Table 1. List of chemical mixtures targeting male reproductive development in the Earl Gray, Jr. laboratory, USEPA (as of October 2016).

Type of mixture	Mixture study design[a]: Chemicals in mixture	Mechanism of individual chemicals
Similar mechanisms of action, same signaling pathway[c]	B, EQ: Vinclozolin (VIN) + Procymidon (PROCYM)	VIN and PROCYM: Androgen receptor (AR) antagonists
	B, EQ: Di(n)butyl phthalate (DBP) + Benzyl butyl phthalate (BBP)	DBP and BBP: inhibitors of fetal testosterone (T) synthesis with a o common active metabolite (monobutyl phthalate (MBP))
	B, EQ: DBP + Diethylhexyl phthlate (DEHP)	DBP and DEHP: inhibitors of fetal T synthesis with different active metabolites (MBP and monoethylhexyl phthalate (MEHP))
	FR-D, EQ: BBP + DBP + DEHP + Diisobutyl phthalate (DiBP) + Dipentyl phthalate (DPeP)	BBP, DBP, DEHP, DiBP, and DPeP: inhibitors of fetal T synthesis
	FR-D, EQ: BBP + DBP + DEHP + DiBP + DPeP + Dihexyl phthlate (DHP) + Diheptyl phthalate (DHeP) + Diisoheptyl phthalate (DiHeP) + dicyclohexyl phthalate (DCHP)	BBP, DBP, DEHP, DiBP, DHP, DHeP, DiHeP, DCHP, and DPeP: inhibitors of fetal T synthesis
Different mechanisms of action, same signaling pathway	B, EQ: BBP + Linuron (LIN)	BBP: inhibitor of fetal T synthesis LIN: AR antagonist and direct inhibitor of T synthesis
	FR-D, EQ: DBP + PROCYM	DBP: inhibitor of fetal T synthesis PROCYM: AR antagonist

	FR-D, EQ: VIN + PROCYM + Prochloraz (PROCL) + LIN + BBP + DBP + DEHP	VIN and PROCYM: AR antagonists LIN: AR antagonist and direct inhibitor of T synthesis PROCL: AR antagonist and direct inhibitor of steroid hormone synthesis BBP, DBP, and DEHP: inhibitors of fetal T synthesis
	FR-D, EQ: VIN + PROCYM + PROCL + LIN + BBP + DBP + DEHP + DiBP + DiHeP + DPeP	VIN and PROCYM: AR antagonists LIN: AR antagonist and direct inhibitor of T synthesis PROCL: AR antagonist and inhibitor of steroid hormone synthesis BBP, DBP, DEHP, DiBP, DiHeP, DPeP: inhibitors of fetal T synthesis
	FR-D, EQ: DBP + Pyrifluquinazon (PFQ)	DBP: inhibitor of fetal T synthesis PFQ: Possible AR antagonist
Different signaling pathways, same target tissue	B, EQ DBP + 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD)	DBP: inhibitor of fetal T synthesis TCDD: Aryl hydrocarbon receptor (AhR) agonist
Converging AOPs, same target tissue	B, EQ: DPeP + Simvastatin (SIM)	DPeP: inhibitor of fetal T synthesis SIM: inhibitor of cholesterol synthesis (via inhibition of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase) resulting in redu fetal T synthesis
Converging AOPs, same target tissue and different mechanisms of action, same signaling pathway	18 chemical, FR-D, LOEL study: VIN + PROCYM + PROCL + PFQ + p,p'- dichlorodiphenyl dichloroethylene (pp'DDE) + LIN + PHTHALATES (BBP + DBP + DEHP + DiBP + DiHeP + DPeP + DHeP + DCHP + DHP) + flutamide (FLUT) + finasteride (FIN) + SIM	VIN, PFQ, FLUT, p,p'DDE and PROCYM: AR antagonists LIN: AR antagonist and direct inhibitor of T synthesis PROCL: AR antagonist and direct inhibitor of steroid hormone synthesis BBP + DBP + DEHP + DiBP + DiHeP + DPeP + DHeP + DCHP + D inhibitors of fetal T synthesis SIM: inhibitor of cholesterol synthesis (via inhibition of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase) resulting in redu fetal T synthesis FIN: direct inhibitor of dihydrotestosterone (DHT) synthesis (via 5 a reductase)
	15 chemical FR-D, NOEL study: VIN + PROCYM + PROCL + PFQ + pp'DDE + LIN + PHTHALATES (BBP + DBP + DEHP + DiBP + DiHeP + DPeP+ DHeP + DCHP + DHP)	VIN, PFQ, p,p'DDE and PROCYM: AR antagonists LIN: AR antagonist and direct inhibitor of T synthesis PROCL: AR antagonist and direct inhibitor of steroid hormone synthesis BBP + DBP + DEHP + DiBP + DiHeP + DPeP + DHeP + DCHP + D inhibitors of fetal T synthesis

Mixture study design: binary (B) or fixed ratio dilution (FR-D) design with equipotent doses (EQ), doses based on one-fifth the lowest observed effect level (LOEL), or doses based on twice the no observed effect level (NOEL) for the individual chemicals for the top dose.

b

Mixture models tested include: dose addition (DA), integrated addition (IA), response addition (RA), and toxic equivalency factor (TEQ). Studies that did not specifically test a mixture model, but compared the data to the individual chemical responses were considered to have tested RA.

c

AOP: adverse outcome pathway