

**Preliminary Draft Under Development
EDSP and Other Validation Chemicals at a
Glance
(December 2005)**

Summary

EDSP & Other Valdiation Chemicals at a Glance Version 1 Dec 05

Modality	Chemical	Hersh-berger	Utero-trophic	TG 407	Pubertal Female	Pubertal Male	Adult Male	Fish repro screen	Frog
Androgen agonist		<u>Agonist</u>	<i>Agonist</i>						
	Methyl testosterone	X		X		X		X	
	Testosterone propionate	X					X		
	Trenbolone	X						X	
Androgen antagonist		<u>Antagonist</u>	<i>Antagonist</i>						
	Cyproterone acetate						X		
	DDE- <i>p,p'</i>	X		X		X	X	X	
	<u>Flutamide</u>	X		X		X	X	X	
	Linuron	X				X	X		
	<u>Methoxychlor (HPTE)**</u>		X		X	X	X	X	
	Procymidone	X							
	Vinclozolin	X				X	X	X	
Estrogen agonist									
	17 β Estradiol						X	X	
	4-tert-pentylphenol							X	
	Bisphenol A		X		X			X	
	Coumestrol						X		
	DDT- <i>o,p'</i>		X						
	Ethynyl estradiol		X	X	X				
	Genistein		X	X					
	<u>Methoxychlor (HPTE)**</u>		X		X	X	X	X	
	<u>Nonylphenol</u>		X	X					
Estrogen antagonist									
	ICI 182,780						X		
	Tamoxifen citrate			X	X				
HPG									
	Atrazine				X	X		X	X
Steroidogenesis									
	<u>Flutamide</u>					X	X	X	
	Ketoconazole				X	X	X	O	
	Prochloraz							X	
	<u>Di-n-butylphthalate</u>		X			X			
(5α reductase)									
	Finasteride	X					X		
Aromatase									
	Anastrozole						X		
	Fadrozole						X	X	
	CGS 183201			X					

** Needs metabolism to the active form, which is not expected to occur in vitro.

X Chemical has been run using either pre-validation or validation protocols

O Planned or underway.

Summary

Modality	Chemical	Hershberger	Uterotrophic	TG 407	Pubertal Female	Pubertal Male	Adult Male	Fish repro screen	Frog
	Fenarimol				X				
	Ketoconazole				X	X	X		
Thyroid									
	Iopanoic acid (monodeiodinases)								O
	Methimazole								X
	PBDE (DE-71)				X	X			O
	Perchlorate (Ammonium or Sodium)				X a	X a		X s	X s
	Phenobarbital				X	X	X		X
	Propylthiouracil			X	X	X	X		X
	Thyroxine			X					X
Other modalities									
Corticosteroids									
	Dexamethasone								X
	Pregnenolone-16-a-carbonitrile								X
Dopamine Receptor Antagonists									
	Apomorphine						X		
	Haloperidol						X		
	Mifepristone RU486						X		
	Oxazepam						X		
	Pimozide				X	X	X		
	Reserpine						X		
Methemoglobinemia	2-chloronitrobenzene				X	X			
Used as negative chemicals									
	Nonylphenol	X							
	Di-n-butylphthalate		X						
	2,4-Dinitrophenol	X							
	Potassium permanganate							X	
	n-propanol							O	

** Needs metabolism to the active form, which is not expected to occur in vitro.

X Chemical has been run using either pre-validation or validation protocols

O Planned or underway.

Androgen Agonist

Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
Hershberger agonist							
Agonist Hershberger assay used group n of 6, 10 days consecutive administration, necropsy on day 11							
Testosterone propionate	OECD Hershberger	Primary reference positive	Rat - both Sprague and Wistar	sub-cutaneous, 10 cons. days	0.1, 0.2, 0.4, 0.8, and 1.6 mg/kg/d (Test series in Phase 1A, 0.2 and 0.4 mg/kg/d were selected for subsequent work)	VP, SVCG, LABC, GP, COWS	
Methyl testosterone	OECD Hershberger	Test compound positive	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.5, 2, 10, 40 mg/kg/d 0.05, 0.5, 5, 50 mg/kg/d (Two series - top is outside of Japan, bottom is within Japan)	VP, SVCG, LABC, GP, COWS	
Trenbolone	OECD Hershberger	Test compound positive	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.3, 1.5, 8, 40 mg/kg/d	VP, SVCG, LABC, GP, COWS	
Nonylphenol	OECD Hershberger	Test compound negative	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	150 mg/kg/d	VP, SVCG, LABC, GP, COWS	
2,4-Dinitrophenol	OECD Hershberger	Test compound negative	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	10 mg/kg/d	VP, SVCG, LABC, GP, COWS	

Androgen Antagonist

Antagonist Hershberger assay used group n of 6, 10 days consecutive administration, necropsy on day 11 - the stimulating androgen was coadministered with test substance on each day

Hershberger Antagonist

	Venue	Overview	Species	Dosing	TP doses (TP was the coadministered stimulating androgen; sc, in mg/kg/d)	Doses	Endpoints	Labs	Summary
Flutamide	OECD Hershberger	Primary reference compound	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.2 and 0.4		VP, SVCG, LABC, GP, COWS		
Procymidone	OECD Hershberger	Test compound positive	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.4	3, 10, 30, 100 mg/kg/d	VP, SVCG, LABC, GP, COWS		
Vinclozolin	OECD Hershberger	Test compound positive	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.2 and 0.4	3, 10, 30, 100 mg/kg/d	VP, SVCG, LABC, GP, COWS		
Linuron	OECD Hershberger	Test compound positive	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.4	3, 10, 30, 100 mg/kg/d	VP, SVCG, LABC, GP, COWS		

VP- ventral prostate, SVCG - seminal vesicles and coagulating glands, LABC - levator ani bulbocavernosus, GP - glans penis, COWS - Cowper's or bulbourethral glands

Androgen Antagonist

	Venue	Overview	Species	Dosing	TP doses (TP was the coadministered stimulating androgen; sc, in mg/kg/d)	Doses	Endpoints	Labs	Summary
<i>p,p'</i>-DDE	OECD Hershberger	Test compound positive	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.2 and 0.4	5, 16, 50, 160 mg/kg/d and 3, 10, 30, 100 mg/kg/d (top series was run outside of Japan, and bottom series of doses within Japan)	VP, SVCG, LABC, GP, COWS		
Nonylphenol	OECD Hershberger	Test compound negative	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.4	150 mg/kg/d	VP, SVCG, LABC, GP, COWS		
2,4- Dinitrophenol	OECD Hershberger	Test compound negative	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.4	10 mg/kg/d	VP, SVCG, LABC, GP, COWS		
5α-reductase inhibitor - not androgen receptor antagonist									
Finasteride	OECD Hershberger	Test compound positive of enzyme inhibition	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.4	0.2, 1, 5, 25 mg/kg/d	VP, SVCG, LABC, GP, COWS		

VP- ventral prostate, SVCG - seminal vesicles and coagulating glands, LABC - levator ani bulbocavernosus, GP - glans penis, COWS - Cowper's or bulbourethral glands

Estrogen Agonist

Uterotrophic assay									
	Venue	Overview	Species	Dosing	Doses		Endpoints	Labs	Summary
Ethinyl Estradiol	OECD Uterotrophic	Primary reference positive	Rat - both Sprague and Wistar	sc, 3 cons. days	oral gavage - 0.01, 0.03, 0.1, 0.3, 1, 3, and 10 µg/kg/d (With Phase 2, 1 and 3 mg EE/kg/d were used as positive control)	sc - 0.01, 0.03, 0.1, 0.3, 1, 3, and 10 µg/kg/d (With Phase 2, 0.3 and 1 mg EE/kg/d were used as positive control)	wet and blotted uterine wt		
Genistein	OECD Uterotrophic	Test compound positive	Rat - both Sprague and Wistar	oral gavage and sc, 3 cons. days	oral gavage - 20, 60, 120, 300, and 500 mg/kg/d	sc - 1, 15, 35, 50, and 80 mg/kg/d	wet and blotted uterine wt		
Methoxychlor	OECD Uterotrophic	Test compound positive	Rat - both Sprague and Wistar	oral gavage and sc, 3 cons. days	oral gavage - 20, 50, 120, 300, and 500 mg/kg/d	sc - 20, 100, 250, 500, and 800 mg/kg/d	wet and blotted uterine wt		
Nonylphenol	OECD Uterotrophic	Test compound negative	Rat - both Sprague and Wistar	oral gavage and sc, 3 cons. days	oral gavage - 15, 75, 125, 250, and 350 mg/kg/d	sc - 5, 15, 35, 80, and 100 mg/kg/d	wet and blotted uterine wt		
Bisphenol A	OECD Uterotrophic	Test compound negative	Rat - both Sprague and Wistar	oral gavage and sc, 3 cons. days	oral gavage - 60, 200, 375, 600 and 1000 mg/kg/d	sc - 10, 100, 300, 600 and 800 mg/kg/d	wet and blotted uterine wt		

Estrogen Agonist

Uterotrophic assay									
	Venue	Overview	Species	Dosing	Doses		Endpoints	Labs	Summary
<i>o,p'</i>-DDT	OECD Uterotrophic	Test compound negative	Rat - both Sprague and Wistar	oral gavage and sc, 3 cons. days	oral gavage - 10, 50, 125, 300 and 600 mg/kg/d	sc - 5, 25, 50, 100, and 200 mg/kg/d	wet and blotted uterine wt		
Dibutyl- phthalate	OECD Uterotrophic	Test compound negative	Rat - both Sprague and Wistar	oral gavage and sc, 3 cons. days	oral gavage - 1000 mg/kg/d	sc - 500 mg/kg/d	wet and blotted uterine wt		

Estrogen Antagonist

	Venue	Overview	Species	Dosing	Doses		Endpoints	Labs	Summary
	Uterotrophic								
ZM 189,154	OECD Uterotrophic	Test compound positive	Rat - both Sprague and Wistar	oral gavage and sc, 3 cons. days	oral gavage	sc	wet and blotted uterine wt		

Uterotrophic

Agonist uterotrophic assay used group n of 6, 3 days consecutive administration, necropsy on day 11 - both immature female (dosing start pnd 18-20) and ovariectomized young adult female								
Agonist uterotrophic assay								
Venue	Overview	Species	Dosing	Doses		Endpoints	Labs	Summary
Ethinyl Estradiol	OECD Uterotrophic	Primary reference positive	Rat - both Sprague and Wistar	sc, 3 cons. days	oral gavage - 0.01, 0.03, 0.1, 0.3, 1, 3, and 10 mg/kg/d (With Phase 2, 1 and 3 mg EE/kg/d were used as positive control)	sc - 0.01, 0.03, 0.1, 0.3, 1, 3, and 10 mg/kg/d (With Phase 2, 0.3 and 1 mg EE/kg/d were used as positive control)	wet and blotted uterine wt (The wet weight includes the imbibed luminal fluid; blotted is after the incision of the wall and blotting of the uterus under mild pressure)	
Genistein	OECD Uterotrophic	Test compound positive	Rat - both Sprague and Wistar	oral gavage and sc, 3 cons. days	oral gavage - 20, 60, 120, 300, and 500 mg/kg/d	sc - 1, 15, 35, 50, and 80 mg/kg/d	wet and blotted uterine wt	
Methoxychlor	OECD Uterotrophic	Test compound positive	Rat - both Sprague and Wistar	oral gavage and sc, 3 cons. days	oral gavage - 20, 50, 120, 300, and 500 mg/kg/d	sc - 20, 100, 250, 500, and 800 mg/kg/d	wet and blotted uterine wt	
Nonylphenol	OECD Uterotrophic	Test compound negative	Rat - both Sprague and Wistar	oral gavage and sc, 3 cons. days	oral gavage - 15, 75, 125, 250, and 350 mg/kg/d	sc - 5, 15, 35, 80, and 100 mg/kg/d	wet and blotted uterine wt	
Bisphenol A	OECD Uterotrophic	Test compound negative	Rat - both Sprague and Wistar	oral gavage and sc, 3 cons. days	oral gavage - 60, 200, 375, 600 and 1000 mg/kg/d	sc - 10, 100, 300, 600 and 800 mg/kg/d	wet and blotted uterine wt	

Uterotrophic

	Venue	Overview	Species	Dosing	Doses		Endpoints	Labs	Summary
<i>o,p'</i>-DDT	OECD Uterotrophic	Test compound negative	Rat - both Sprague and Wistar	oral gavage and sc, 3 cons. days	oral gavage - 10, 50, 125, 300 and 600 mg/kg/d	sc - 5, 25, 50, 100, and 200 mg/kg/d	wet and blotted uterine wt		
Dibutyl- phthalate	OECD Uterotrophic	Test compound negative	Rat - both Sprague and Wistar	oral gavage and sc, 3 cons. days	oral gavage - 1000 mg/kg/d	sc - 500 mg/kg/d	wet and blotted uterine wt		
	Antgonist uterotrophic assay used group n of 6, EE was coadministered as a stimulating estrogen, 3 days consecutive administration of the test substgance, necropsy on day 11 - both immature female (dosing start pnd 18-20) and								
	Antagonist uterotrophic assay								
	Venue	Overview	Species	Dosing	Doses		Endpoints	Labs	Summary
ZM 189,154	OECD Uterotrophic	Test compound positive	Rat - both Sprague and Wistar	oral gavage and sc, 3 cons. days	oral gavage	sc	wet and blotted uterine wt		

Hershberger

Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
Hershberger agonist							
Agonist Hershberger assay used group n of 6, 10 days consecutive administration, necropsy on day 11							
Testosterone propionate		Primary reference positive	Rat - both Sprague and Wistar	sub-cutaneous, 10 cons. days	0.1, 0.2, 0.4, 0.8, and 1.6 mg/kg/d (Test series in Phase 1A, 0.2 and 0.4 mg/kg/d were selected for subsequent work)	VP, SVCG, LABC, GP, COWS (see H64:72)	
Methyl testosterone	OECD Hershberger	Test compound positive	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.5, 2, 10, 40 mg/kg/d 0.05, 0.5, 5, 50 mg/kg/d (Two series - top is outside of Japan, bottom is within Japan)	VP, SVCG, LABC, GP, COWS	
Trenbolone	OECD Hershberger	Test compound positive	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.3, 1.5, 8, 40 mg/kg/d	VP, SVCG, LABC, GP, COWS	
Nonylphenol	OECD Hershberger	Test compound negative	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	150 mg/kg/d	VP, SVCG, LABC, GP, COWS	

VP- ventral prostate, SVCG - seminal vesicles and coagulating glands, LABC - levator ani bulbocavernosus, GP - glans penis, COWS - Cowper's or bulbourethral glands

Hershberger

2,4-Dinitrophenol	OECD Hershberger	Test compound negative	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	10 mg/kg/d	VP, SVCG, LABC, GP, COWS			
	Hershberger antagonist								
	Antagonist Hershberger assay used group n of 6, 10 days consecutive administration, necropsy on day 11 - the stimulating androgen was coadministered with test substance on each day								
	Venue	Overview	Species	Dosing	TP doses (TP was the coadministered stimulating androgen; sc, in mg/kg/d)	Doses	Endpoints	Labs	Summary
Flutamide	OECD Hershberger	Primary reference compound	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.2 and 0.4	0.1, 0.3, 1, 3, and 10 mg/kg/d (doses in Phase 1B, subsequently, as positive antagonist control, 10 was used for maximum effect, 3 for ability of assays to detect modest effect)	VP, SVCG, LABC, GP, COWS		
Procymidone	OECD Hershberger	Test compound positive	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.4	3, 10, 30, 100 mg/kg/d	VP, SVCG, LABC, GP, COWS		

VP- ventral prostate, SVCG - seminal vesicles and coagulating glands, LABC - levator ani bulbocavernosus, GP - glans penis, COWS - Cowper's or bulbourethral glands

Hershberger

					TP doses (TP was the coadministered stimulating androgen; sc, in mg/kg/d)				
	Venue	Overview	Species	Dosing		Doses	Endpoints	Labs	Summary
Vinclozolin	OECD Hershberger	Test compound positive	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.2 and 0.4	3, 10, 30, 100 mg/kg/d	VP, SVCG, LABC, GP, COWS		
Linuron	OECD Hershberger	Test compound positive	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.4	3, 10, 30, 100 mg/kg/d	VP, SVCG, LABC, GP, COWS		
p,p'-DDE	OECD Hershberger	Test compound positive	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.2 and 0.4	5, 16, 50, 160 mg/kg/d and 3, 10, 30, 100 mg/kg/d (top series was run outside of Japan, and bottom series of doses within Japan)	VP, SVCG, LABC, GP, COWS		
Nonylphenol	OECD Hershberger	Test compound negative	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.4	150 mg/kg/d	VP, SVCG, LABC, GP, COWS		

VP- ventral prostate, SVCG - seminal vesicles and coagulating glands, LABC - levator ani bulbocavernosus, GP - glans penis, COWS - Cowper's or bulbourethral glands

Hershberger

	Venue	Overview	Species	Dosing	TP doses (TP was the coadministered stimulating androgen; sc, in mg/kg/d)	Doses	Endpoints	Labs	Summary
2,4-Dinitrophenol	OECD Hershberger	Test compound negative	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.4	10 mg/kg/d	VP, SVCG, LABC, GP, COWS		
5α-reductase inhibitor - not androgen receptor antagonist									
Finasteride	OECD Hershberger	Test compound positive of enzyme inhibition	Rat - both Sprague and Wistar	oral gavage, 10 cons. days	0.4	0.2, 1, 5, 25 mg/kg/d	VP, SVCG, LABC, GP, COWS		

VP- ventral prostate, SVCG - seminal vesicles and coagulating glands, LABC - levator ani bulbocavernosus, GP - glans penis, COWS - Cowper's or bulbourethral glands

TG 407

Assay is based on groups of 5 males and 5 females, validation study explored increasing the number and internal replication at lab by running a second group of 5 and 5, then combining to 10 for a statistical run								
	Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
Ethinyl Estradiol	OECD TG 407	Test compound positive, estrogen	Rat - both Sprague and Wistar	oral gavage, 28 cons. days	10, 50, and 200 mg/kg/d	Battery, see note L3:O30	Two	Topline outcome - what was positive @ what dose?
Genistein	OECD TG 407	Test compound positive, weak estrogen	Rat - both Sprague and Wistar	oral gavage, 28 cons. days	120, 400, and 1000 mg/kg/d	Battery, see note	Two	
Nonylphenol	OECD TG 407	Test compound positive, weak estrogen	Rat - both Sprague and Wistar	oral gavage, 28 cons. days	20 and 80 mg/kg/d, then 150 in lab #1 and 250 in lab #2 for high dose	Battery, see note	Two	
Tamoxifen	OECD TG 407	Test compound positive, antiestrogen	Rat - both Sprague and Wistar	oral gavage, 28 cons. days	5, 30, and 200 mg/kg/d	Battery, see note	Two	
CGS 18320B	OECD TG 407	Test compound positive, aromatase inhibitor	Rat - both Sprague and Wistar	oral gavage, 28 cons. days	0.3, 3, and 30 mg/kg/d	Battery, see note	Two	
Methyl Testosterone	OECD TG 407	Test compound positive, androgen	Rat - both Sprague and Wistar	oral gavage, 28 cons. days	males 10, 40, 200 mg/kg/d females 10, 100, and 600 mg/kg/d	Battery, see note	Two	

TG 407

	Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
Flutamide	OECD TG 407	Test compound positive, antiandrogen	Rat - both Sprague and Wistar	oral gavage, 28 cons. days	1, 10, and 100 mg/kg/d	Battery, see note	Two	
<i>p,p'</i>-DDE	OECD TG 407	Test compound positive, weak androgen	Rat - both Sprague and Wistar	oral gavage, 28 cons. days	Lab #1 12.5, 50, and 200 mg/kg/d Lab #2 6.5, 25, and 100 mg/kg/d	Battery, see note	Two	
Propylthiouracil	OECD TG 407	Test compound positive, thyroid toxicant	Rat - both Sprague and Wistar	oral gavage, 28 cons. days	0.1, 1, and 10 mg/kg/d	Battery, see note	Two	
Thyroxine (T4)	OECD TG 407	Test compound positive, thyroid hormone, suppress pituitary	Rat - both Sprague and Wistar	oral gavage, 28 cons. days	0.1, 1, and 10 mg/kg/d	Battery, see note	Two	

**Summary of Key Endpoints
TG 407**

Summary of key endpoints, including general and hormone sensitive			
	Tissue Wt	Histology	Other
Males	thyroid liver, kidney, adrenals, thymus, spleen, brain, heart brain, spinal cord, stomach, small and large intestines, liver; kidneys, adrenals, spleen; heart, thymus, trachea, lungs, gonads, accessory sex organs (i.e., uterus, prostate), urinary bladder, lymph nodes, peripheral nerve, bone marrow, all gross lesions testes, epididymides, seminal + coagulating glands, ventral prostate pituitary	thyroid liver, kidney, adrenals, thymus, spleen, brain, heart brain, spinal cord, stomach, small and large intestines, liver; kidneys, adrenals, spleen; heart, thymus, trachea, lungs, gonads, accessory sex organs (i.e., uterus, prostate), urinary bladder, lymph nodes, peripheral nerve, bone marrow, all testes, epididymides, seminal + coagulating glands, ventral prostate pituitary	T3, T4 epididyma l sperm
Females	thyroid liver, kidney, adrenals, thymus, spleen, brain, heart brain, spinal cord, stomach, small and large intestines, liver; kidneys, adrenals, spleen; heart, thymus, trachea, lungs, gonads, accessory sex organs (i.e., uterus, prostate), urinary bladder, lymph nodes, peripheral nerve, bone marrow, all gross lesions ovaries, uterus pituitary	mammary gland thyroid liver, kidney, adrenals, thymus, spleen, brain, heart brain, spinal cord, stomach, small and large intestines, liver; kidneys, adrenals, spleen; heart, thymus, trachea, lungs, gonads, accessory sex organs (i.e., uterus, prostate), urinary bladder, lymph nodes, peripheral nerve, bone marrow, all ovaries, uterus pituitary mammary gland, vagina	T3, T4 daily vaginal

Pubertal Female

15 females per dose group, 2 or more dose levels, gavage pnd 22 through pnd 42

		Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
1	Ethinyl Estradiol	USEPA Pubertal Female	Potent Estrogen agonist	Rat - Sprague Dawley	oral gavage/ diet/sc?	What mg/kg/d?	vaginal opening, organ wts, histology, hormones (growth, daily body wt)	Number & who?	Topline outcome - what was positive @ what dose?
2	17β-Estradiol?	USEPA Pubertal Female	Potent Estrogen agonist	Rat - Sprague Dawley			vaginal opening, organ wts, histology, hormones		
3	Coumestrol	USEPA Pubertal Female	Modest Estrogen agonist	Rat - Sprague Dawley			vaginal opening, organ wts, histology, hormones		
4	Nonylphenol	USEPA Pubertal Female	Weak Estrogen agonist	Rat - Sprague Dawley			vaginal opening, organ wts, histology, hormones		
5	Octylphenol	USEPA Pubertal Female	Weak Estrogen agonist	Rat - Sprague Dawley			vaginal opening, organ wts, histology, hormones		

Pubertal Female

		Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
12	PBDE (DE-71)	USEPA	Accelerates hepatic	Rat - Sprague Dawley			vaginal opening, organ wts, histology, hormones		
		Pubertal Female	thyroid metabosim/excretion						
13	Finasteride	USEPA	5 α -reductase inhibitor	Rat - Sprague Dawley			vaginal opening, organ wts, histology, hormones		
		Pubertal Female							
14	Ketoconazole	USEPA	General P450 steroidogenesis inhibitor	Rat - Sprague Dawley			vaginal opening, organ wts, histology, hormones		
		Pubertal Female							
15	Fenarimol?	USEPA	General P450 steroidogenesis inhibitor	Rat - Sprague Dawley			vaginal opening, organ wts, histology, hormones		
		Pubertal Female							
16	Fadrozole	USEPA	Aromatase inhibitor	Rat - Sprague Dawley			vaginal opening, organ wts, histology, hormones		
		Pubertal Female							
17	Testolactone	USEPA	Aromatase inhibitor	Rat - Sprague Dawley			vaginal opening, organ wts, histology, hormones		
		Pubertal Female							

Pubertal Female

		Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
18	Atrazine	USEPA	Neuroendocr	Rat -			vaginal opening,		
		Pubertal	ine impact	Sprague			organ wts,		
		Female	on pituitary	Dawley			histology,		
							hormones		
							What tissues wts		
							What tissues histo		
							What hormones		

Pubertal Male

15 males per dose group, 2 or more dose levels, gavage pnd 23 through pnd 53

		Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
1	Diethylstilbestrol	USEPA Pubertal Male	Potent Estrogen agonist	Rat - Sprague Dawley	oral gavage/ diet/sc?	What mg/kg/d?	preputial separation, organ wts, histology, hormones (growth, daily body wt)	Number & who?	Topline outcome - what was positive @ what dose?
2	Bisphenol A	USEPA Pubertal Male	Weak Estrogen agonist	Rat - Sprague Dawley					
3	Dibutylphthalate	USEPA Pubertal Male	Testosterone synthesis inhibitor	Rat - Sprague Dawley					
4	Methoxychlor	USEPA Pubertal Male	Weak Estrogen agonist	Rat - Sprague Dawley					
5	Testosterone (or Methyl T?)	USEPA Pubertal Male	Potent Androgen agonist	Rat - Sprague Dawley					

Pubertal Male

		Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
6	Flutamide	USEPA Pubertal Male	Potent Androgen antagonist	Rat - Sprague Dawley					
7	Cyproterone Acetate	USEPA Pubertal Male	Modest Androgen antagonist	Rat - Sprague Dawley					
8	Vinclozolin	USEPA Pubertal Male	Modest Androgen antagonist	Rat - Sprague Dawley					
9	<i>p,p'</i>-DDE	USEPA Pubertal Male	Weak Androgen antagonist	Rat - Sprague Dawley					
10	Bromocryptine	USEPA Pubertal Male	D2 receptor agonist	Rat - Sprague Dawley					
11	Haloperidol	USEPA Pubertal Male	D2 receptor antagonist	Rat - Sprague Dawley					

Pubertal Male

		Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
12	Propylthiouraci I	USEPA Pubertal Male	Inhibit thyroid hormone synthesis	Rat - Sprague Dawley					
13	Phenobarbital	USEPA Pubertal Male	Accelerates hepatic thyroid metabosim/ excretion	Rat - Sprague Dawley					
14	PBDE (DE-71)	USEPA Pubertal Male	Accelerates hepatic thyroid metabosim/ excretion	Rat - Sprague Dawley					
15	Finasteride	USEPA Pubertal Male	5 α -reductase inhibitor	Rat - Sprague Dawley					
16	Ketoconazole	USEPA Pubertal Male	General P450 steroidogenesis inhibitor	Rat - Sprague Dawley					
17	Fadrozole	USEPA Pubertal Male	Aromatase inhibitor	Rat - Sprague Dawley					

Pubertal Male

		Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
18	Anastrozole	USEPA Pubertal Male	Aromatase inhibitor	Rat - Sprague Dawley					
19	Testolactone	USEPA Pubertal Male	Aromatase inhibitor	Rat - Sprague Dawley					
20	Atrazine	USEPA Pubertal Male	Neuroendocrine impact on pituitary	Rat - Sprague Dawley					
							What tissues wts		
							What tissues histo		
							What hormones		

Adult Male

pnd 72 intact males, 15/group, up to 4 dose groups, 15-day consecutive administration, oral gavage

		Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
1	17β-Estradiol	15day Adult Male	Potent Estrogen agonist	Rat - Sprague Dawley	oral gavage/ diet/sc?	What mg/kg/d?	See notes M4:O8	DuPont & who else?	Topline outcome - what was positive @ what dose?
2	Coumestrol	15day Adult Male	Modest Estrogen agonist	Rat - Sprague Dawley			See notes	DuPont	
3	ICI-182,780	15day Adult Male	Potent Estrogen antagonist	Rat - Sprague Dawley			See notes	DuPont	
4	Testosterone Propionate	15day Adult Male	Potent Androgen agonist	Rat - Sprague Dawley			See notes	DuPont	
5	Flutamide	15day Adult Male	Potent Androgen antagonist	Rat - Sprague Dawley			See notes	DuPont	
6	Cyproterone Acetate	15day Adult Male	Modest Androgen antagonist	Rat - Sprague Dawley			See notes	DuPont	

Adult Male

		Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
7	Vinclozolin	15day Adult Male	Modest Androgen antagonist	Rat - Sprague Dawley			See notes	DuPont	
8	Linuron	15day Adult Male	Weak Androgen antagonist	Rat - Sprague Dawley			See notes	DuPont	
9	<i>p,p'</i>-DDE	15day Adult Male	Weak Androgen antagonist	Rat - Sprague Dawley				DuPont	
10	Progesterone	15day Adult Male	Progesterone agonist	Rat - Sprague Dawley				DuPont	
11	Mifepristone (RU486)	15day Adult Male	Progesterone antagonist	Rat - Sprague Dawley				DuPont	
12	Apomorphine	15day Adult Male	D2 Receptor agonist	Rat - Sprague Dawley				DuPont	
13	Haloperidol	15day Adult Male	D2 Receptor antagonist	Rat - Sprague Dawley				DuPont	

Adult Male

		Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
14	Reserpine	15day Adult Male	Depletes dopamine	Rat - Sprague Dawley				DuPont	
15	Phenobarbital	15day Adult Male	Accelerates hepatic thyroid metabosim/excretion	Rat - Sprague Dawley				DuPont	
16	Oxazepam	15day Adult Male	Accelerates hepatic thyroid metabosim/excretion	Rat - Sprague Dawley				DuPont	
17	Propylthiouracil	15day Adult Male	Inhibit thyroid hormone synthesis	Rat - Sprague Dawley				DuPont	
18	Propylimidazole-2-thione	15day Adult Male	Inhibit thyroid hormone synthesis	Rat - Sprague Dawley				DuPont	
19	Finasteride	15day Adult Male	5 α -reductase inhibitor	Rat - Sprague Dawley				DuPont	
20	Ketoconazole	15day Adult Male	General P450 steroidogenesis inhibitor	Rat - Sprague Dawley				DuPont	

Adult Male

		Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
21	Dibutyl-phthalate	15day Adult Male	Testosterone synthesis inhibitor	Rat - Sprague Dawley				DuPont	
22	Anastrozole	15day Adult Male	Aromatase inhibitor	Rat - Sprague Dawley				DuPont	
23	Fadrozole	15day Adult Male	Aromatase inhibitor	Rat - Sprague Dawley				DuPont	
24	Ammonium perfuluro-octanate	15day Adult Male	Aromatase inhibitor	Rat - Sprague Dawley				DuPont	

Tissue Wts

Histopath

Hormones

liver, testes,
thyroid,
epididymides,
prostate,
seminal vesicles,
accessory sex gland (ASG) unit

testis,
epididymides,
thyroid

testosterone,
DHT, estradiol,
prolactin, LH,
FSH, T3, T4,
TSH

Fish Repro Screen

	Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
USEPA Protocols								
Methoxychlor	USEPA Fish repro screen		Fathead minnow	Diluter into water column? Nominal or analysis?	1 and 5 µg/L		Duluth, Battelle	
Trenbolone	USEPA Fish repro screen		Fathead minnow		0.1 and 1 µg/L		Duluth, Battelle	
Flutamide	USEPA Fish repro screen		Fathead minnow		65 and 650 µg/L		Battelle	
Vinclozolin	USEPA Fish repro screen		Fathead minnow		1 and 5 µg/L		Duluth	
Fadrozole	USEPA Fish repro screen		Fathead minnow		5 and 50 µg/L		Battelle	
Atrazine	USEPA Fish repro screen		Fathead minnow		25 and 250 µg/L		Battelle	

Fish Repro Screen

	Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
OECD Non-reproduction Protocol (Phase 1A)								
17β-Estradiol	OECD Fish repro screen	Potent Estrogen agonist	Japanese medaka, fathead minnow, zebrafish		10, 32 and 100 ng/L			
Trenbolone	OECD Fish repro screen	Potent Androgen agonist	Japanese medaka, fathead minnow, zebrafish		50, 500 and 5000 ng/L			
OECD Reproduction Protocol (Phase 1B)								
17β-Estradiol	OECD Fish repro screen	Potent Estrogen agonist	Japanese medaka, fathead minnow, zebrafish		100 ng/L			
4-tert-pentylphenol	OECD Fish repro screen	Weak Estrogen agonist	Japanese medaka, fathead minnow, zebrafish		100, 320 and 1000 µg/L			
Fadrozole	OECD Fish repro screen	Aromatase inhibitor	Japanese medaka, fathead minnow, zebrafish		100 µg/L			
Prochloraz	OECD Fish repro screen	P450 Inhibitor	Japanese medaka, fathead minnow, zebrafish		20, 100 and 300 µg/L			
Flutamide	OECD Fish repro screen	Potent Androgen agonist	Japanese medaka, fathead minnow, zebrafish		100, 500 and 1000 µg/L			

Frog Metamorphosis

	Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
Propylthio-uracil	USEPA Frog Metamorphosis		Xenopus levis?	Diluter into water column? Nominal or analysis?				
Methimazole	USEPA Frog Metamorphosis							
Phenobarbital	USEPA Frog Metamorphosis							
Sodium Perchlorate	USEPA Frog Metamorphosis							
PBDE (DE-71)	USEPA Frog Metamorphosis							
Iopanoic acid (monodeiodinases)	USEPA Frog Metamorphosis							
Thyroxine	USEPA Frog Metamorphosis							

Frog Metamorphosis

	Venue	Overview	Species	Dosing	Doses	Endpoints	Labs	Summary
Atrazine	USEPA Frog Metamorphosis							
Dexametha-son	USEPA Frog Metamorphosis							
Pregnenolone-16-α-carbonitrile	USEPA Frog Metamorphosis							
	USEPA Frog Metamorphosis							