Table 2. Earl Gray's Anticipated Effects of Various Endocrine-Active Chemicals with Various Mechanisms on Maternal and Offspring Endpoints in the *In Utero*/Lactational Screening Protocol

Chemical:	TCDD	MXC	DBP	VIN	PRO	LIN	KETO	FEN	PER
Class:	RM	RM	NRM	RM (M1 and M2)	RM	RM	NRM	NRM	NRM
Function:	Ah R agonist	EAG EAN AAN	Inhibit fetal T synthesis; AAN	AAN	AAN	AAN may also inhbit fetal T synthesis	SBI	ARI	Inhibit I transport into thyroid; "TAG"
A. FO Dams									
Fertility/pregnancy indices				–	–			delayed parturition	–
Postimplantation (*in utero)* loss	–			–	–	–		–	–
Serum T4/TSH		TSH, T4	–	–	–	–	–	–	TSH, T4
B. F1 Offspring									
1. <u>During Lactation</u>									
No. total, live/litter				–	–	–			–
Sex ratio	–	–	–	–	–	–	–	–	–
AGD (pnd 0)	??	-	males	males	males	males	-	-	--
Retained nipples (both sexes, pnd 11-13)	-	-	males	males	males	males	-	-	--
Gross necropsy, culled pups (pnd 4)	–	–	MAL males	-	-	MAL males	--	–	–

Chemical:	TCDD	MXC	DBP	VIN	PRO	LIN	KETO	FEN	PER
Class:	RM	RM	NRM	RM (M1 and M2)	RM	RM	NRM	NRM	NRM
Function:	Ah R agonist	EAG EAN AAN	Inhibit fetal T synthesis; AAN	AAN	AAN	AAN may also inhbit fetal T synthesis	SBI	ARI	Inhibit I transport into thyroid; "TAG"
2. Postwean Cohort									
a. Female Uterotrophic									
AGD on pnd 21	–	-	–	–	–	–	–	-	–
Uterine weight and histology			–	–	–	–	-	-	-
Necropsy (pnd 24)									
Retained nipples???????	–	–	–	–	–	–	–	-	–
Ovary (paired) weight	-	-	–	–	–	--			--
Uterine weight (wet)			–	–	–	–		-	--
Uterine histopathology	?		–	–	–	–	-	-	--
Serum E2, T4, and TSH	E2	THS, T4	–	–	–	–	–	_	E2, TSH, T4
b. Female Pubertal Cohort									
AGD on pnd 21	–	-	–	–	–	–	--	-	–
Age of Vaginal Patency			–	–	–	–			
Age at first estrus	–	_	–	–	–	–	?	?	?
Necropsy (pnd 42/43)									
AGD	-	-	–	–	–	–	–	–	–
Retained nipples	-	–	–	–	–	–	–	–	–
Serum TSH, T3, T4	–	TSH, T3, T4	–	–	–	–	–	–	TSH, T3, T4

Chemical:	TCDD	MXC	DBP	VIN	PRO	LIN	KETO	FEN	PER
Class:	RM	RM	NRM	RM (M1 and M2)	RM	RM	NRM	NRM	NRM
Function:	Ah R agonist	EAG EAN AAN	Inhibit fetal T synthesis; AAN	AAN	AAN	AAN may also inhbit fetal T synthesis	SBI	ARI	Inhibit I transport into thyroid; "TAG"
Organ Weights									
Uterus (wet and blotted)	?	--	–	–	–	–			–
Ovaries (paired)	--	-	–	–	–	–		?	–
Thyroid	–	–	–	–	–	–	–	–	
Liver		–	–	?	?	–		–	–
Kidneys (paired)	–	–	–	–	–	–	–	–	–
Adrenal glands (paired	–	–	?	?	?	?		–	--
Histopathology	ovarian histo Vaginal Threads	–	–	–	–	–	–	ovary	thyroid histo
c. Male Pubertal Cohort									
AGD on pnd 21	-	-					-	–	–
Age at Preputial Separation								–	
Necropsy (pnd 60)									
AGD	-	-						–	–
Retained nipples	-	-					-	–	--
Serum TSH, T3, T4		TSH, T3/T4	–	–	–	–	–	–	TSH, T3/T4

Chemical:	TCDD	MXC	DBP	VIN	PRO	LIN	KETO	FEN	PER
Class:	RM	RM	NRM	RM (M1 and M2)	RM	RM	NRM	NRM	NRM
Function:	Ah R agonist	EAG EAN AAN	Inhibit fetal T synthesis; AAN	AAN	AAN	AAN may also inhbit fetal T synthesis	SBI	ARI	Inhibit I transport into thyroid; "TAG"
Organ Weights									
Paired testes	?		MAL		?	MAL	-	–	
Paired epididymides			MAL			MAL		–	–
Prostate (whole and ventral and dorsolateral lobes)				MAL	MAL			–	–
Seminal visicles with coagulating glands				MAL	MAL	T and LH		–	–
Cowper's glands								–	–
Glans penis								--	–
LABC complex			–					–	–
Adrenal glands (paired)	–	–						–	–
Thyroid	–	–	–	–	–	–	–	–	
Serum TSH, T3/T4 Serum Testosterone and LH	T3/T4	TSH, T3/T4	T?	T and LH	T and LH	–	LH and T	–	TSH, T3/T4, T and LH
Liver			–			–			?
Kidneys (paired)	–	–	–		–	–	–	–	?
Epididymal sperm number								--	
Testicular homogenization-resistant spermatid head counts	-	-		-	-			-	
Histopathology	-	-	epididymides, testes	VP, SV	–	epididymides, testes	adrenal	--	thyroid

Key:

Class:

RM	=	receptor mediated
NRM	=	not receptor mediated

Function:

EAG	=	estrogen agonist
EAN	=	estrogen antagonist
AAN	=	androgen antagonist
TAN	=	thyroid agonist
TAG	=	thyroid antagonist
SBI	=	steroid biosynthesis inhibitor
ARI	=	aromatase inhibitor (prevents conversion of T to E)
5 RI	=	5 -reductase inhibitor (prevents conversion of T to DHT)
T	=	testosterone (mammalian endogenous androgen)
E	=	17 -estradiol (mammalian endogenous estrogen)
DHT	=	dihydrotestosterone (potent *in utero* androgen
HPG	=	hypothalamic-pituitary-gonadal axis

Chemicals:

TCDD	=	2,3,7,8-tetrachlorodibenzo-*p*-dioxin
MXC	=	methoxychlor (metabolite HPTE, high affinity for estrogen receptor alpha; ER)
DBP	=	di-n-butyl phthalate
VIN	=	vinclozolin (metabolites M1 and M2)
PRO	=	procymidone
LIN	=	linuron
FEN	=	fenarimol
PER	=	perchlorate

Activity:

	=	increases, stimulates, accelerates
	=	decreases, inhibits, delays
–	=	no change
?	=	associated with arrows; likely, not confirmed
MAL	=	male/female reproductive tract malformations with *in utero* exposure

NOTE: For effects indicated in this table, the following assumptions were made:

(1) The predictions were made based upon EPA studies and then the chemicals were evaluated in the RTI *in utero*/lactational screening protocol
(2) The route employed was effective
(3) The doses employed were effective
(4) The time(s) of evaluation detected effects