

US EPA ARCHIVE DOCUMENT

## Appendix O

### Examples of Weight of Evidence Determinations

*[NOTE TO THE READER: The following charts were developed, at the request of the EDSTAC, by one EDSTAC member and one STWG member (not an EDSTAC member). The chart has not been seen by all EDSTAC members and should be considered as a draft for further discussion.]*

**T1S RESPONSE/WOE TABLE.** These three tables (parts 1, 2, and 3) include known or expected responses of well characterized toxicants in the assays included in the proposed EDSTAC T1S battery. The list includes only required endpoints. After the responses which are as follows: + is a positive, - is negative, +? is a possible positive response, and shaded responses are more certain than unshaded ones, weight of evidence determinations are made to determine the next steps for the chemical in question. The three possible decisions are: 1) hold, 2) go to T2T, and 3) other. Most chemicals truly exist and in *in vivo* dosage levels are provided while a few are fictitious, generated to provide examples of likely outcomes in T1S. The substances are identified by brief descriptions.

**Part 1.**

T1S ASSAY	ENDPOINT	Anti-androgenic Fungicide	Estrogenic Toxic Substance	Estrogenic Pesticide	Anti-androgenic Drug	PCB Mixture	Anti-A pesticide
<b>IN VITRO HTPS OR BENCH ASSAYS</b>							
HTPS ER/MVLN	ER AGONIST	-	+	++	-	-	-
ABOVE PLUS E2	ER ANTAGONIST	-	-	-	-	-	-
HTPS ER PLUS METABOLISM	METAB IS ER AGONIST	-	-	++	-	-	-
ABOVE PLUS E2	METAB IS ER ANTAGONIST	-	-	-	-	-	-
HTPS AR/CV-1	AR AGONIST	-	-	-	-	-	-
ABOVE PLUS DHT	AR ANTAGONIST	+	+?	++	-	-	+
HTPS AR PLUS METABOLISM	METAB IS AR AGONIST	-	-	-	-	-	-
ABOVE PLUS DHT	METAB IS AR ANTAGONIST	++	-	++	-	-	-
HTPS TR	TR AGONIST	-	-	-	-	-	-
ABOVE PLUS T3	TR ANTAGONIST	-	-	-	-	-	-
HTPS TR PLUS METABOLISM	METAB IS TR AGONIST	-	-	-	-	-	-
ABOVE PLUS T3	METAB IS TR ANTAGONIST	-	-	-	-	-	-
<b>IN VITRO TESTIS CULTURE</b>	<b>INHIBITION OF P4 OR T SYNTHESIS</b>	-	-	-	-	-	-
<b>IN VIVO ASSAYS</b>							
<b>3 DAY UTEROTROPIC IN ADULT OVX'D RAT</b>	<b>UTERINE WEIGHT WITH AND WITHOUT FLUID</b>	-	+	+?	-	-	-
	<b>UTERINE HISTOLOGY</b>	-	+	+?	-	-	-
	<b>BODY WEIGHT</b>	-	-	-	-	-	-

	VAGINAL CORNIFICATION	-	+?	-	-	-	-

3 DAY UTEROTROPHIC IN ADULT OVX'D RAT PLUS E2	UTERINE WEIGHT WITH AND WITHOUT FLUID	-	-	-	-	-	-
	UTERINE HISTOLOGY	-	-	-	-	-	-
	BODY WEIGHT	-	-	-	-	-	-
	VAGINAL CORNIFICATION	-	-	-	-	-	-
PUBERTAL/THYROID ASSAY IN WEANLING FEMALE RAT	GROWTH	-	-	-	-	-	-
	AGE AT VAGINAL OPENING	-	++	++	-	-	-
	WEIGHT AT VAGINAL OPENING	-	++	++	-	-	-
	SERUM T4	-	-	-	-	++	-
	SERUM TSH	-	-	-	-	+?	-
	UTERINE WEIGHT WITH AND WITHOUT FLUID	-	-	+? <sup>-</sup>	-	-	-
	OVARIAN WEIGHT	-	-	+? <sup>-</sup>	-	-	-
	THYROID HISTOLOGY	-	-	-	-	+-	-
	NONREPRODUCTIVE ORGAN WEIGHTS	LIVER n	-	-	-	LIVER n	LIV n
7-10 DAY HERSHBERGER-TYPE ASSAY IN CASTRATED MALE RAT	SEMINAL VESICLE WEIGHT, WITH AND WITHOUT FLUID	-	-	-	-	-	-
	VENTRAL PROSTATE WEIGHT	-	-	-	-	-	-
	LEVATOR ANI PLUS BULBOCAVERNOSUS WEIGHT	-	-	-	-	-	-
	GROWTH	-	-	-	-	+-?	-
	NONREPRODUCTIVE ORGAN WEIGHTS	LIVER n	-	-	-	LIVER n	LIV n
7-10 DAY HERSHBERGER-TYPE ASSAY IN CASTRATED MALE RAT: PLUS T	SEMINAL VESICLE WEIGHT, WITH AND WITHOUT FLUID	+ <sup>-</sup>	-?	+? <sup>-</sup>	-	+-?	+
	VENTRAL PROSTATE WEIGHT	+ <sup>-</sup>	-?	+? <sup>-</sup>	++	+-?	+
	LEVATOR ANI PLUS BULBOCAVERNOSUS WEIGHT	+ <sup>-</sup>	-?	+? <sup>-</sup>	-	+-?	+
	GROWTH	-	-	+	-	+-?	-
	NONREPRODUCTIVE ORGAN WEIGHTS	LIVER n	-	-	-	LIVER n	LIV n

<b>Weight of Evidence Determination:</b> <b>Hold, Go to T2T, Other</b>		<b>T2T</b>	<b>T2T</b>	<b>T2T</b>	<b>Repeat T1S</b> <b>T2T</b>	<b>T2T</b>	<b>T2T</b>
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<b>PUBERTAL/THYROID ASSAY IN WEANLING FEMALE RAT</b>	<b>GROWTH</b>	-	-?	-	-	-	+-?
	<b>AGE AT VAGINAL OPENING</b>	+n	-?	+n	+?n	+	+-?
	<b>WEIGHT AT VAGINAL OPENING</b>	+n	-?	+n	+?n	+	-
	<b>SERUM T4</b>	-	+ <sup>-</sup> ?	-	-	-	++
	<b>SERUM TSH</b>	-	+ <sup>-</sup> ?	-	-	-	++
	<b>UTERINE WEIGHT WITH AND WITHOUT FLUID</b>	+? <sup>-</sup>	-?	+? <sup>-</sup>	-	-	+-?
	<b>OVARIAN WEIGHT</b>	+n	-?	+n	-	-	+-?
	<b>THYROID HISTOLOGY</b>	-	+? <sup>-</sup>	-	-	-	-
	<b>NONREPRODUCTIVE ORGAN WEIGHTS</b>	LIVER ?n	-?	LIVER n	LIVER n?	LIVERn	THYROI Dn
<b>7-10 DAY HERSHBERGER-TYPE ASSAY IN CASTRATED MALE RAT</b>	<b>SEMINAL VESICLE WEIGHT, WITH AND WITHOUT FLUID</b>	-	-	-	-	-	-
	<b>VENTRAL PROSTATE WEIGHT</b>	-	-	-	-	-	-
	<b>LEVATOR ANI PLUS BULBOCAVERNOSUS WEIGHT</b>	-	-	-	-	-	-
	<b>GROWTH</b>	-	-?	-	-	-	+-?
	<b>NONREPRODUCTIVE ORGAN WEIGHTS</b>	LIVER ?n	-	+?n	-	LIVERn	+-?
<b>7-10 DAY HERSHBERGER-TYPE ASSAY IN CASTRATED MALE RAT: PLUS T</b>	<b>SEMINAL VESICLE WEIGHT, WITH AND WITHOUT FLUID</b>	-	-	-	-	+	+-?
	<b>VENTRAL PROSTATE WEIGHT</b>	-	-	-	-	+	+-?
	<b>LEVATOR ANI PLUS BULBOCAVERNOSUS WEIGHT</b>	-	-	-	-	+?	+-?
	<b>GROWTH</b>	-	-?	-	-	-	+-?
	<b>NONREPRODUCTIVE ORGAN WEIGHTS</b>	LIVER ?n	-	LIVERn	-	LIVERn	+-?
<b>Weight of Evidence Determination: hold, go to T2T or other</b>		T2T	REPEAT T1S, T2T	T2T	MAY REPEAT T1S, T2T	T2T	T2T





<b>PUBERTAL/THYROID ASSAY IN WEANLING FEMALE RAT</b>	<b>GROWTH</b>	+	-	-	-	-	-
	<b>AGE AT VAGINAL OPENING</b>	-	-	-	+?	+ <sup>-</sup> ?	-
	<b>WEIGHT AT VAGINAL OPENING</b>	-	-	-	+?	+ <sup>-</sup> ?	-
	<b>SERUM T4</b>	-	-	-	-	-	-
	<b>SERUM TSH</b>	-	-	-	-	-	-
	<b>UTERINE WEIGHT WITH AND WITHOUT FLUID</b>	-	-	-	+	-	-
	<b>OVARIAN WEIGHT</b>	-	-	-	+	-	-
	<b>THYROID HISTOLOGY</b>	-	-	-	-	-	-
	<b>NONREPRODUCTIVE ORGAN WEIGHTS</b>	+	-	-	-	-	-
							-
<b>7-10 DAY HERSHBERGER-TYPE ASSAY IN CASTRATED MALE RAT</b>	<b>SEMINAL VESICLE WEIGHT, WITH AND WITHOUT FLUID</b>	-	-	-	-	-	-
	<b>VENTRAL PROSTATE WEIGHT</b>	-	-	-	-	-	-
	<b>LEVATOR ANI PLUS BULBOCAVERNOSUS WEIGHT</b>	-	-	-	-	-	-
	<b>GROWTH</b>	+	-	-	-	-	-
	<b>NONREPRODUCTIVE ORGAN WEIGHTS</b>	+	-	-	-	-	-
<b>7-10 DAY HERSHBERGER-TYPE ASSAY IN CASTRATED MALE RAT: PLUS T</b>	<b>SEMINAL VESICLE WEIGHT, WITH AND WITHOUT FLUID</b>	-	+?	++	-	-	-
	<b>VENTRAL PROSTATE WEIGHT</b>	-	+?	++	-	-	-
	<b>LEVATOR ANI PLUS BULBOCAVERNOSUS WEIGHT</b>	-	+?	+	-	-	-
	<b>GROWTH</b>	+	-	-	-	-	-
	<b>NONREPRODUCTIVE ORGAN WEIGHTS</b>	+	-	-	-	-	-
<b>Weight of Evidence Determination: Hold, or go to T2T or Other</b>		<b>REPEAT T1S, Hold<sup>1</sup></b>	<b>T2T</b>	<b>T2T</b>	<b>T2T</b>	<b>REPEAT T1S, T2T</b>	<b>Other</b>