Reference Chemicals Used in EDSP Tier 1 Prevalidation Studies

Prepared for the Endocrine Methods Validation Subcommittee
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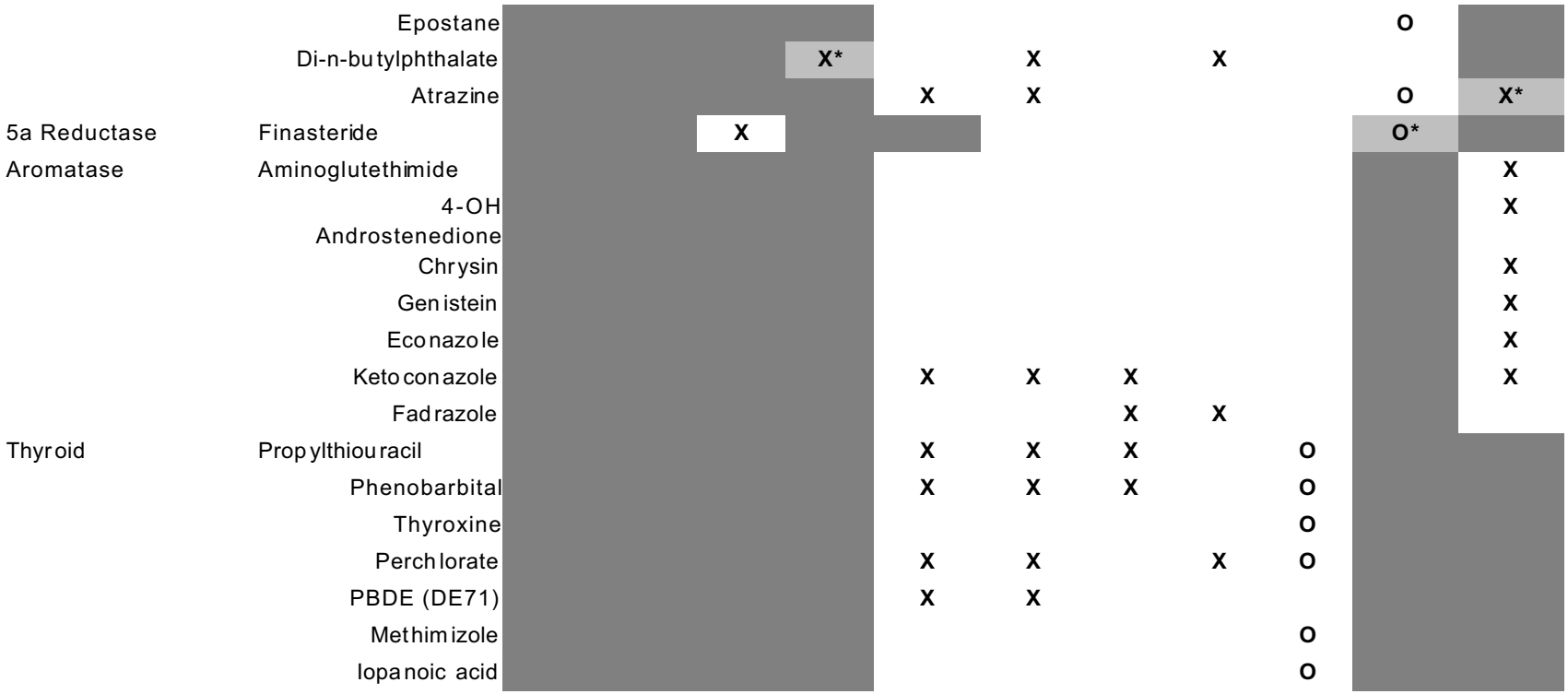
The chemicals contained in this document were selected as reference chemicals for prevalidation studies in the EDSP assay validation program because they produced a well-documented positive response in one or more Tier 1 assays by an identified mode of action. Some chemicals may act by more than one mode of action. It should be noted that this is **not** intended to be a list of endocrine disruptors, and it should not be concluded a chemical on this list is necessarily an endocrine disruptor since that designation also requires an association with an adverse effect identified in a Tier 2 study. Although some chemicals on this list have been studied extensively, others have not been studied in Tier 2 assays.

The chemicals in the attached chart do not represent all of the chemicals used in the prevalidation or validation of the assays but, in general, those that are common across several assays. The chemicals used in prevalidation appear in the following table grouped into eight modes of action:, androgen, antiandrogen, estrogen, antiestrogen, hypothalamic-pituitary-gonadal axis, steroidogenesis, aromatase, and thyroid. Some chemicals appear more than once because they act by more than one mode of action.

For the most part, chemicals used in tests in the general literature have not been included in these tables as such studies raise questions about comparability of protocols and data. Thus, the entries in the tables represent studies conducted in the EDSP validation program, EPA ORD laboratories, and the OECD assay validation program. The exception to this are the studies shown for the adult or intact male assay, which was developed by the US chemical industry and tested in various industry laboratories.

EDSP Reference Chemicals at a Glance

Modality	Chemical	ER binding	AR binding	Hersh-berger	Utero-trophic	Pubertal Female	Pubertal Male	Adult Male	Fish repro screen	Frog	Steroid	Arom
Androgen	Methyl testosterone		X	X			X		X			
	Trenbolone			X					X	O		
Anti androgen	DDE-p,p'		X	X			X	X	X			
	Vinclozolin		X	X			X	X	X		O*	
	Linuron		X	X			X	X				
	Procymidone		X	X								
	Methoxychlor (HPTE)**		X**				X	X	X			
	Flutamide			X			X	X	X			
	Cyproterone acetate		X					X				
Estrogen	Estradiol	X	X					X	X			
	Ethynyl estradiol	X			X	X						
	Nonylphenol	X			X							X*
	Bisphenol A	X			X	X			X			
	Genistein	X			X							
	Methoxychlor	X	X		X	X		X	X			
	DDT-o,p'				X							
Anti estrogen	ICI 182,780	X						X				
	Tamoxifen citrate	X				X						
HPG	Atrazine					X	X		X	X		
	Pimozide					X	X					
Steroidogenesis	Dimethoate										O	
	Aminoglutethimide										O	
	Flutamide						X	X	X		O	
	Ketoconazole					X	X	X			O	



*** Lightly shaded box indicates a chemical selected to be negative in this assay.**
**** Needs metabolism to the active form, which is not expected to occur in vitro.**
X Chemical has been run in this assay.
O Planned or underway.