including persistent estrus in rats at LOAELs of 25-400 mg/kg-day after short-term and

		<p>estrous cyclicity and vaginal opening at a NOAEL of 10 mg/kg-day in rats exposed from GD 1- PND 21 (Makita, 2008)</p>	<p>subchronic exposures (Chapin et al., 1997; Gray et al., 1988, 1989; Harris et al., 1974; Okasaki et al., 2001; Martinez and Swartz 1991)</p> <ul style="list-style-type: none"> • Gross and histopathological changes in female reproductive organs (including changes in ovarian and uterine weights, ovarian cysts, atrophic/degenerative lesions in the ovaries and uterus, increased lipid accumulation in interstitial and thecal cells of the ovary and delayed regression of endometriosis) in rats and mice at LOAELs of 50-400 mg/kg-day after subchronic exposure (Bal 1984; Chapin et al., 1997; Cummings and Metcalf 1995b; Gray et al., 1988, 1989; Harris et al., 1974; Martinez and Swartz 1991, 1992) • Induction of uterine decidualization at a LOAEL of 75 mg/kg-day (Cummings 1993) and decreased uterine receptivity to implantation at a LOAEL of 200 mg/kg-day (Cummings and Gray 1987) in rats after short-term exposure (8 days) • Decreased serum progesterone in rats at LOAELs of 50-100 mg/kg-day after short-term (3-8 days) (Cummings and Gray 1989) and in utero exposure (GD 1-8) (Cummings and Laskey 1993) • Altered mating behavior including decreased mating frequency in rats at LOAELs of 60-150 mg/kg-day after exposure for 6-12 weeks (Harris et al., 1974)
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^aData show reproductive effects and associated effect levels (no-observed-adverse-effect levels [NOAEL] and lowest-observed-adverse-effect levels [LOAEL]) from repeated-dose animal toxicity studies via oral administration reported by ATSDR (2002a, b) and U.S. EPA (2017 b, c). Studies for DDT, DDD, and methoxychlor include technical grade and analytical formulations of the *p,p'* isomers.

Table A-3. AC50 Values (µM) for <i>p,p'</i>-DDD and Analogues from ToxCast Assays in Human Liver Cells Grouped by Biological Response/Target^a							
Biological Response/Target	Assay Name^b	<i>p,p'</i>-DDD	<i>p,p'</i>-DDT	<i>p,p'</i>-DDE	Methoxychlor	Assay Design	Cell Line
Mitochondrial damage	APR_HepG2_MitoMass_24h_dn	89.3	45	55.1	Inactive	Morphology reporter	HepG2
	APR_HepG2_MitoMass_72h_dn	Inactive	Inactive	61	Inactive	Morphology reporter	HepG2
	APR_HepG2_MitoMembPot_1h_dn	NA	NA	NA	98	Membrane potential reporter	HepG2
	APR_HepG2_MitoMembPot_24h_dn	64.9	25.7	18.4	Inactive	Membrane potential reporter	HepG2
	APR_HepG2_MitoMembPot_72h_dn	Inactive	25.8	Inactive	Inactive	Membrane potential reporter	HepG2
	TOX21_MMP_ratio_down	17.5	22.1	32.5	59.4	Membrane potential reporter	HepG2
Cellular stress/cytotoxicity	APR_HepG2_CellLoss_24h_dn	104	57.6	56.5	71.4	Viability reporter	HepG2
	APR_HepG2_CellLoss_72h_dn	97.3	53.5	30.3	75.1	Viability reporter	HepG2
	APR_HepG2_OxidativeStress_24h_up	109	52	59.4	Inactive	Viability reporter	HepG2
	APR_HepG2_OxidativeStress_72h_up	104	55.4	Inactive	98.2	Viability reporter	HepG2
	APR_HepG2_p53Act_24h_up	108	54.5	58.9	Inactive	Viability reporter	HepG2
	APR_HepG2_p53Act_72h_up	89.2	Inactive	Inactive	76.6	Viability reporter	HepG2
	APR_HepG2_StressKinase_24h_up	Inactive	52.6	Inactive	Inactive	Enzyme reporter	HepG2
	APR_HepG2_StressKinase_72h_up	115	Inactive	Inactive	Inactive	Enzyme reporter	HepG2
Cell cycle	APR_HepG2_CellCycleArrest_24h_dn	101	Inactive	Inactive	Inactive	Morphology reporter	HepG2

	APR_HepG2_CellCycleArrest_24h_up	Inactive	82.1	Inactive	Inactive	Morphology reporter	HepG2
	APR_HepG2_CellCycleArrest_72h_dn	102	26	17.3	Inactive	Morphology reporter	HepG2
	APR_HepG2_MitoticArrest_24h_up	90.2	50.5	60	Inactive	Morphology reporter	HepG2
	APR_HepG2_MitoticArrest_72h_up	69.6	44.3	17.8	68.3	Morphology reporter	HepG2
Cellular/organelle conformation	APR_HepG2_MicrotubuleCSK_24h_dn	133	Inactive	Inactive	Inactive	Conformation reporter	HepG2
	APR_HepG2_MicrotubuleCSK_24h_up	Inactive	Inactive	Inactive	71.6	Conformation reporter	HepG2
	APR_HepG2_MicrotubuleCSK_72h_dn	132	Inactive	Inactive	Inactive	Conformation reporter	HepG2
	APR_HepG2_MicrotubuleCSK_72h_up	Inactive	Inactive	Inactive	80.9	Conformation reporter	HepG2
	APR_HepG2_NuclearSize_24h_dn	109	59.9	Inactive	Inactive	Morphology reporter	HepG2
Transcriptional factors^c	ATG_AP_1_CIS_up	42	49.9	79.1	44.6	Inducible reporter	HepG2
	ATG_C_EBP_CIS_up	57.2	Inactive	Inactive	Inactive	Inducible reporter	HepG2
	ATG_CRE_CIS_up	57.2	Inactive	Inactive	Inactive	Inducible reporter	HepG2
	ATG_EGR_CIS_up	38.1	Inactive	Inactive	Inactive	Inducible reporter	HepG2
	ATG_GLI_CIS_up	25.2	Inactive	64.5	Inactive	Inducible reporter	HepG2
	ATG_HIF1a_CIS_up	Inactive	Inactive	56	Inactive	Inducible reporter	HepG2
	ATG_HSE_CIS_up	57.2	Inactive	Inactive	Inactive	Inducible reporter	HepG2
	ATG_MRE_CIS_up	42.7	72.9	Inactive	12.7	Inducible reporter	HepG2
	ATG_Myc_CIS_up	38.8	Inactive	121	Inactive	Inducible reporter	HepG2
	ATG_NFI_CIS_up	57.2	48.1	111	Inactive	Inducible reporter	HepG2

	ATG_NRF1_CIS_up	Inactive	Inactive	78.1	Inactive	Inducible reporter	HepG2
	ATG_NRF2_ARE_CIS_up	42.1	26.9	50.5	3.4	Inducible reporter	HepG2
	ATG_Oct_MLP_CIS_up	41.8	70.6	90.9	Inactive	Inducible reporter	HepG2
	ATG_Pax6_CIS_up	57.2	Inactive	Inactive	Inactive	Inducible reporter	HepG2
	ATG_Sox_CIS_up	57.2	Inactive	Inactive	Inactive	Inducible reporter	HepG2
	ATG_Sp1_CIS_up	57.2	69.3	86.6	Inactive	Inducible reporter	HepG2
	ATG_SREBP_CIS_up	57.2	79.9	104	Inactive	Inducible reporter	HepG2
	ATG_Xbp1_CIS_up	46.8	Inactive	97.4	Inactive	Inducible reporter	HepG2
	TOX21_ARE_BLA_agonist_ratio	68.7	Inactive	78.5	Inactive	Inducible reporter	HepG2
Nuclear receptors^c	ATG_CAR_TRANS_up	Inactive	20.9	Inactive	Inactive	Inducible reporter	HepG2
	ATG_DR5_CIS_up	57.2	Inactive	Inactive	Inactive	Inducible reporter	HepG2
	ATG_ERa_TRANS_up	17.3	4.41	2.83	0.913	Inducible reporter	HepG2
	ATG_ERE_CIS_up	19.5	4.74	14.7	2.5	Inducible reporter	HepG2
	ATG_FXR_TRANS_up	13.1	Inactive	Inactive	Inactive	Inducible reporter	HepG2
	ATG_PXR_TRANS_up	8.34	8.2	7.49	1.03	Inducible reporter	HepG2
	ATG_PXRE_CIS_up	5.99	4.31	3.14	2.62	Inducible reporter	HepG2
	ATG_RXRb_TRANS_up	36.3	10.6	15	Inactive	Inducible reporter	HepG2
	ATG_THRa1_TRANS_up	28.8	Inactive	Inactive	Inactive	Inducible reporter	HepG2
	ATG_VDRE_CIS_up	16.9	Inactive	Inactive	5.43	Inducible reporter	HepG2

Metabolism enzymes	CLD_CYP1A1_48hr	NA	NA	NA	29.6	Inducible reporter	Primary hepatocytes
	CLD_CYP1A1_6hr	NA	NA	NA	15.1	Inducible reporter	Primary hepatocytes
	CLD_CYP1A2_24hr	NA	NA	NA	5.06	Inducible reporter	Primary hepatocytes
	CLD_CYP1A2_48hr	NA	NA	NA	4.59	Inducible reporter	Primary hepatocytes
	CLD_CYP1A2_6hr	NA	NA	NA	16	Inducible reporter	Primary hepatocytes
	CLD_CYP2B6_24hr	NA	NA	NA	10.5	Inducible reporter	Primary hepatocytes
	CLD_CYP2B6_48hr	NA	NA	NA	10.5	Inducible reporter	Primary hepatocytes
	CLD_CYP2B6_6hr	NA	NA	NA	10.4	Inducible reporter	Primary hepatocytes
	CLD_CYP3A4_24hr	NA	NA	NA	29.5	Inducible reporter	Primary hepatocytes
	CLD_CYP3A4_48hr	NA	NA	NA	22.7	Inducible reporter	Primary hepatocytes
	CLD_CYP3A4_6hr	NA	NA	NA	31.5	Inducible reporter	Primary hepatocytes
	CLD_UGT1A1_24hr	NA	NA	NA	5.44	Inducible reporter	Primary hepatocytes
	CLD_UGT1A1_48hr	NA	NA	NA	10.2	Inducible reporter	Primary hepatocytes

^aData were sourced from the EPA's CompTox Chemistry Dashboard (U.S. EPA, 2017a).

^bAssays for which all chemicals were inactive are not displayed.

^cNuclear receptor and transcriptional factor assays were designed to measure inducible activity. Therefore, responses from assays analyzed in the negative fitting direction relative to the control ('_dn') are considered non-specific and are not presented in this table.

NA = Not available

Table A-4. Activity Summary for *p,p'*-DDD and Analogues from ToxCast Assays Evaluating Regulation of Transcriptional Factor Activity in Human Hepatoma HepG2 Cells^a

Nuclear receptor gene ^b	Organism	<i>p,p'</i> -DDD		<i>p,p'</i> -DDT		<i>p,p'</i> -DDE		Methoxychlor	
		Active Assays	Total Assays	Active Assays	Total Assays	Active Assays	Total Assays	Active Assays	Total Assays
AR (AR)	Human	0	1	0	1	0	1	0	1
CAR (NR1I3)	Human	0	2	1	2	0	2	0	2
ER (ESR1)	Human	2	2	2	2	2	2	2	2
ERR (ESRRA, ESRRG)	Human	0	2	0	2	0	2	0	2
FXR (NR1H4)	Human	1	2	0	2	0	2	0	2
GR (NR3C1)	Human	0	2	0	2	0	2	0	2
HNF4A	Human	0	1	0	1	0	1	0	1
LXR (NR1H3, NR1H2)	Human	0	3	0	3	0	3	0	3
NURR1 (NR4A2)	Human	0	1	0	1	0	1	0	1
PPAR (PPARA, PPARG, PPARG)	Human	0	4	0	4	0	4	0	4
PXR (NR1I2)	Human	2	2	2	2	2	2	2	2
RAR (RARA, RARB, RARG)	Human	1	4	0	4	0	4	0	4
ROR (RORA, RORB, RARG)	Human	0	3	0	3	0	3	0	3
RXR (RXRA, RXRB)	Human	1	2	1	2	1	2	0	2
TR (THRA)	Human	1	1	0	1	0	1	0	1
VDR	Human	1	2	0	2	0	2	1	2

^aData were sourced from the EPA's CompTox Chemistry Dashboard (U.S. EPA, 2017a).

^bNuclear receptor abbreviation (gene symbol).

Abbreviations: AR, androgen receptor; CAR, constitutive androgen receptor; ER, estrogen receptor; ERR, estrogen-related receptor; FXR, farnesoid X receptor; GR, glucocorticoid receptor; HNF4A, hepatocyte nuclear factors 4 alpha; LXR, liver X receptor; NURR1, nuclear receptor related-1 protein; PPAR, peroxisome proliferator-activated receptor; PXR, pregnane X receptor; RAR, retinoid acid receptor; ROR, RAR-related orphan receptor; RXR, retinoid X receptor; TR, thyroid hormone receptor; VDR, vitamin D receptor.

Table A-5. AC50 Values (µM) for <i>p,p'</i> -DDD and Analogues from ToxCast Assays Evaluating Key Signaling Events in the ER and AR pathways ^a							
Assay Name ^b		<i>p,p'</i> -DDD	<i>p,p'</i> -DDT	<i>p,p'</i> -DDE	Methoxychlor	Organism	Tissue
ER pathway							
Receptor binding	NVS_NR_hER	1.0E+06	1.0E+06	1.0E+06	6.0	Human	NA
Receptor dimerization	OT_ER_ERaERa_0480	1.0E+06	59.8	46.2	11.1	Human	Kidney
	OT_ER_ERaERa_1440	1.0E+06	1.0E+06	1.0E+06	4.0	Human	Kidney
	OT_ER_ERaERb_0480	32.4	56.7	38.1	9.6	Human	Kidney
	OT_ER_ERaERb_1440	1.0E+06	5.1	16.1	3.9	Human	Kidney
	OT_ER_ERbERb_0480	18.7	14.5	20.5	5.3	Human	Kidney
	OT_ER_ERbERb_1440	1.0E+06	6.1	12.8	3.5	Human	Kidney
DNA binding	OT_ERa_EREGFP_0120	17.0	4.7	17.0	2.7	Human	Cervix
	OT_ERa_EREGFP_0480	14.0	3.3	1.0E+06	3.1	Human	Cervix
RNA transcription	ATG_ERa_TRANS_up	17.3	4.4	3.5	0.9	Human	Liver
	ATG_ERE_CIS_up	19.5	4.7	14.7	2.5	Human	Liver
Agonist transactivation	Tox21_ERa_BLA_Agonist_ratio	1.0E+06	43.7	1.0E+06	1.0E+06	Human	Kidney
	Tox21_ERa_LUC_BG1_Agonist	19.3	11.1	1.0E+06	10.0	Human	Ovary
Cell proliferation	ACEA_T47D_80hr_Positive	1.0E+06	1.0E+06	1.0E+06	10.2	Human	Breast
Antagonist transactivation	Tox21_ERa_BLA_Antagonist_ratio	1.0E+06	1.0E+06	1.0E+06	44.2	Human	Kidney
AR pathway							
Receptor binding	NVS_NR_cAR	1.0E+06	1.0E+06	21.9	1.0E+06	Chimpanzee	NA
Co-factor recruitment	OT_AR_ARSRC1_0480	62.8	72.0	58.7	1.0E+06	Human	Kidney
	OT_AR_ARSRC1_0960	49.7	47.0	37.3	34.2	Human	Kidney
Antagonist transactivation	TOX21_AR_BLA_Antagonist_ratio	40.0	1.0E+06	1.0E+06	29.3	Human	Kidney
	TOX21_AR_LUC_MDAKB2_Antagonist	31.0	17.8	7.0	40.8	Human	Breast

^a Data for ER and AR activities were sourced from Judson et al., (2015) and Kleinstreuer et al., (2016), respectively.

^b Assays for which all chemicals were inactive are not displayed.

An AC50 value of 1.0E+06 indicates that the chemical was inactive in that assay.

NA = not applicable (cell-free binding assay).