Estrogen Receptor Expert Systems (ERES) for Chemical Prioritization

The Food Quality Protection Act of 1996 requires the US EPA to screen pesticidal actives and inert ingredients for the potential to act as endocrine disruptors. Given the significant time and money required to conduct hazard assessments for the large numbers of chemicals covered by this mandate, there is a need for a strategic approach to prioritize chemicals to be nominated to move forward into higher tiered targeted testing. One approach being taken to address this need is through decision support tools called “expert systems” that are founded on quantitative structure activity relationships (QSAR) and development of effects-based chemical categories. Expert Systems are automated rule-based decision trees that can be used to predict which chemicals have the potential to disrupt endocrine systems. This is done by testing key chemicals within a chemical group to represent others, determining what is similar about the chemical structures and properties that explain their similar biological activity, and writing rules that help predict the activity of untested chemicals that fit the parameters of the chemical group. The ER Expert System (ERES) developed at the USEPA, NHEERL, Mid-Continent Ecology Division (MED) used the OECD QSAR Validation Principles to maximize transparency and usefulness by using well-defined endpoints in well-characterized assays that are appropriate for testing the types of chemicals on EPA inventories, and striving for a mechanistic understanding of all assay results (Hornung et al., 2014; 2017; Schmieder et al., 2014).

The conceptual approach providing the foundation for the expert system is the description of the chemically-initiated perturbation of the ER system in fish within the framework of an adverse outcome pathway (AOP). The ER-mediated reproductive impairment AOP (Figure 1; Schmieder et al., 2004) describes the linkage between the event that initiates the pathway (e.g., a chemical binding the ER) and measures made at successively higher and more complex levels of biological organization. The pathway progresses from the molecular initiating event (MIE), through cell and tissue level gene transcription and translation, continuing through organ effects to an adverse outcome observed in the individual and/or population. With a plausible pathway to an adverse outcome described, a rationale is provided for using chemical interaction at the MIE as a basis for prioritizing chemicals for further screening using in vivo assays which incorporate endpoints at higher levels of biological organization.

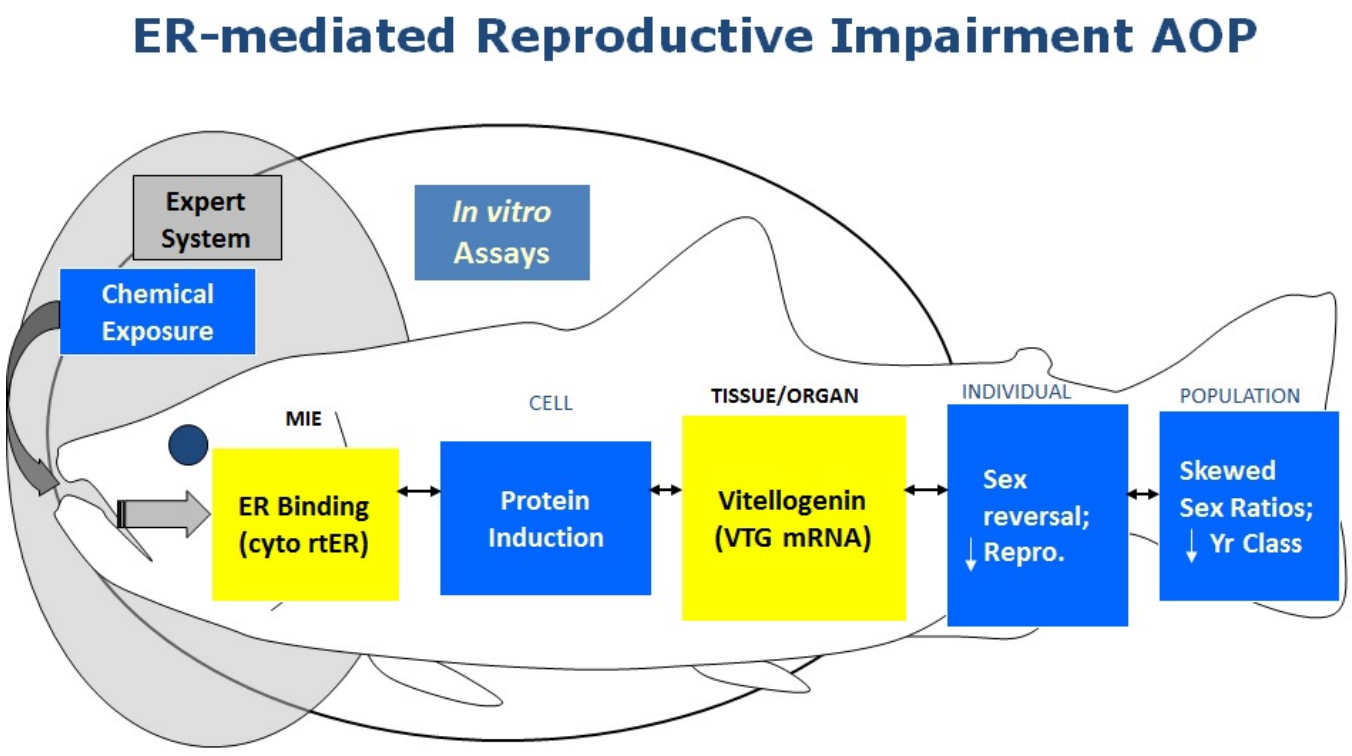


Figure 1. The in vitro assays used at MED to develop the ERES (yellow boxes) are: i) measured chemical binding to the rainbow trout $ER_{\alpha/\beta}$ to detect the potential for a chemical to initiate the $ER_{\alpha/\beta}$-mediated pathway; and ii) $ER_{\alpha/\beta}$-mediated vitellogenin induction in rainbow trout liver slices to confirm that ER binding translates to an effect at a point further along the ER-mediated AOP (Schmieder et al., 2004; Hornung et al., 2014; Schmieder et al., 2014).

2009 ERES SAP

In August 2009, the effects-based chemical category approach developed using the in vitro assays within the ER-mediated AOP, and presented as the ER Expert System (ERES) decision trees and logic rules, titled: *The Use of Structure Activity Relationships of Estrogen Binding Affinity to Support Prioritization of Pesticide Inert Ingredients and Antimicrobial Pesticides for Screening and Testing,* was presented to a FIFRA Science Advisory Panel (SAP) to obtain feedback on the use of the approach for prioritizing chemicals for further screening (USEPA FIFRA SAP, 2009

2013 Chemical Prioritization SAP

In January 2013, a FIFRA SAP was convened in which the Agency sought further comment on the concepts, decision logic, and computational (*in silico* and *in vitro*) methods used to prioritize chemicals for advancement into the EDSP Tier I screening assays. The document prepared for this meeting presented the expansion of the ERES and presented how computational toxicology tools, including high throughput assays data, may be used to expand the ERES to prioritize chemicals for screening (USEPA FIFRA SAP, 2013).

A set of 295 chemicals that were tested in the ER expert system trout ER binding and liver slice assays and also tested in the ER high throughput (HTP) assays were discussed in Section 7 of the chemical prioritization SAP document. The relative binding affinity (RBA) data for these chemicals derived from the trout $ER_{\alpha/\beta}$ competitive binding assay can be accessed in Appendix H in the docket folder from the 2013 SAP. The decision process for assigning the chemicals an RBA is presented in Appendix G of the 2013 SAP meeting documents.

ER Expert System in the OECD (Q)SAR Toolbox

In response to the recommendations of a 2009 Organisation for Economic Cooperation and Development (OECD) expert consultation (OECD, 2009) and the 2009 FIFRA SAP, the ERES has been automated and incorporated into the OECD (Q)SAR Toolbox. The Toolbox is a freely available software tool that can be used for assessing the hazards of chemicals for which limited or no hazard information is available.

Related References:

1. P.K. Schmieder, R.C. Kolanczyk, M.W. Hornung, M.A. Tapper, J.S. Denny, B.R. Sheedy & H. Aladjov. 2014. A rule-based expert system for chemical prioritization using effects-based chemical categories, SAR and QSAR in Environmental Research, 25:4, 253-287.

2. M.W. Hornung, M.A. Tapper, J.S. Denny, R.C. Kolanczyk, B.R. Sheedy, P.C. Hartig, H. Aladjov, T.R. Henry & P.K. Schmieder. 2014. Effects-based chemical category approach for prioritization of low affinity estrogenic chemicals, SAR and QSAR in Environmental Research, 25:4, 289-323.

3. M.W. Hornung, M.A. Tapper, J.S. Denny, B.R. Sheedy, R. Erickson, T.J. Sulerud, R.C. Kolanczyk, P.K. Schmieder. 2017. Avoiding False Positives and Optimizing Identification of True Negatives in Estrogen Receptor Binding and Agonist/Antagonist Assays. Applied In Vitro Toxicology. In Press. DOI: 10.1089/aivt.2016.0021

4. P.K. Schmieder, M.A. Tapper, J.S. Denny, R.C. Kolanczyk, B.R. Sheedy, T.R. Henry, and G.D. Veith. 2004. Use of trout liver slices to enhance mechanistic interpretation of estrogen receptor binding for cost-effective prioritization of chemicals within large inventories, Environ. Sci. Technol. 38, pp. 6333–6342.

5. J.S. Denny, M.A. Tapper, P.K. Schmieder, M.W. Hornung, K.M. Jensen, G.T. Ankley, and T.R. Henry. 2005. Comparison of relative binding affinities of endocrine active compounds to fathead minnow and rainbow trout estrogen receptors. Environmental Toxicology and Chemistry, 24:11, 2948–2953.

6. US EPA, Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Science Advisory Panel (SAP). 2009. An effects-based expert system to predict estrogen receptor binding affinity for food use inert ingredients and antimicrobial pesticides: Application in a prioritization scheme for endocrine disruptor screening, FIFRA Science Advisory Panel Meeting, Arlington, VA, 2009.

7. US EPA, FIFRA SAP. 2013. Prioritization of the endocrine disruptor screening program universe of chemicals for an estrogen receptor adverse outcome pathway using computational toxicology tools, FIFRA Science Advisory Panel Meeting, Arlington, VA, 2013

8. OECD, 2009. Report of the Expert Consultation to Evaluate an Estrogen Receptor Binding Affinity Model for Hazard Identification. Series on Testing and Assessment, No. 111 (2009) ENV/JM/MONO(2009)33.

ERES and Training Set Data

ERES Decision Tree

The schematic of the initial version of the ERES decision tree (ERESv1) from 2009 [3, 5] is shown in Figure 2. In 2013 [6] this was expanded to ERESv2 with additional chemical groups that fit within the decision framework (Figure 3). The ERES was recently expanded further to ERESv3 (Figure 4) to cover all groups in the training set presented in the tables below. ERESv3 is based upon rtER competitive binding data for 556 chemicals with trout liver slice Vtg gene expression data for 267 of the chemicals. As a chemical list passes through the ERES decision tree, structures are classified into effects-based groups of similar structure, and binding activity is assigned [2, 3, 6]. Where there are multiple functional groups found within a chemical structure (i.e., where the structure fails to meet criteria of a more strictly defined chemical group), the structure is evaluated for classification within a 'mixed' group. The 'Mixed Phenols' are found in ERESv3 Node VI ('Site A' binders). 'Mixed Anilines' are found in Node VII ('Site B' binders). The remaining 'Mixed Organics' in Node VIII include a mixture of diverse one-of-a-kind structures which do not contain a phenol or aniline moiety. Where a chemical structure is an 'Exact Match' [3, 5, 6] to a chemical within a mixed group it is assigned the binding activity measured for that training set chemical. [The automated version of ERESv1 is found in the OECD QSAR Toolbox. ERESv3 will be available with the release of OECD QSAR Toolbox v4 anticipated in 2016.]

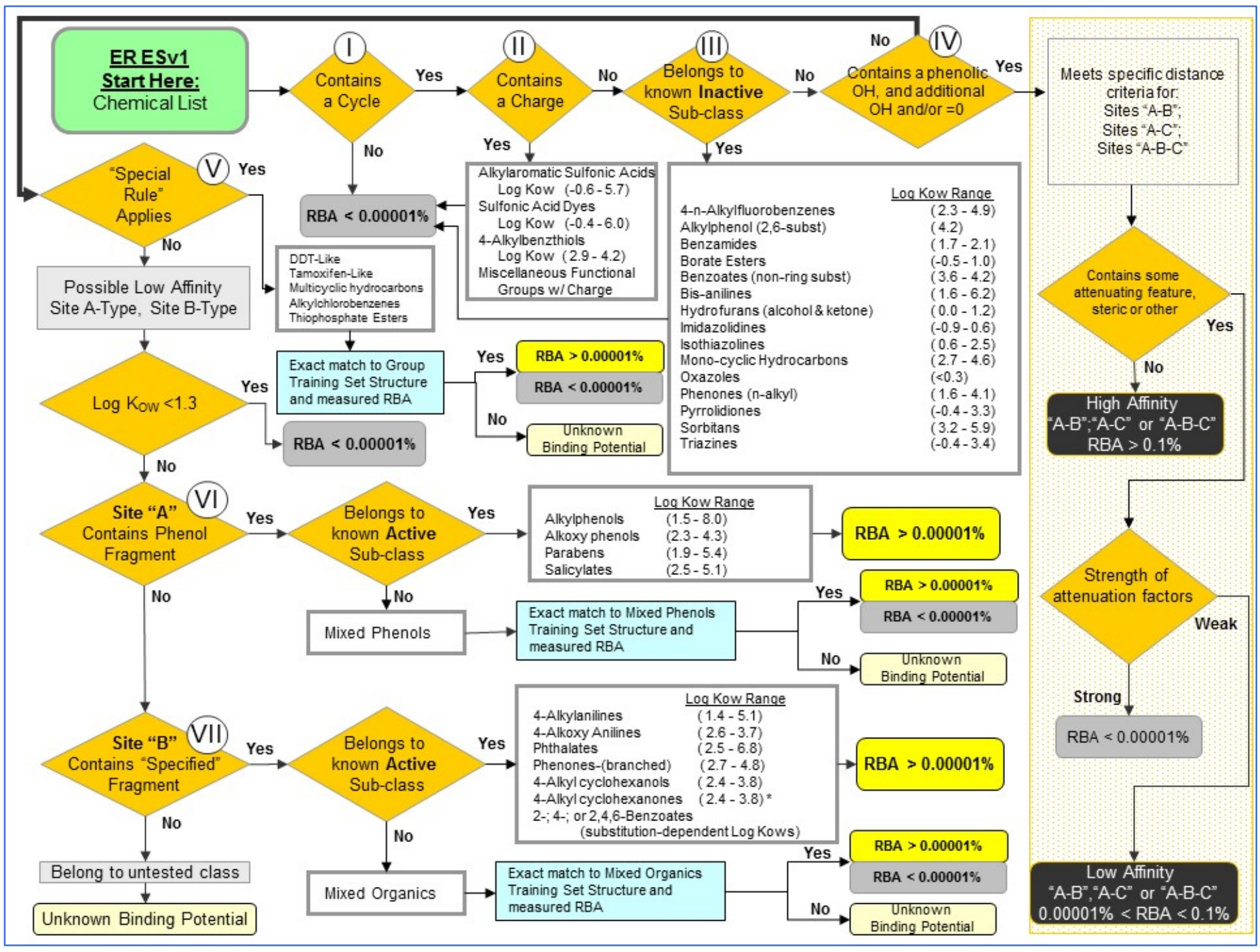


Figure 2. Rule-based ERESv1 decision tree for predicting ER binding potential for low affinity chemicals [3, 5, 6, 7].

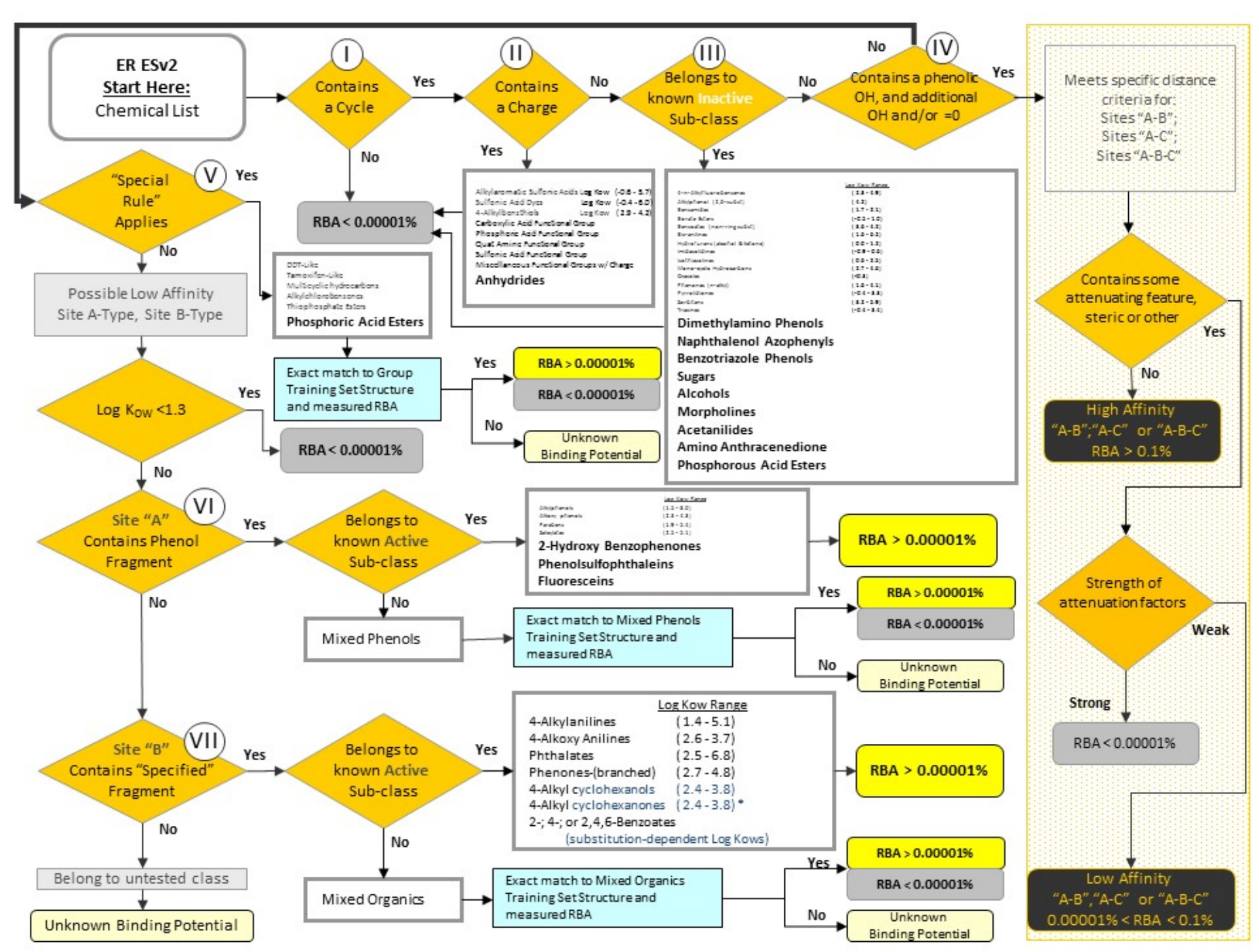


Figure 3. ERESv2 showing expansion of the system from ERESv1 with additional effects-based chemical categories at multiple decision rule Nodes [6].

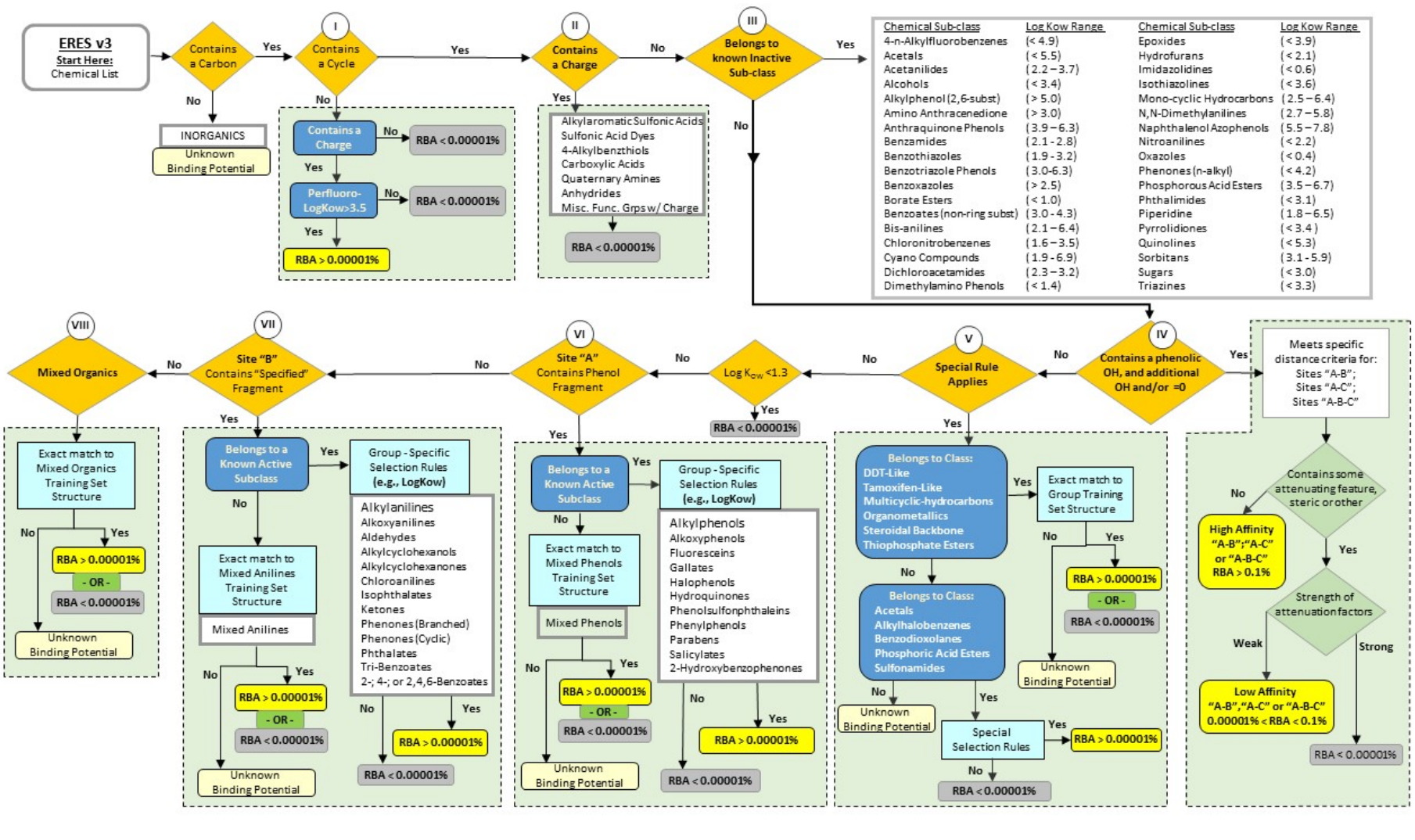


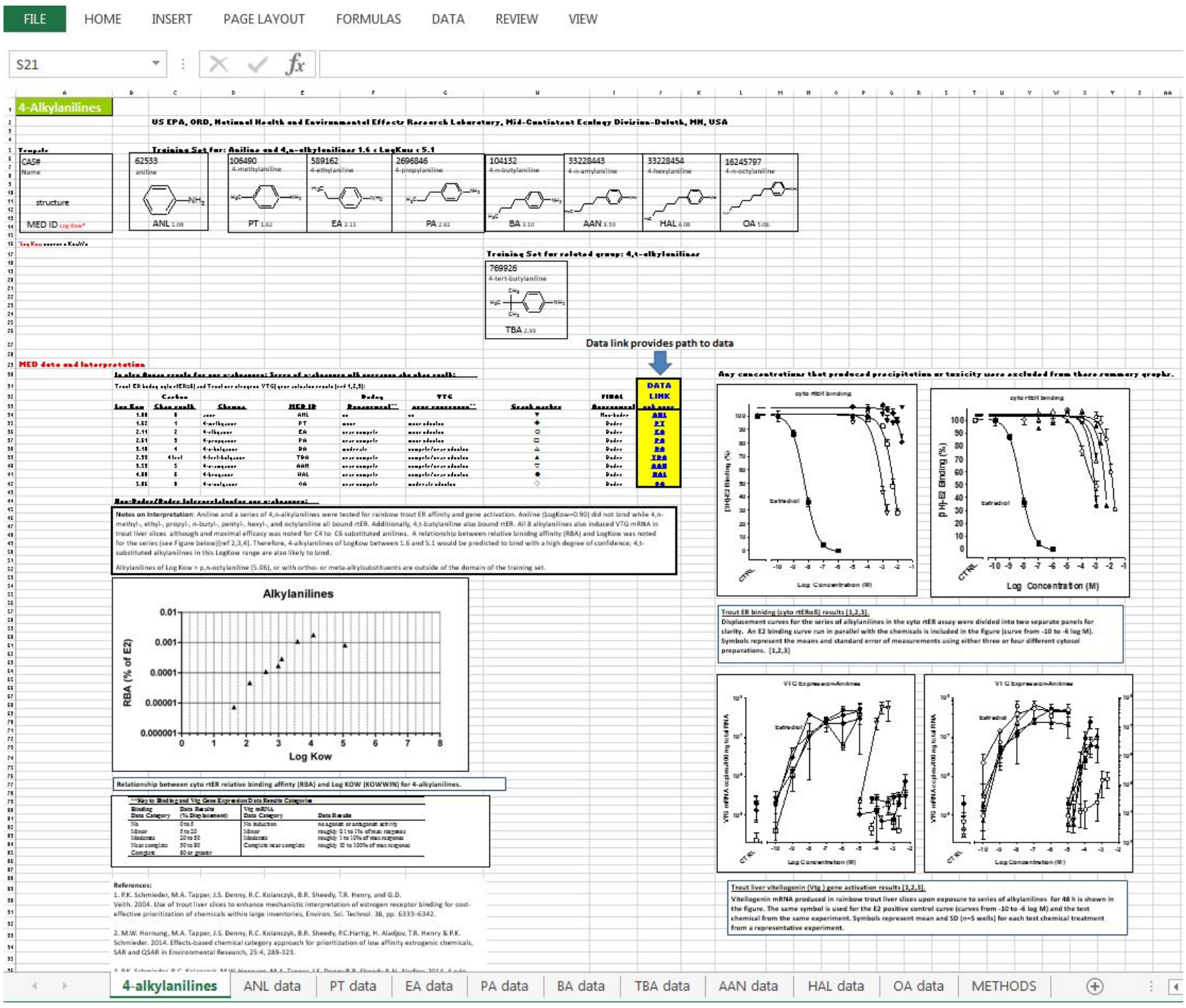
Figure 4. The rule-based decision tree ERESv3 (11/2015).

TRAINING SET DATA:

Data used to develop the ERES can be obtained via links in the **INSTRUCTIONS FOR OBTAINING DATA** section below. The following screen shots captured from the Excel data file for the Chemical Group - 4-alkylanilines are provided here to help orient the user to the layout and structure of these data files that are available for download.

DATA EXAMPLE: Downloaded Excel file with data for each chemical within their chemical group will include:

1. Summary sheet includes structures of all chemicals tested within a chemical group, and related chemicals where applicable. This includes a table of results for the ER binding and liver slice vitellogenin (Vtg) gene expression assays, and column indicating the final assessment of each chemical as an ER BINDER or a NON-BINDER. Note that in some instances where there was experimental evidence that the activity was due to a metabolite and not the parent chemical the result was noted in the Summary Table as 'Non-Binder; active metabolite'. However, not all chemicals were tested for metabolic activation. Refer to the '3. Decision Scheme' below (and associated references provided) for more information on when the liver slice/Vtg gene expression assay was run. Notes describing assay interpretations leading to the final activity determinations are provided in a text box below this summary table. Plots of the RBA vs. Log Kow relationship for the group, and graphs of ER competitive binding displacement and liver slice vitellogenin (Vtg mRNA) induction are included on the summary sheet. The summary worksheet tab has the name of the chemical group. Additional worksheet tabs contain individual chemical data (see #2 below). The example shown is for the ERES 'Site B' active group, 4-alkylanilines.

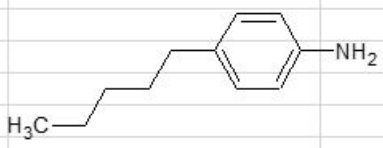


2. Individual chemical data (competitive binding dose-response in comparison to 17ß-Estradiol (E2); IC50s; Relative Binding Affinities (RBA); liver slice Vtg mRNA production with viability assay results (and additional information where applicable) is found by clicking on a chemical's MED ID (yellow cell 'DATA LINK') within the Summary sheet, or the worksheet tab for each chemical of the downloaded file. The chemical structure, CAS and final 'Classification' of the chemical as an ER BINDER or ER NON-BINDER, and the rationale used in making the determination are presented first. Next is a list of Assays performed for that chemical, followed by the individual chemical data. All final assessments are also done within the context of the other chemicals within the group and the information on the Summary sheet for that chemical group (See #3 for Decision Scheme). Additional details are found in: Schmieder et al., 2004; Hornung et al., 2014; Schmieder et al., 2014; USEPA FIFRA SAP, 2009; USEPA FIFRA SAP, 2013.

Example of 4-amylaniline information found under "**data**" tab. More detail about assay METHODS are found under '**METHODS**' tab (example screen shot not shown);

DATA	to METHODS	to summary page

Chemical: 4-n-amylaniline
MED acronym: AAN
CAS#: 33228-44-3



Classification: BINDER
Justification: Chemical produced complete displacement curves in both the cytosol and recombinant rainbow trout estrogen receptor assays
Chemical induced Vtg to maxiumum efficacy in the rainbow trout liver slice/ Vtg mRNA assay

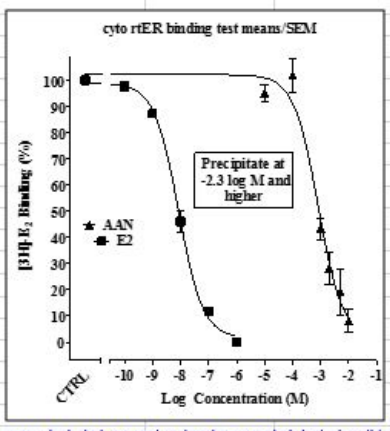
Assays available	Performed
Cyto rtER binding	yes
Cytosol chemical analysis	yes
Ki rtER binding	no
Rec rtER binding	yes
Recombinant chemical analysis	yes
Gene expression Vtg in liver slices-AGONIST	yes
Gene expression Vtg in liver slices-ANTAGONIST	no
Gene expression Vtg in liver slices-AGONIST with chemicals analysis	yes

ER BINDING

'**ER BINDING**' section: Includes cyto rtER$_{\alpha/\beta}$ competitive binding data with additional rec rtER$_{\alpha}$ competitive binding data where applicable (Hornung et al., 2014). Information shown includes: a graph of the chemical's response compared to E2 run in the same experiments, a table listing of the dose-response data, the formula used for RBA calculations, RBAs and IC50s for each chemical and corresponding E2 runs, and the procedure and equation used for generating IC50s.

Cyto rtER Binding

Cyto rtER Binding Summary Graph



Result Summary

precipitation: visual precipitation at -2.3 log M and higher concentrations
matrix pH: not measured
E2 displacement: yes

SUMMARY DATA

Nominal Conc log M	AAN binding Mean	AAN binding SEM	AAN binding N	E2 Binding Mean	E2 Binding SEM	E2 Binding N
control	100.0	0.0	3	100.0	0.0	3
-10				97.7	1.4	3
-9				87.2	1.4	3
-8				46.1	3.8	3
-7				11.9	1.2	3
-6				0.0	0.0	3
-5	95.1	3.2	3			
-4	102.1	6.5	3			
-3	43.2	4.3	3			
-2.7	28.1	6.2	3			
-2.3	19.2	8.7	3			
-2	8.1	4.4	3			

RBA Calculation

$$RBA = \frac{IC50\ estradiol}{IC50\ test\ chemical} \times 100$$

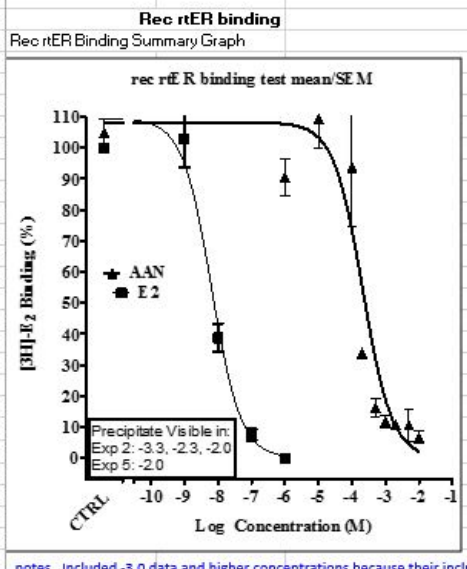
Exp	RBA(%) AAN	IC50 (M) AAN	IC50 (M) E2
1	0.0014	0.00062	8.84E-09
2	0.0016	0.00075	1.19E-08
3	0.0005	0.00105	5.48E-09
mean	0.0012	0.00080	8.73E-09
SEM	0.0003	0.00013	1.84E-09

Used One site competition equation as found in GraphPad Prism 5 for Windows to generate IC50 values. The bottom of the curve was constrained to zero
Y=Bottom + (Top-Bottom)/(1+10^(X-LogEC50))

note: included -2.3 and -2 data because their inclusion did not pull the regression curve off of measured data points.and completed curve

Rec rtER binding

Rec rtER Binding Summary Graph



Result Summary

precipitation: visual precipitation at -3.3 log M and higher concentrations
matrix pH: not measured
E2 displacemer yes

SUMMARY DATA

Nominal Conc. log M	AAN Binding Mean	AAN Binding SEM	AAN Binding N	E2 Binding Mean	E2 Binding SEM	E2 Binding N
control	103.8	3.8	5	100.0	0.0	5
-10				111.6	7.7	5
-9				102.9	9.3	5
-8	102.9	0.0	1	38.8	4.5	5
-7	117.3	0.0	1	7.6	1.8	5
-6	96.6	7.1	3	0.0	0.0	5
-5	109.6	7.1	5			
-4	93.2	14.8	5			
-3.7	33.8	0.0	1			
-3.3	16.3	2.8	3			
-3	11.8	2.0	4			
-2.7	10.7	0.0	1			
-2.3	10.6	5.2	2			
-2	6.7	2.0	4			

RBA Calculation

$$RBA = \frac{IC50\ estradiol}{IC50\ test\ chemical} \times 100$$

Exp	RBA(%) AAN	IC50 (M) AAN	IC50 (M) E2
1	0.0014	0.00036	5.10E-09
2	0.0052	0.00010	5.44E-09
3	0.0005	0.00136	7.32E-09
4	0.0033	0.00034	1.11E-08
5	0.0029	0.00018	5.26E-09
mean	0.0027	0.00047	6.85E-09
SEM	0.0009	0.0002	0.0000

Used One site competition equation as found in GraphPad Prism 5 for Windows to generate IC50 values. The bottom of the curve was constrained to zero
Y=Bottom + (Top-Bottom)/(1+10^(X-LogEC50))

notes. Included -3.0 data and higher concentrations because their inclusion was necessary to make the regression curve best fit data at 50% displacement.

'GENE EXPRESSION-Male rainbow trout liver slice/Vtg mRNA' section: Includes Vtg mRNA dose-response data from the trout liver slice experiments for Control, Chemical, and E2. Slice viability assay data for the chemical, and additional media pH and chemical solubility information where applicable, is also shown. For chemicals that produced apparent receptor binding but not significant Vtg mRNA agonist activity, data from experiments run to determine antagonism activity are also included.

GENE EXPRESSION-Male rainbow trout liver slice/Vtg mRNA

Gene expression Vtg in liver slices-AGONIST

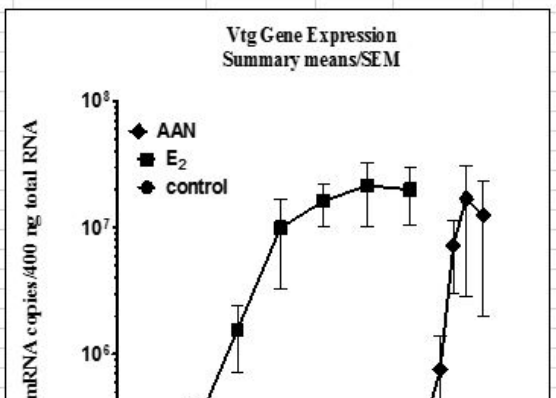
Result Summary

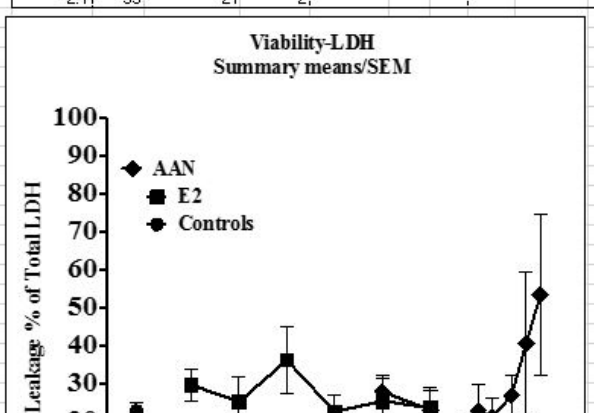
precipitation: precipitation at -3 nephelometry analysis
media pH: within acceptable range at all concentrations
LDH: significant toxicity at -3 and -2.7 log M AAN tested concentrations
Vtg mRNA expression: Vtg agonist-significant induction at -4, -3.7, -3.3 log M

SUMMARY DATA

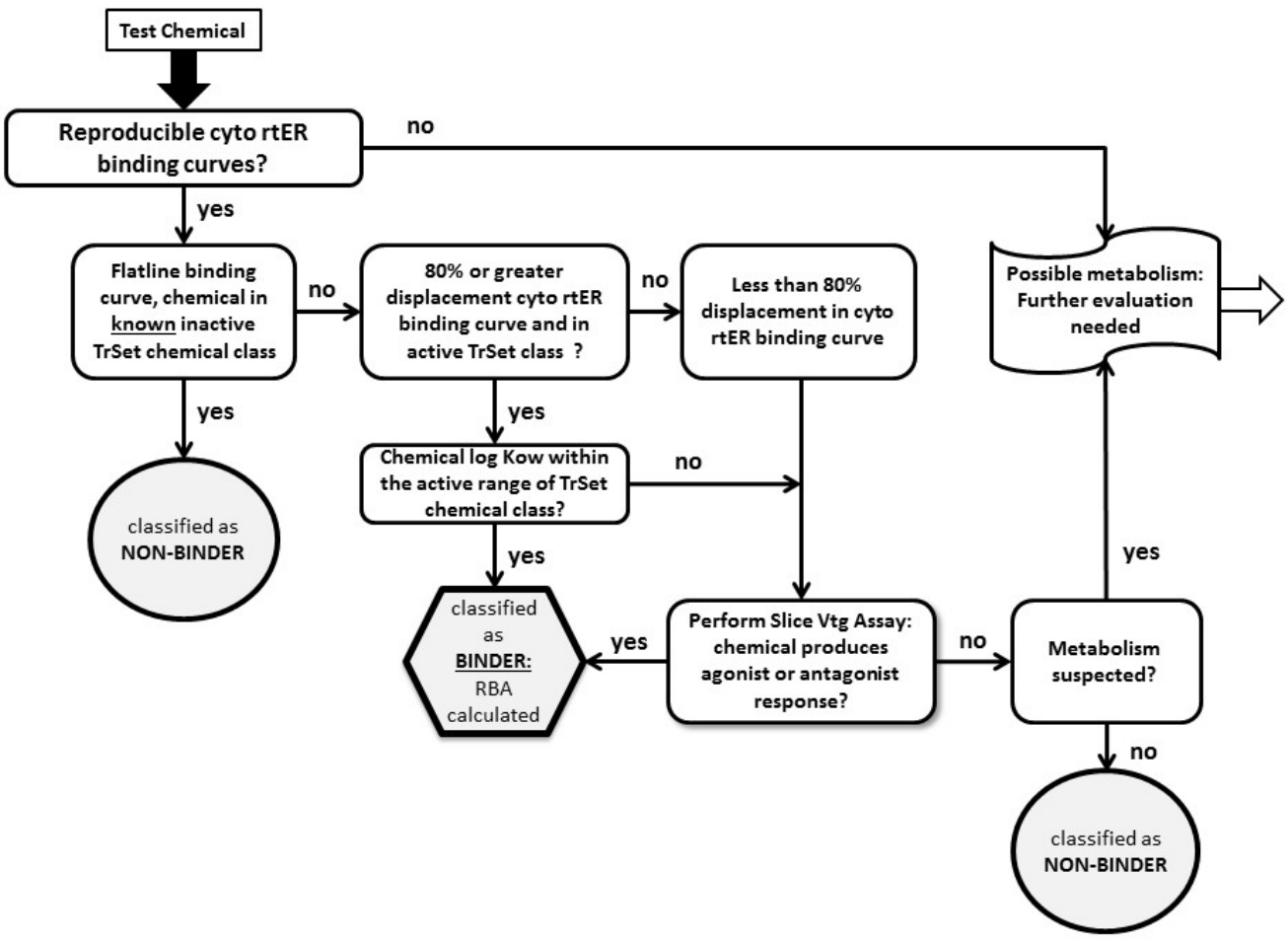
Nominal Concentration log M	AAN Vtg Gene Expression Vtg mRNA copies/400 ng total RNA Mean	AAN Vtg Gene Expression SEM	AAN Vtg Gene Expression N	E2 Vtg Gene Expression Mean	E2 Vtg Gene Expression SEM	E2 Vtg Gene Expression N	Control Gene Expression Mean	Control Gene Expression SEM	Control Gene Expression N
control							109297.6	43773.1	5
-10				241671	187548.6	5			
-9				1556822	845354.3	5			
-8				9949959	6661859	5			
-7				1.6E+07	5952574	5			
-6	135310.2	110139.6	2	2.1E+07	11302550	5			
-5	173021.3	36431.84	5	2E+07	9545763	5			
-4.7	249812.4	0	1						
-4.3	754872.1	644213.9	2						
-4	7230270	4180856	5						
-3.7	16962620	14085000	4						
-3.3	12572890	10563950	5						

Nominal Conc. log M	AAN Viability-LDH Mean	AAN Viability-LDH SEM	AAN Viability-LDH N	E2 Viability-LDH Mean	E2 Viability-LDH SEM	E2 Viability-LDH N	Control Viability-LDH Mean	Control Viability-LDH SEM	Control Viability-LDH N
control							23	2	5
-10.0				30	4	5			
-9.0				25	6	5			
-8.0				36	9	5			
-7.0				23	4	5			
-6.0	28	4	2	25	6	5			
-5.0	23	5	5	24	6	5			
-4.7	13	0	1						
-4.3	20	0	1						
-4.0	23	7	4						
-3.7	21	5	5						
-3.3	27	5	5						
-3.0	41	19	3						
-2.7	53	21	2						





3. Decision scheme using a chemical category-based strategy for testing unknown chemicals and assignment as either rtER 'BINDERS' or 'NON-BINDERS' is shown below and described further in Hornung et al. 2014 and USEPA FIFRA SAP, 2013 (Appendix G). Abbreviations: cyto rtER = rainbow trout estrogen receptor(s) isolated from trout liver cytosol; TrSet = training set chemicals; Vtg = vitellogenin; RBA = relative binding affinity.



INSTRUCTIONS FOR OBTAINING DATA:

The ERES training set chemicals are listed in the tables below based upon their assignment to Nodes I – VIII as shown above in the ERESv3 decision tree (Figure 4). Chemicals listed in the tables below are those currently available for download.

Data Download:
The data for each ERES Node are available from the ERES webpage from which this "Description & Instructions" pdf file was downloaded.

The "ERES Node # data.zip" download for each node includes one Excel file named "ERES Node # Table" organized similarly to what is shown in the tables below for each node. The zip download also includes Excel files that contain the data specific to the Chemical Groups within that node.

For example the download "ERES Node I data.zip" contains ten Excel files:

ERES Node I Table
Chemical Group-Acyclic Alcohols
Chemical Group-Acyclic Aldehydes & Ketones
Chemical Group-Acyclic Amines
... *through*
Chemical Group-Perfluoro Acyclics

Working through the downloaded Excel data files:

1. Locate chemical of interest in the "ERES Node # Table" file by chemical name, CAS number or MED ID.
2. A highlighted row above each chemical group in the "ERES Node # Table" file indicates which "Chemical Group- "file contains the summary data for that chemical group and data for the individual chemicals in that group.
3. In the Chemical Group file, find the chemical of interest in the chemical group Summary worksheet and click on links in that worksheet to open worksheets within that file containing $rtER_{\alpha/\beta}$ binding and trout liver slice Vtg mRNA expression data for each chemical (**see above in the Data Example section of this webpage**).
    a. Worksheet tabs labeled "MED ID_data" contain data for individual ER binding and Vtg mRNA assay runs for a given chemical.
    b. Worksheet tab labeled "METHODS" lists assays performed and assay methods.

The following links jump to the sections below that list the chemicals associated with each specified ERES Node:

Node I Node II Node III Node IV Node V Node VI Node VII Node VIII

Node I

Primary Node. I. Acyclics

Sub-Node: Non-Ionic Acyclics

ERES Chemical Group	Sub-group	log Kow	CASRN	Chemical Name
Acyclic Alcohols	Acyclic Alcohols	-7.24	637398	triethanolamine HCl
Acyclic Alcohols	Acyclic Alcohols	0.19	77996	1,1,1-tris (hydroxymethyl)propane
Acyclic Alcohols	Acyclic Alcohols	1.82	111273	1-hexanol
Acyclic Alcohols	Acyclic Alcohols	3.79	112301	1-decanol
Acyclic Alcohols	Acyclic Alcohols	2.73	104767	2-ethyl-1-hexanol
Acyclic Aldehydes & Ketones	Acyclic Aldehydes	1.86	4313035	(2E,4E)-2,4-heptadienal
Acyclic Aldehydes & Ketones	Acyclic Ketones	2.68	504201	2,6-dimethyl-2,5-heptadien-4-one
Acyclic Amines	Acyclic Amines	-3.16	112572	1,2-ethanediamine, n-(2-aminoethyl)-n'-2-(2-aminoethyl)amino ethyl-
Acyclic Amines	Acyclic Amines	-1.20	78900	1,2-diaminopropane
Acyclic Amines	Acyclic Amines	3.29	2783177	1,12-diaminedodecane
Acyclic Carboxy Esters	Acyclic Carboxy Esters	1.77	97632	ethyl methacrylate
Acyclic Carboxy Esters	Acyclic Carboxy Esters	1.91	689894	methylsorbate
Acyclic Carboxy Esters	Acyclic Carboxy Esters	2.45	55406536	3-iodo-2-propynyl N-butylcarbamate
Acyclic Fumerates & Maleates	Acyclic Fumerates	4.16	105759	Dibutyl fumarate
Acyclic Fumerates & Maleates	Acyclic Fumerates	7.94	141026	Bis (2-ethylhexyl)fumarate
Acyclic Fumerates & Maleates	Acyclic Maleates	4.16	105760	Dibutyl maleate
Acyclic Fumerates & Maleates	Acyclic Maleates	7.94	142165	Bis (2-ethylhexyl)maleate
Acyclic Halogenated	Acyclic Brominated	2.99	110521	1,4-Dibromobutane
Acyclic Halogenated	Acyclic Chlorinated	3.11	76017	Pentachloroethane
Acyclic Halogenated	Acyclic Chlorinated	4.52	111853	1-Chlorooctane
Acyclic Halogenated	Acyclic Chlorinated	4.72	87683	Hexachloro-1,3-butadiene
Acyclic Others	Acyclic Others	-1.90	121437	trimethylborate
Acyclic Others	Acyclic Others	3.67	97778	Disulfiram (Tetraeethylthiuram disulfide)

Sub-node: Ionic Acyclics

ERES Chemical Group	Sub-group	log Kow	CASRN	Chemical Name
Ionic Non-Perfluoro Acyclics	Acyclic Carboxylic Acids	-11.36	139899	Trisodium (2-hydroxyethyl) ethylenediaminetriacetate
Ionic Non-Perfluoro Acyclics	Acyclic Carboxylic Acids	-4.91	67436	Diethylenetriamine-pentaacetic acid
Ionic Non-Perfluoro Acyclics	Acyclic Carboxylic Acids	1.62	110441	2,4-hexadienoic acid
Ionic Non-Perfluoro Acyclics	Acyclic Carboxylic Acids	2.37	38916426	DL-Aspartic acid, N-(3-carboxy-1-oxo-3-sulfopropyl)-N-octadecyl-, tetrasodium salt
Ionic Non-Perfluoro Acyclics	Acyclic Phosphates	0.28	4672382	Propylphosphonic acid
Ionic Non-Perfluoro Acyclics	Acyclic Quat Amines	-3.45	35141367	1-Propanaminium, N,N,N,-trimethyl-3(trimethoxysilyl)-, chloride
Ionic Non-Perfluoro Acyclics	Acyclic Quat Amines	0.24	56375792	Tributylmethylammonium chloride
Ionic Non-Perfluoro Acyclics	Acyclic Quat Amines	1.22	112005	N-Dodecyltrimethylammonium chloride
Ionic Non-Perfluoro Acyclics	Acyclic Quat Amines	6.43	67633630	N-Ethyl-N,N-dimethyl-3-[(1-oxoisooctadecyl) amino]-1-propanaminium, ethyl sulfate
Ionic Non-Perfluoro Acyclics	Acyclic Sulfates	-0.35	126921	sodium 2-ethylhexylsulfate
Ionic Non-Perfluoro Acyclics	Acyclic Sulfates	-0.27	142314	sodium octylsulfate
Ionic Non-Perfluoro Acyclics	Acyclic Sulfates	5.09	42808366	Octadecanoic acid, 9(or 10)-(sulfooxy)-, 1-butyl ester, sodium salt
Ioinic Perfluoro Acyclics	PerfluoroCarboxylic Acid [LogKow<3.5]	2.43	375224	Perfluorobutyric acid
Ioinic Perfluoro Acyclics	PerfluoroCarboxylic Acid [LogKow<3.5]	2.81	2706903	Perfluoropentanoic acid
Ioinic Perfluoro Acyclics	PerfluoroCarboxylic Acid [LogKow<3.5]	3.48	307244	Undecafluorohexanoic acid
Ioinic Perfluoro Acyclics	PerfluoroCarboxylic Acid [LogKow>3.5]	4.15	375859	Perfluoroheptanoic acid
Ioinic Perfluoro Acyclics	PerfluoroCarboxylic Acid [LogKow>3.5]	4.81	335671	Perfluorooctanoic acid
Ioinic Perfluoro Acyclics	PerfluoroCarboxylic Acid [LogKow>3.5]	5.48	375951	Perfluorononanoic acid
Ioinic Perfluoro Acyclics	PerfluoroCarboxylic Acid [LogKow>3.5]	6.15	335762	Perfluorodecanoic acid
Ioinic Perfluoro Acyclics	PerfluoroSulfonic Acids [LogKow>3.1]	3.16	3871996	Tridecafluorohexane-1-sulfonic acid, potassium salt
Ioinic Perfluoro Acyclics	PerfluoroSulfonic Acids [LogKow>3.10]	7.36	56773423	Heptadecafluorooctanesulfonic acid, tetraethyl ammonium salt

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Primary Node II. Contains a Charge

Sub-node: Belongs to Known Charged Group

ERES Chemical Group	Sub-group	Log Kow	CASRN	Chemical Name
4-Alkylbenzthiols	4-Alkylbenzthiols	3.23	106456	p-Toluene thiol
4-Alkylbenzthiols	4-Alkylbenzthiols	4.59	2396681	4-tert-Butylthiophenol
Alkylaromatic Sulfonic Acids	Alkylaromatic Sulfonic Acids	-2.40	657841	p-Toluenesulfonate, sodium salt
Alkylaromatic Sulfonic Acids	Alkylaromatic Sulfonic Acids	-1.78	532025	Naphthalene-2-sulfonic acid, sodium salt
Alkylaromatic Sulfonic Acids	Alkylaromatic Sulfonic Acids	-1.78	130143	Naphthalene-1-sulfonic acid, sodium salt
Alkylaromatic Sulfonic Acids	Alkylaromatic Sulfonic Acids	-0.13	98691	4-Ethylbenzenesulfonic acid
Alkylaromatic Sulfonic Acids	Alkylaromatic Sulfonic Acids	1.03	6149037	4-Octylbenzenesulfonic acid, sodium salt
Alkylaromatic Sulfonic Acids	Alkylaromatic Sulfonic Acids	5.77	27176870	4-Dodecylbenzenesulfonic acid
Anhydrides	Anhydrides	6.41	19780111	2-Dodecen-1-yl succinic acid anhydride
Charged Functional Groups	Sulfonic Acid Functional Group	1.76	23386529	Dicyclohexyl sulfosuccinate, sodium salt
Charged Functional Groups	Carboxylic Acid Functional Group	0.57	499832	2,6-Pyridinedicarboxylic acid
Charged Functional Groups	Carboxylic Acid Functional Group	1.76	121915	Isophthalic acid
Charged Functional Groups	Carboxylic Acid Functional Group	2.24	69727	Salicylic acid
Charged Functional Groups	Carboxylic Acid Functional Group	3.26	93765	2,4,5-T
Charged Functional Groups	Carboxylic Acid Functional Group	3.81	4365600	(2-carboxyethyl)triphenyl phosphonium hydroxide
Charged Functional Groups	Carboxylic Acid Functional Group	3.95	81903	Phenolphthalin
Charged Functional Groups	Quat Amine Functional Group	3.91	139082	Benzyldimethyl tetradecyammonium chloride
Charged Functional Groups	Quat Amine Functional Group	4.00	121540	Benzethonium chloride
Charged Functional Groups	Quat Amine Functional Group	4.85	56951	Chlorhexidine, diacetate salt, dihydrate
Sulfonic Acid Dyes	Sulfonic Acid Dyes	-6.74	1934210	Acid Yellow 23
Sulfonic Acid Dyes	Sulfonic Acid Dyes	-2.50	3844459	C.I. Acid Blue 9, disodium salt
Sulfonic Acid Dyes	Sulfonic Acid Dyes	-1.18	2783940	C.I. Food Yellow 3
Sulfonic Acid Dyes	Sulfonic Acid Dyes	1.82	3567257	Sulcofuron, sodium salt, monohydrate
Sulfonic Acid Dyes	Sulfonic Acid Dyes	3.12	27344418	4,4'-bis(2-Sulfostyryl)biphenyl, disodium salt
Sulfonic Acid Dyes	Sulfonic Acid Dyes	3.23	4404437	Flourescent Brightener 28
Sulfonic Acid Dyes	Sulfonic Acid Dyes	3.63	5281049	Pigment Red 57-1
Sulfonic Acid Dyes	Sulfonic Acid Dyes	4.03	25956176	C.I. Food Red 17
Sulfonic Acid Dyes	Sulfonic Acid Dyes	5.38	7023612	2-Naphthalenecarboxylic acid, 4-[(5-chloro-4-methyl-2-sulfophenyl)azo]-3-hydroxy-, calcium salt

Primary Node III. Known Inactive Class

Sub-node: Belongs to Known Inactive Group

ERES Chemical Group	Sub-group	log Kow	CASRN	Chemical Name
Acetals	Acetals [LogKow <= 5.5]	0.49	828002	2,6-Dimethyl-1,3-dioxan-4-ol acetate
Acetals	Acetals [LogKow <= 5.5]	1.30	6413101	Ethyl (2-methyl-1,3-dioxolan-2-yl) acetate
Acetals	Acetals [LogKow <= 5.5]	1.55	6175457	2,2-Diethoxyacetophenone
Acetals	Acetals [LogKow <= 5.5]	5.47	57345194	Amberketal IPM
Acetanilides	Acetanilides [2.2<LogKow<3.7]	2.21	24367940	4,4'-Diaminodiphenylmethane, mono-acetylated
Acetanilides	Acetanilides [2.2<LogKow<3.7]	2.23	2719053	4,4'-Diaminodiphenylmethane, di-acetylated
Acetanilides	Acetanilides [2.2<LogKow<3.7]	3.12	20330454	N-(4-butylphenyl) Acetamide
Acetanilides	Acetanilides [2.2<LogKow<3.7]	3.61	20330523	N-(4-pentylphenyl) Acetamide
Alcohols	Alcohols [LogKow<=3.4]	1.08	100516	Benzene methanol
Alcohols	Alcohols [LogKow<=3.4]	1.84	104541	Cinnamyl alcohol
Alcohols	Alcohols [LogKow<=3.4]	3.33	98555	Alpha-terpineol
4-Alkylfluorobenzenes	4-Alkylfluorobenzene [LogKow<=4.8]	2.19	462066	Fluorobenzene
4-Alkylfluorobenzenes	4-Alkylfluorobenzene [LogKow<=4.8]	3.65	403394	4-isopropyl Fluorobenzene
4-Alkylfluorobenzenes	4-Alkylfluorobenzene [LogKow<=4.8]	4.71	28593148	4-pentyl Fluorobenzene
Amino Anthracenedione	Amino Anthracenedione (LogKow>=3.0)	3.16	128950	9,10-Anthracenedione, 1,4-diamino-
Amino Anthracenedione	Amino Anthracenedione (LogKow>=3.0)	7.20	17354142	Sudan Blue II
Amino Anthracenedione	Amino Anthracenedione (LogKow>=3.0)	8.69	128803	Quinizarin Green SS
Anthraquinone Phenols	Anthraquinone Phenols [3.9<LogKow<6.3]	3.94	117102	1,8-Dihydroxyanthraquinone
Anthraquinone Phenols	Anthraquinone Phenols [3.9<LogKow<6.3]	6.24	81481	1-Hydroxy-4-(p-toluidino)anthraquinone
Benzoates (non-ring Subst)	Benzoates (non-ring Subst)[3.3<LogKow<4.3]	3.30	136607	n-butyl Benzoate
Benzoates (non-ring Subst)	Benzoates (non-ring Subst)[3.3<LogKow<4.3]	3.72	94462	isoamyl Benzoate
Benzoates (non-ring Subst)	Benzoates (non-ring Subst)[3.3<LogKow<4.3]	4.28	6789884	hexyl Benzoate
Benzoates (non-ring Subst)	Benzoates (non-ring Subst)[3.0<LogKow<4.1]	3.04	93992	phenyl Benzoate
Benzoates (non-ring Subst)	Benzoates (non-ring Subst)[3.0<LogKow<4.1]	4.03	94473	phenethyl Benzoate
Benzamides	Benzamides [2.1<LogKow<2.8]	2.19	10546700	N-propyl Benzamide
Benzamides	Benzamides [2.1<LogKow<2.8]	2.73	n/a	2-methyl-N-propyl Benzamide
Benzothiazoles	Benzothiazoles [1.9<LogKow<3.2]	2.00	136958	2-amino Benzothiazole
Benzothiazoles	Benzothiazoles [1.9<LogKow<3.2]	2.86	149304	2-mercapto Benzothiazole
Benzothiazoles	Benzothiazoles [1.9<LogKow<3.2]	3.12	21564170	2-thiocyanomethylthio Benzothiazole
Benzotriazole Phenol	Benzotriazole Phenol [3.0<LogKow<6.3]	3.00	2440224	2-(2-hydroxy-5-methyl phenyl) Benzotriazole
Benzotriazole Phenol	Benzotriazole Phenol [3.0<LogKow<6.3]	6.21	3147759	2-(2-hydroxy-5-t-octyl phenyl) Benzotriazole
Benzoxazoles	Benzoxazoles [LogKow>=2.5]	2.54	68427350	5-Benzoxazole sulfonamide, 2-(7-(diethylamino)-2-oxo-2H-1-benzopyran-3-yl)-
Benzoxazoles	Benzoxazoles [LogKow>=2.5]	8.61	7128645	Benzoxazole, 2,2'-(2,5-thiophenediyl) bis (5-tert-butyl)-
Bis-Anilines	Bis-Anilines [2.1<LogKow<6.4]	2.18	101779	4,4'-Methylenebis(aniline)
Bis-Anilines	Bis-Anilines [2.1<LogKow<6.4]	3.93	2390592	Ethanaminium,N-[4-[bis[4-(diethylamino) phenyl]methylene]-2,5-cyclohexadien-1-ylidene]-N-ethyl-, chloride;
Bis-Anilines	Bis-Anilines [2.1<LogKow<6.4]	4.00	54628216	4,4'-Diamino-2,2'-dimethylbibenzyl
Bis-Anilines	Bis-Anilines [2.1<LogKow<6.4]	4.37	101611	4,4'-Methylenebis[N,N-dimethyl]aniline
Bis-Anilines	Bis-Anilines [2.1<LogKow<6.4]	4.37	4073987	4,4'-Methylenebis(2,6-dimethylaniline)
Bis-Anilines	Bis-Anilines [2.1<LogKow<6.4]	5.22	101688	1,1'-Methylenebis(4-isocyanatobenzene)
Bis-Anilines	Bis-Anilines [2.1<LogKow<6.4]	5.38	2716101	4,4'-[1,4-phenylenebis(1-methylethylidene)] bis-benzenamine
Bis-Anilines	Bis-Anilines [2.1<LogKow<6.4]	6.34	13680358	4,4'-Methylenebis(2,6-diethylanilne)
Borate Esters	Borate Esters [LogKow<=1]	-1.64	2665136	Tributyleneglycol biborate
Borate Esters	Borate Esters [LogKow<=1]	-0.53	14697508	Hexyleneglycol biborate
Borate Esters	Borate Esters [LogKow<=1]	0.98	100890	Trihexyleneglycol biborate
Chloro Nitrobenzenes	Chloro Nitrobenzenes [1.6<LogKow<3.5]	1.64	6358072	2-Amino-4-chloro-5-nitrophenol
Chloro Nitrobenzenes	Chloro Nitrobenzenes [1.6<LogKow<3.5]	2.12	121879	1-Amino-2-chloro-4-nitrobenzene
Chloro Nitrobenzenes	Chloro Nitrobenzenes [1.6<LogKow<3.5]	2.46	100005	4-Chloronitrobenzene
Chloro Nitrobenzenes	Chloro Nitrobenzenes [1.6<LogKow<3.5]	3.10	99547	3,4-Dichloronitrobenzene
Chloro Nitrobenzenes	Chloro Nitrobenzenes [1.6<LogKow<3.5]	3.42	121175	2-Chloro-5-(trifluoromethyl)nitrobenzene
Cyano Compounds	Cyano Compounds [1.8<LogKow<6.9]	1.84	1885387	Cinnamonitrile
Cyano Compounds	Cyano Compounds [1.8<LogKow<6.9]	2.21	140534	(4-Chlorophenyl) acetonitrile
Cyano Compounds	Cyano Compounds [1.8<LogKow<6.9]	6.64	120068373	Fipronil
Cyano Compounds	Cyano Compounds [1.8<LogKow<6.9]	6.88	6197304	2-Ethylhexyl 2-cyano-3,3-diphenylacrylate
2,6-Dialkylphenols	2,6-Dialkylphenols	3.57	2078548	2,6-diisopropylphenol
2,6-Dialkylphenols	2,6-Dialkylphenols	5.03	128370	2,6-di-tert-butyl-4-methylphenol
2,6-Dialkylphenols	2,6-Dialkylphenols	7.97	119471	2,2'-methylenebis 6-(1,1-dimethylethyl)-4-methyl-phenol
2,6-Dialkylphenols	2,6-Dialkylphenols	8.95	88244	2,2'-methylenebis 6-(1,1-dimethylethyl)-4-ethyl-phenol
2,6-Dialkylphenols	2,6-Dialkylphenols	13.41	2082793	octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionate
2,6-Dialkylphenols	2,6-Dialkylphenols	17.17	1709702	1,3,5-trimethyl-2,4,6-tris(3,5-ditertbutyl-4-hydroxybenzyl)benzene
Dichloro Acetamide	Dichloro Acetamide [2.3<LogKow<3.2]	2.38	98730042	Benoxacor
Dichloro Acetamide	Dichloro Acetamide [2.3<LogKow<3.2]	2.86	39085182	N-cyclohexyl-2,2-dichloro-N-methylacetamide
Dichloro Acetamide	Dichloro Acetamide [2.3<LogKow<3.2]	3.19	71526073	Ethanone, 2,2-dichloro-1-(1-oxa-4-azaspiro(4.5)dec-4-yl)-
Dimethylamino Phenols	Dimethylamino Phenol [LogKow<=1.4]	0.77	90722	2,4,6-tris(dimethylaminomethyl) phenol
Dimethylamino Phenols	Dimethylamino Phenol [LogKow<=1.4]	1.27	120650	2-(dimethylaminomethyl) phenol
Dimethylamino Phenols	Dimethylamino Phenol [LogKow<=1.4]	1.34	99070	3-(dimethylamino) phenol
Epoxides	Epoxides [LogKow<=3.9]	0.23	17557232	Neopentyl Glycol Diglycidyl Ether
Epoxides	Epoxides [LogKow<=3.9]	2.55	121391	Ethyl phenylglycidate
Epoxides	Epoxides [LogKow<=3.9]	3.00	77838	Ethyl 3-methyl-3-phenylglycidate
Epoxides	Epoxides [LogKow<=3.9]	3.84	1675543	oxirane, 2,2'-(1-methylethylidene)bis (4,1-phenyleneoxymethylene) bis-
Hydrofurans	Hydrofurans [LogKow<=2.1]	-0.11	97994	tetrahydrofurfuryl alcohol
Hydrofurans	Hydrofurans [LogKow<=2.1]	1.59	105215	5-butyldihydrofuran-2(3H)-one
Hydrofurans	Hydrofurans [LogKow<=2.1]	2.08	104610	2(3h)-furanone,dihydro-5-pentyl-
Imidazolidines	Imidazolidines [LogKow<=0]	-1.53	116256	5,5-Dimethyl-1-hydroxymethylhydantoin
Imidazolidines	Imidazolidines [LogKow<=0]	-0.45	82925960	1,3-Dibromo-5-ethyl-5-methylhydantoin
Imidazolidines	Imidazolidines [LogKow<=0]	-0.94	118525	1,3-Dichloro-5,5-dimethylhydantoin
Imidazolidines	Imidazolidines [LogKow<=0]	-0.94	77485	1,3-Dibromo-5,5-dimethylhydantoin
Imidazolidines	Imidazolidines [LogKow<=0]	-0.94	16079882	1-Bromo-3-chloro-5,5-dimethylhydantoin
Isothiazolines	Isothiazolines [LogKow<=3.6]	0.45	81072	1,2-Benzisothiazol-3(2h)-one, 1,1-dioxide
Isothiazolines	Isothiazolines [LogKow<=3.6]	0.64	2634335	1,2-Benzisothiazol-3-one
Isothiazolines	Isothiazolines [LogKow<=3.6]	3.12	26530201	2-Octyl-3(2H)-isothiazolone
Isothiazolines	Isothiazolines [LogKow<=3.6]	3.61	64359815	4,5-Dichloro-2-octyl-isothiazolone
Monocyclic Hydrocarbons	Mono-cyclic Hydrocarbons [2.5<LogKow<6.4]	2.54	108883	Toluene
Monocyclic Hydrocarbons	Mono-cyclic Hydrocarbons [2.5<LogKow<6.4]	3.09	106423	p-Xylene
Monocyclic Hydrocarbons	Mono-cyclic Hydrocarbons [2.5<LogKow<6.4]	3.45	98828	Cumene
Monocyclic Hydrocarbons	Mono-cyclic Hydrocarbons [2.5<LogKow<6.4]	4.83	5989275	(R)-(+)-Limonene
Monocyclic Hydrocarbons	Mono-cyclic Hydrocarbons [2.5<LogKow<6.4]	6.36	717748	1,3,5-triisopropylbenzene
Naphthalenol Azophenyl	Naphthalenol_Azophenyl [5.5<LogKow<7.8]	5.51	842079	Sudan 1
Naphthalenol Azophenyl	Naphthalenol_Azophenyl [5.5<LogKow<7.8]	7.75	85869	C.I. Solvent Red 23
Nitro Anilines	Nitro Anilines [LogKow<=2.2]	0.99	121880	2-hydroxy-4-Nitroaniline
Nitro Anilines	Nitro Anilines [LogKow<=2.2]	1.47	100016	4-Nitroaniline
Nitro Anilines	Nitro Anilines [LogKow<=2.2]	2.10	96968	4-methoxy-2-Nitroaniline
N,N-Dimethylanilines	N,N-Dimethylanilines [2.7<LogKow<5.8]	2.72	99978	N,N-Dimethyl-p-toluidine (4,N,N- Trimethylaniline)
N,N-Dimethylanilines	N,N-Dimethylanilines [2.7<LogKow<5.8]	3.50	90948	Michler's ketone
N,N-Dimethylanilines	N,N-Dimethylanilines [2.7<LogKow<5.8]	4.02	61734	Methylene Blue
N,N-Dimethylanilines	N,N-Dimethylanilines [2.7<LogKow<5.8]	4.95	1552427	Crystal Violet lactone
N,N-Dimethylanilines	N,N-Dimethylanilines [2.7<LogKow<5.8]	5.77	21245023	2-Ethylhexyl 4 (dimethylamino) Benzoate
Oxazoles	Oxazoles [LogKow<=0.4]	-1.55	6542376	5-Hydroxymethyl-1-aza-3,7-dioxabicyclo(3.3.0)octane
Oxazoles	Oxazoles [LogKow<=0.4]	0.40	7747355	5-ethyl-1-aza-3,7-dioxabicyclo(3.3.0)-octane
Phenones (n-alkyl)	Phenones (n-alkyl)[LogKow<=4.2]	1.67	98862	Acetophenone
Phenones (n-alkyl)	Phenones (n-alkyl)[LogKow<=4.2]	3.64	942927	n-Hexanophenone
Phenones (n-alkyl)	Phenones (n-alkyl)[LogKow<=4.2]	4.13	1671756	n-Heptanophenone
Phosphorous Acid Ester	Phosphorous Acid Esters [LogKow>6.6]	6.62	101020	Phosphorous acid, triphenyl ester
Phosphorous Acid Ester	Phosphorous Acid Esters [LogKow>6.6]	8.00	25550985	Phosphorous acid, diisodecyl phenyl ester
Phthalimides	Phthalimides [LogKow<=3.1]	-1.46	69932	Uric acid
Phthalimides	Phthalimides [LogKow<=3.1]	0.16	58082	Caffeine
Phthalimides	Phthalimides [LogKow<=3.1]	1.23	5450-40-8	2-(2-Hydroxyethyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione
Phthalimides	Phthalimides [LogKow<=3.1]	1.30	85416	Phthalimide
Phthalimides	Phthalimides [LogKow<=3.1]	2.84	133073	Folpet

Phthalimides	Phthalimides [LogKow<=3.1]	3.03	50471448	Vinclozolin
Piperidines	Piperidines [1.85<LogKow<6.5]	1.89	766096	1-Ethylpiperidine
Piperidines	Piperidines [1.85<LogKow<6.5]	6.50	52829079	Decanedioic acid, bis(2,2,6,6-tetramethyl-4-piperidinyl) ester
Pyrrolidiones	Pyrrolidiones [LogKow<=3.4]	-0.11	872504	1-Methyl-2-pyrrolidone
Pyrrolidiones	Pyrrolidiones [LogKow<=3.4]	3.33	2687947	N-Octylpyrrolidone
Quinolines	Quinolines [LogKow<=5.3]	-3.79	207386923	8-Hydroxy-5-quinolinesulfonic acid hydrate
Quinolines	Quinolines [LogKow<=5.3]	-1.50	207386912	8-Hydroxyquinoline hemisulfate salt hemihydrate
Quinolines	Quinolines [LogKow<=5.3]	2.29	66717	1,10-Phenanthroline, Anhydrous
Quinolines	Quinolines [LogKow<=5.3]	4.21	8003223	Quinoline Yellow
Quinolines	Quinolines [LogKow<=5.3]	5.28	99607702	Cloquintocet-Mexyl
Sorbitans	Sorbitans [3.1<LogKow<5.9]	3.15	1338392	Sorbitan, monododecanoate
Sorbitans	Sorbitans [3.1<LogKow<5.9]	5.89	1338438	Sorbitan, mono-9-octadecenoate, (Z)-
Sugars	Sugars [LogKow<=3.0]	-7.77	10016203	α-Cyclodextrin
Sugars	Sugars [LogKow<=3.0]	-4.27	57501	Sucrose
Sugars	Sugars [LogKow<=3.0]	-1.98	90802	D-Gluconic acid, delta-lactone
Sugars	Sugars [LogKow<=3.0]	2.93	29836268	Octyl beta-d-glucopyranoside
Triazines	Triazines [LogKow<=3.3]	-5.92	51229788	1-(cis-3-chloroallyl)-3,5,7-triaza-1-azoniaadamantane chloride
Triazines	Triazines [LogKow<=3.3]	-4.15	100970	Hexamethyltetramine
Triazines	Triazines [LogKow<=3.3]	-0.38	7673098	N,N',N-trichloro-1,3,5-triazine-2,4,6-triamine
Triazines	Triazines [LogKow<=3.3]	-0.06	2893789	1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3-dichloro-, sodium salt
Triazines	Triazines [LogKow<=3.3]	0.61	108805	2,4,6-Trihydroxy-1,3,5-triazine
Triazines	Triazines [LogKow<=3.3]	3.27	5915413	6-chloro-n(1,1-dimethylethyl)-n'-ethyl-1,3,5-triazine-2,4-diamine
Triazines	Triazines [LogKow<=3.3]	4.07	28159980	N'-tert-butyl-n-cyclopropyl-6-(methylthio)-1,3,5-triazine-2,4-diamine

Node IV <return to Node list>

Chemicals in Node IV have a phenolic -OH and a second –OH or =O. The distances between these substituents are hypothesized to enable them to interact with the ER at multiple sub-pockets (A-, B- and/or C-site) within the ligand binding domain of the ER (see Figure 1 and accompanying text in Hornung et al. 2014 and Katzenellenbogen et al. 2003. Pure Appl. Chem. 75, 2397-2403).

Primary Node IV. Phenolic OH + 2nd -OH or =O_spec. dist.

Sub-node	Chemical Group	Sub-group	log Kow	CASRN	Chemical Name
# of Nucleophilic Sites = 3	A_B-type	A_B-type	2.81	50271	Estriol
# of Nucleophilic Sites = 2	A_B-type	A_B-type	3.43	53167	Estrone
# of Nucleophilic Sites = 2	A_B-type	A_B-type	3.94	57910	17-alpha-Estradiol
# of Nucleophilic Sites = 2	A_B-type	A_B-type	3.94	50282	17-beta-Estradiol
# of Nucleophilic Sites = 2	A_B-type	A_B-type	4.12	57636	Ethynylestradiol
# of Nucleophilic Sites = 2	A_B-type	A_B-type [Atten.]	5.70	6088513	6-Hydroxy-2-naphthyl disulfide
# of Nucleophilic Sites = 2	A_B-type	A_B-type [Atten.]	8.24	96695	5-tert-butyl-4-hydroxy-2-methylphenyl sulfide
# of Nucleophilic Sites = 2	A_C-type	A_C-type	1.65	80091	4,4'-Sulfonyldiphenol
# of Nucleophilic Sites = 2	A_C-type	A_C-type	4.13	77407	Bisphenol B
# of Nucleophilic Sites = 2	A_C-type	A_C-type	3.64	80057	Bisphenol A
# of Nucleophilic Sites = 2	A_C-type	A_C-type	3.75	14868032	bis-hydroxy-DDE
# of Nucleophilic Sites = 2	A_C-type	A_C-type	4.47	1478611	4,4'-(hexafluoroisopropylidene) diphenol
# of Nucleophilic Sites = 2	A_C-type	A_C-type	4.55	2971360	dihydroxy-Methoxychlor (HPTE)
# of Nucleophilic Sites = 2	A_C-type	A_C-type	5.11	28463038	monohydroxy-Methoxychlor
# of Nucleophilic Sites = 2	A_C-type	A_C-type	5.60	84162	Hexestrol
# of Nucleophilic Sites = 2	A_C-type	A_C-type	5.64	56531	Diethylstilbestrol
# of Nucleophilic Sites = 2	A_C-type	A_C-type - Antagonist	5.82	68047063	4-hydroxy-Tamoxifen
# of Nucleophilic Sites = 2	A_C-type	A_C-type [Atten. Steric Hind.]	7.20	79947	4,4'-Isopropylidenebis(2,6-dibromophenol)
# of Nucleophilic Sites = 2	A_C-type	A_C-type [Atten. Steric Hind.]	9.09	85609	4,4'-Butylidene bis(6-tert-butyl-m-cresol)
# of Nucleophilic Sites = 3	A_B_C-type	A_B_C-type - Flavones	1.48	480160	Morin
# of Nucleophilic Sites = 3	A_B_C-type	A_B_C-type - Flavones	1.57	479130	Coumestrol
# of Nucleophilic Sites = 3	A_B_C-type	A_B_C-type - Flavones	1.96	520183	Kaemferol
# of Nucleophilic Sites = 3	A_B_C-type	A_B_C-type	2.37	97290	Resorcinol sulfide
# of Nucleophilic Sites = 3	A_B_C-type	A_B_C-type - Flavones	2.55	486668	Daidzein
# of Nucleophilic Sites = 3	A_B_C-type	A_B_C-type - Flavones	2.84	446720	Genistein
# of Nucleophilic Sites = 3	A_B_C-type	A_B_C-type	3.06	77098	Phenolphthlein
# of Nucleophilic Sites = 3	A_B_C-type	A_B_C-type -Antagonist	9.09	129453618	ICI 182780
# of Nucleophilic Sites = 3	A_B_C-type	A_B_C-type -Antagonist	10.23	101908229	ZM189154

Node V <return to Node list>

Primary Node V. Special Rules Groups

Sub-node: Alkyl Halobenzenes Selection Rules

ERES Chemical Group	Sub-group	log Kow	CASRN	Chemical Name
4-Alkylchlorobenzenes	Alkylchlorobenzene [LogKow<4.5]	2.64	108907	Chlorobenzene
4-Alkylchlorobenzenes	Alkylchlorobenzene [LogKow<4.5]	3.68	622980	4-Chloroethylbenzene
4-Alkylchlorobenzenes	Alkylchlorobenzene [LogKow<4.5]	4.17	52944340	4-Chloropropylbenzene
4-Alkylchlorobenzenes	Alkylchlorobenzenes [LogKow=4.5-5.5]	4.66	15499271	4-Chlorobutylbenzene
4-Alkylchlorobenzenes	Alkylchlorobenzenes [LogKow=4.5-5.5]	5.15	79098207	4-Chloropentylbenzene
Bromo- and Alkylbromobenzenes	Alkylbromobenzenes [3.4<LogKow<4.7]	3.43	106387	4-Bromotoluene
Bromo- and Alkylbromobenzenes	Bromobenzenes [3.4<LogKow<4.7]	3.77	106376	1,4-Dibromobenzene
Bromo- and Alkylbromobenzenes	Bromobenzenes [3.4<LogKow<4.7]	4.66	615543	1,2,4-Tribromobenzene

Sub-node: Anisole Selection Rules

ERES Chemical Group	Sub-group	Log Kow	CAS	Chemical Name
Anisoles (a)	Anisoles [RBA<0.00001%]	1.79	123115	4-Methoxybenzaldehyde
Anisoles (b)	Anisoles [RBA<0.00001%]	1.36	120149	3,4-Dimethoxybenzaldehyde
Anisoles (b)	Anisoles [RBA<0.00001%]	1.67	487069	5,7-Dimethoxycoumarin
Anisoles (b)	Anisoles [RBA<0.00001%]	2.03	7443256	Dimethyl 4-methoxybenzylidene malonate
Anisoles (b)	Anisoles [RBA<0.00001%]	2.15	150787	1,4-Dimethoxylbenzene
Anisoles (b)	Anisoles [RBA<0.00001%]	2.93	24393564	Ethyl-4-methoxycinnamate
Anisoles (b)	Anisoles [RBA<0.00001%]	5.80	5466773	2-Propenoic acid, 3-(4-methoxyphenyl)-, 2-ethylhexyl ester
Anisoles (c)	Anisoles [RBA<0.00001%]	3.39	104461	Anethole
Anisoles (c)	Anisoles [RBA<0.00001%]	3.39	4180238	trans-Anethole
Anisoles (c)	Anisoles [RBA<0.00001%]	3.60	104450	p-Propyl anisole
Anisoles (d)	Anisoles [RBA<0.00001%]	1.60	343271	Harmine hydrochloride
Anisoles (d)	Anisoles [RBA<0.00001%]	1.86	64868	Colchicine
Anisoles (d)	Anisoles [RBA<0.00001%]	4.17	83669	4-tert-Butyl-3-methoxy-2,6-dinitrotoluene
Anisoles (d)	Anisoles [RBA<0.00001%]	4.63	61813987	Solvent yellow 72
Anisoles (d)	Anisoles [RBA>0.00001%]	5.67	72435	Methoxychlor

Sub-node: Benzodioxolane Selection Rules

ERES Chemical Group	Sub-group	Log Kow	CAS	Chemical Name
Benzodioxolane	Benzodioxolane (Exact Match) [RBA<0.00001%]	1.77	120570	Piperonal
Benzodioxolane	Benzodioxolane (Exact Match) [RBA<0.00001%]	4.29	51036	Piperonyl Butoxide

Sub-node: DDT-Like Selection Rules

ERES Chemical Group	Sub-group	Log Kow	CAS	Chemical Name
DDT-Like	DDT-Like (Exact Match) [RBA>0.00001%]	5.87	53190	o,p'-DDD
DDT-Like	DDT-Like (Exact Match) [RBA>0.00001%]	5.87	72548	p,p'-DDD
DDT-Like	DDT-Like (Exact Match) [RBA>0.00001%]	6.00	3424826	o,p'-DDE
DDT-Like	DDT-Like (Exact Match) [RBA>0.00001%]	6.00	72559	p,p'-DDE
DDT-Like	DDT-Like (Exact Match) [RBA>0.00001%]	6.79	50293	p,p'-DDT
DDT-Like	DDT-Like (Exact Match) [RBA>0.00001%]	6.79	no cas	o,p'-DDT (- enantiomer)
DDT-Like	DDT-Like (Exact Match) [RBA>0.00001%]	6.79	789026	o,p'-DDT
DDT-Like	DDT-Like (Exact Match) [RBA>0.00001%]	6.79	no cas	o,p'-DDT (+ enantiomer)
DDT-Like	DDT-Like (Exact Match) [RBA>0.00001%]	6.79	789026	o,p'-DDT-Racemic mixture (50:50)

Sub-node: Multicyclic Hydrocarbons Selection Rules

ERES Chemical Group	Sub-group	Log Kow	CAS	Chemical Name
Multicyclic Hydrocarbons	Multicyclic Hydrocarbons (Exact Match) [RBA<0.00001%]	3.17	91203	Naphthalene
Multicyclic Hydrocarbons	Multicyclic Hydrocarbons (Exact Match) [RBA<0.00001%]	4.02	86737	Fluorene
Multicyclic Hydrocarbons	Multicyclic Hydrocarbons (Exact Match) [RBA<0.00001%]	4.27	80568	alpha-Pinene
Multicyclic Hydrocarbons	Multicyclic Hydrocarbons (Exact Match) [RBA<0.00001%]	4.27	613310	9,10-Dihydroanthracene
Multicyclic Hydrocarbons	Multicyclic Hydrocarbons (Exact Match) [RBA<0.00001%]	4.52	103300	trans-Stilbene
Multicyclic Hydrocarbons	Multicyclic Hydrocarbons (Exact Match) [RBA<0.00001%]	4.93	206440	Fluoranthene
Multicyclic Hydrocarbons	Multicyclic Hydrocarbons (Exact Match) [RBA<0.00001%]	4.93	129000	Pyrene
Multicyclic Hydrocarbons	Multicyclic Hydrocarbons (Exact Match) [RBA<0.00001%]	6.45	632519	Tetraphenylethylene
Multicyclic Hydrocarbons	Multicyclic Hydrocarbons (Exact Match) [RBA<0.00001%]	7.58	1625918	4,4-Ditertbutylbiphenyl
Multicyclic Hydrocarbons	Multicyclic Hydrocarbons (Exact Match) [RBA>0.00001%]	3.86	530483	1,1-Diphenylethylene
Multicyclic Hydrocarbons	Multicyclic Hydrocarbons (Exact Match) [RBA>0.00001%]	4.52	645498	cis-Stilbene
Multicyclic Hydrocarbons	Multicyclic Hydrocarbons (Exact Match) [RBA>0.00001%]	5.37	519733	Triphenylmethane
Multicyclic Hydrocarbons	Multicyclic Hydrocarbons (Exact Match) [RBA>0.00001%]	5.49	58720	Triphenylethylene
Multicyclic Hydrocarbons	Multicyclic Hydrocarbons (Exact Match) [RBA>0.00001%]	5.52	84151	o-Terphenyl

Sub-node: Organometallics Selection Rules

ERES Chemical Group	Sub-group	Log Kow	CAS	Chemical Name
Organometallics	Organometallics [LogKow<1.3]	-10.42	39208156	Ethylenediaminetetraacetic acid copper (II)
Organometallics	Organometallics [LogKow<1.3]	-1.99	13463417	1-Hydroxypyridine-2-thione, zinc salt
Organometallics	Organometallics (Exact Match) [RBA<0.00001%]	2.32	10380286	Bis(8-quinolinolato) Copper (II)
Organometallics	Organometallics (Exact Match) [RBA<0.00001%]	4.69	4342363	Tributyl tin benzoate
Organometallics	Organometallics (Exact Match) [RBA<0.00001%]	7.51	58366	10,10-oxybis-10H-phenoxarsine
Organometallics	Organometallics (Exact Match) [RBA<0.00001%]	8.71	147148	Copper(II) phthalocyanine
Organometallics	Organometallics (Exact Match) [RBA<0.00001%]	19.02	1328536	Pigment Green 7

Sub-node: Phosphoric Acid Ester Selection Rules

ERES Chemical Group	Sub-group	Log Kow	CAS	Chemical Name
Phosphoric Acid Esters	Phosphoric Acid Esters [RBA<0.00001%]	2.88	838857	Phosphoric acid, diphenyl ester
Phosphoric Acid Esters	Phosphoric Acid Esters [RBA>0.00001%]	4.70	115866	Phosphoric acid, triphenyl ester
Phosphoric Acid Esters	Phosphoric Acid Esters [RBA>0.00001%]	6.30	1241947	Phosphoric acid, 2-ethylhexyl diphenyl ester

Sub-node: Steroidal Backbone Selection Rules

ERES Chemical Group	Sub-group	Log Kow	CAS	Chemical Name
Steroidal Backbone	Steroidal Backbone (Exact Match) [RBA<0.00001%]	1.92	564352	11-keto-Testosterone
Steroidal Backbone	Steroidal Backbone (Exact Match) [RBA<0.00001%]	1.99	50226	Corticosterone
Steroidal Backbone	Steroidal Backbone (Exact Match) [RBA<0.00001%]	2.65	80657176	alpha-Trenbolone
Steroidal Backbone	Steroidal Backbone (Exact Match) [RBA>0.00001%]	2.65	10161338	beta-Trenbolone
Steroidal Backbone	Steroidal Backbone (Exact Match) [RBA>0.00001%]	3.07	521186	Stanolone
Steroidal Backbone	Steroidal Backbone (Exact Match) [RBA<0.00001%]	3.27	58220	Testosterone
Steroidal Backbone	Steroidal Backbone (Exact Match) [RBA>0.00001%]	3.51	68235	Norethynodrel
Steroidal Backbone	Steroidal Backbone (Exact Match) [RBA<0.00001%]	3.67	57830	Progesterone
Steroidal Backbone	Steroidal Backbone (Exact Match) [RBA<0.00001%]	3.72	58184	Methyl-Testosterone

Sub-node: Sulfonamides Selection Rules

ERES Chemical Group	Sub-group	Log Kow	CAS	Chemical Name
Sulfonamides	Sulfonamides (ring subst.)	0.84	7080504	Chloramine T trihydrate
Sulfonamides	Sulfonamides (ring subst.)	0.84	59405	Sulfaquinoxaline
Sulfonamides	Sulfonamides (ring subst.)	1.87	80397	N-Ethyl-p-toluenesulfonamide
Sulfonamides	Sulfonamides (ring subst.)	2.73	19044883	Oryzalin
Sulfonamides	Sulfonamides (ring subst.)	2.86	1907659	N-n-Butyl-p-toluenesulfonamide
Sulfonamides	Sulfonamides (non-subst. ring)	2.31	3622842	N-Butylbenzenesulfonamide

Sub-node: Tamoxifen-Like Selection Rules

ERES Chemical Group	Sub-group	Log Kow	CAS	Chemical Name
Tamoxifen-Like	Tamoxifen-Like [RBA>0.00001%]	6.30	10540291	Tamoxifen
Tamoxifen-Like	Tamoxifen-Like [RBA>0.00001%]	6.30	54965241	Tamoxifen Citrate
Tamoxifen-Like	Tamoxifen-Like [RBA>0.00001%]	6.74	50419	Clomiphene Citrate

Sub-node: Thiophosphate Ester Selection Rules

ERES Chemical Group	Sub-group	Log Kow	CAS	Chemical Name
Thiophosphate Esters	Thiophosphate Esters [RBA<0.00001%]	3.30	122145	Fenitrothion
Thiophosphate Esters	Thiophosphate Esters [RBA<0.00001%]	4.47	56724	Coumaphos
Thiophosphate Esters	Thiophosphate Esters [RBA>0.00001%]	2.73	56382	Parathion
Thiophosphate Esters	Thiophosphate Esters [RBA>0.00001%]	3.44	29232937	Pirimiphos-methyl
Thiophosphate Esters	Thiophosphate Esters [RBA>0.00001%]	4.02	944229	Dyfonate
Thiophosphate Esters	Thiophosphate Esters [RBA>0.00001%]	5.20	97176	Dichlofenthion

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Node VI <return to Node list>

Chemicals in Node VI contain a phenolic -OH hypothesized to interact with the A-site sub-pocket within the ligand binding domain of the ER (see Figure 1 and accompanying text in Hornung et al. 2014 and Katzenellenbogen et al. 2003. Pure Appl. Chem. 75, 2397-2403).

Primary Node VI: Site A, Contains Phenol Fragment

Sub-node: Belongs to known Active sub-class

Chemical Group	Sub-group	log Kow	CASRN	Chemical Name
2-Hydroxy Benzophenones	2-Hydroxy Benzophenones	2.78	131555	2,2′,4,4′-tetra-HydroxyBenzophenone
2-Hydroxy Benzophenones	2-Hydroxy Benzophenones	2.96	131566	2,4-di-HydroxyBenzophenone
2-Hydroxy Benzophenones	2-Hydroxy Benzophenones	3.44	117997	2-HydroxyBenzophenone
2-Hydroxy Benzophenones	2-Hydroxy Benzophenones	3.52	131577	2-Hydroxy 4-methoxyBenzophenone
2-Hydroxy Benzophenones	2-Hydroxy Benzophenones [Atten. - Charged]	0.37	4065456	2-Hydroxy-4-methoxyBenzophenone-5-sulfonic acid
2-Hydroxy Benzophenones	2-Hydroxy Benzophenones [Atten. - Steric Hind.]	6.96	1843056	2-Hydroxy-4-(octyloxy)Benzophenone
Alkoxyphenols	Alkoxyphenols [LogKow<4.1]	1.59	150765	4-methoxyphenol
Alkoxyphenols	Alkoxyphenols [LogKow<4.1]	2.58	18979505	4-propoxyphenol
Alkoxyphenols	Alkoxyphenols [LogKow<4.1]	2.73	97530	4-allyl-2-methoxypheno
Alkoxyphenols	Alkoxyphenols [LogKow<4.1]	3.07	122941	4-butoxyphenol
Alkoxyphenols	Alkoxyphenols [LogKow<4.1]	3.50	25013165	2(3)-tert-butyl-4-methoxyphenol (mixture of isomers)
Alkoxyphenols	Alkoxyphenols [LogKow<4.1]	3.50	121006	2-tert-butyl-4-methoxyphenol
Alkoxyphenols	Alkoxyphenols [LogKow<4.1]	4.05	18979550	4-hexyloxyphenol
Alkoxyphenols	Alkoxyphenols [Atten. - Steric Hind.]	4.56	489010	2,6-di-tert-butyl-4-methoxyphenol
Alkylphenols	4-n-Alkylphenols	1.31	108952	phenol
Alkylphenols	4-n-Alkylphenols	2.06	106445	4-methylphenol
Alkylphenols	4-n-Alkylphenols	2.55	123079	4-ethylphenol
Alkylphenols	4-sec-Alkylphenols	2.97	99898	4-isopropylphenol
Alkylphenols	4-n-Alkylphenols	3.04	645567	4-n-propylphenol
Alkylphenols	4-tert-Alkylphenols	3.42	98544	4-tert-butylphenol
Alkylphenols	3-tert--Alkylphenols	3.42	585342	3-tert-butylphenol
Alkylphenols	2-tert--Alkylphenols	3.42	88186	2-tert-butylphenol
Alkylphenols	multi-subst.-Alkylphenols	3.52	89838	2-isopropyl-5-methylphenol
Alkylphenols	2-sec--Alkylphenols	3.46	89725	2-sec-butylphenol
Alkylphenols	4-sec-Alkylphenols	3.46	99718	4-sec-butylphenol
Alkylphenols	4-n-Alkylphenols	3.53	1638228	4-n-butylphenol
Alkylphenols	4-tert-Alkylphenols	3.91	80466	4-tert-amylphenol
Alkylphenols	4-n-Alkylphenols	4.02	14938353	4-n-pentylphenol
Alkylphenols	4-tert-Alkylphenols	4.40	32390468	4-tert-hexylphenol
Alkylphenols	4-n-Alkylphenols	4.52	2446697	4-n-hexylphenol
Alkylphenols	4-tert-Alkylphenols	4.90	72624023	4-tert-heptylphenol
Alkylphenols	4-n-Alkylphenols	5.01	1987504	4-n-heptylphenol
Alkylphenols	4-tert-Alkylphenols	5.28	140669	4-t-octylphenol
Alkylphenols	multi-subst.-Alkylphenols	5.33	96764	2,4-ditert-butylphenol
Alkylphenols	4-n-Alkylphenols	5.50	1806264	4-n-octylphenol
Alkylphenols	4-n-Alkylphenols	5.99	104405	4-n-nonylphenol
Alkylphenols	4-Mixed isomer-Alkylphenols	5.99	84852153	4-nonylphenol; mixed branched isomers
Alkylphenols	4-sec-Alkylphenols	6.41	17408592	4-sec-decylphenol
Alkylphenols	4-Mixed isomer-Alkylphenols	7.24	27193868	4-dodecylpheno
Alkylphenols	Alkylphenol Ethoxylate	5.12	20427843	nonylphenol diethoxylate
Alkylphenols	Alkylphenol Ethoxylate	5.39	104358	nonylphenol ethoxylate
Alkylphenols	Alkylphenol Carboxylate	5.35	106807787	nonylphenoxy ethoxy acetic acid
Alkylphenols	Alkylphenol Carboxylate	5.62	3115499	nonylphenoxy acetic acid
Fluoresceins	Fluorescein [LogKow<1.3]	-4.25	518478	Flourescein sodium salt
Fluoresceins	Fluorescein	3.35	2321075	Fluorescein
Fluoresceins	Fluorescein [Atten.- Charged]	5.47	18472872	Phloxine B
Gallates	Gallates (Exact Match) [RBA>0.00001%]	1.79	121799	Propyl gallate
Gallates	Gallates (Exact Match) [RBA<0.00001%]	6.21	1166525	n-Dodecyl gallate
Halophenols	Halophenols [# of Halogens<3]	1.71	371415	4-Fluorophenol
Halophenols	Halophenols [# of Halogens<3]	2.68	540385	4-Iodophenol
Halophenols	Halophenols [# of Halogens<3]	2.16	106489	4-Chlorophenol
Halophenols	Halophenols [# of Halogens<3]	2.70	59507	4-Chloro-3-methylphenol
Halophenols	Halophenols [# of Halogens<3]	2.80	120832	2,4-Dichlorophenol
Halophenols	Halophenols [# of Halogens=>3]	4.74	87865	Pentachlorophenol
Halophenols	Halophenols [# of Halogens=>3]	4.18	118796	2,4,6-Tribromophenol
Hydroquinones	Hydroquinone [LogKow<1.3]	1.03	123319	Hydroquinone
Hydroquinones	Hydroquinone [Atten. - Charged]	2.94	31519229	1,4-dihydroxy-2-napthoic acid
Hydroquinones	Hydroquinone	2.94	1948330	tert-butylHydroquinone
Mixed Phenol	Mixed Phenol [LogKow ,1.3]	-0.56	65236	Pyridoxine
Mixed Phenol	Mixed Phenol [LogKow ,1.3]	0.24	123308	4-Aminophenol
Mixed Phenol	Mixed Phenol [LogKow ,1.3]	1.05	121335	Vanillin
Mixed Phenol	Mixed Phenol [LogKow ,1.3]	1.19	99934	4'-Hydroxyacetophenone
Mixed Phenol	Mixed Phenol [LogKow ,1.3]	1.24	95852	2-Amino-4-chlorophenol
Mixed Phenol	Mixed Phenol (Exact Match) [RBA<0.00001%]	1.54	2491385	2-bromo-4'-hydroxyacetophenone
Mixed Phenol	Mixed Phenol (Exact Match) [RBA<0.00001%]	1.91	100027	4-nitrophenol
Mixed Phenol	Mixed Phenol (Exact Match) [RBA<0.00001%]	2.27	534521	2-Methyl-4,6-dinitrophenol
Mixed Phenol	Mixed Phenol (Exact Match) [RBA<0.00001%]	2.52	94917	N,N'-Bis(salicylidene) 1,2-Propanediamine
Mixed Phenol	Mixed Phenol (Exact Match) [RBA>0.00001%]	2.67	1137424	4-hydroxy benzophenone
Mixed Phenol	Mixed Phenol (Exact Match) [RBA>0.00001%]	3.76	97231215	cyclohexyl(2,4-dihydroxyphenyl)ketone
Mixed Phenol	Mixed Phenol (Exact Match) [RBA<0.00001%]	3.94	4638486	5-chlorosalicylanilide
Mixed Phenol	Mixed Phenol (Exact Match) [RBA<0.00001%]	4.66	3380345	5-Chloro-2-(2,4-dichlorophenoxy)phenol
Mixed Phenol	Mixed Phenol (Exact Match) [RBA<0.00001%]	7.79	32687788	1,2-Bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamoyl) hydrazine
Mixed Phenol	Mixed Phenol (Exact Match) [RBA>0.00001%]	2.48	98179	3-(Trifluoromethyl)phenol
Mixed Phenol	Mixed Phenol (Exact Match) [RBA>0.00001%]	4.18	120321	2-Benzyl-4-chlorophenol
Mixed Phenol	Mixed Phenol (Exact Match) [RBA>0.00001%]	4.34	97234	dichlorophen
Parabens	Parabens (-alkyl)	2.00	99763	methyl-4-hydroxybenzoate
Parabens	Parabens (-alkyl)	2.49	120478	ethyl-4-hydroxybenzoate
Parabens	Parabens (-alkyl)	2.98	94133	propyl-4-hydroxybenzoate
Parabens	Parabens (-alkyl)	3.40	4247023	isobutyl 4-hydroxybenzoate
Parabens	Parabens (-alkyl)	3.47	94268	n-butyl-4-hydroxybenzoate
Parabens	Parabens (-alkyl)	4.94	1085127	n-heptyl 4-hydroxybenzoate
Parabens	Parabens (-alkyl)	5.43	1219381	n-octyl 4-hydroxybenzoate
Parabens	Parabens (-alkylphenyl)	3.70	94188	methylphenyl 4-hydroxybenzoate
Parabens	Parabens (-phenyl)	3.21	17696627	phenyl 4-hydroxybenzoate
Parabens	Parabens (other)	3.22	4707475	2,4-dihydroxy-3,6-dimethyl methylbenzoate
Phenolsulfonphthaleins	Phenolsulfonphthaleins	3.21	143748	Phenol red
Phenolsulfonphthaleins	Phenolsulfonphthaleins [Atten. - Steric Hind.]	6.77	115399	Tetrabromophenol blue
Phenyl phenols	Phenyl phenols [2.7<LogKow<4.1]	2.69	135193	2-Naphthol
Phenyl phenols	Phenyl phenols [2.7<LogKow<4.1]	3.28	580518	3-Phenylphenol
Phenyl phenols	Phenyl phenols [2.7<LogKow<4.1]	3.28	90437	2-Phenylphenol
Phenyl phenols	Phenyl phenols [2.7<LogKow<4.1]	3.28	92693	4-Hydroxybiphenyl
Phenyl phenols	Phenyl phenols [2.7<LogKow<4.1]	4.12	599644	4-(Dimethylphenylmethyl)phenol
Salicylate	Salicylate (-alkyl)	2.60	119368	methyl 2-hydroxybenzoate
Salicylate	Salicylate (-alkyl)	4.08	2052144	n-butyl 2-hydroxybenzoate
Salicylate	Salicylate (-alkyl)	5.06	6259763	n-hexyl 2-hydroxybenzoate
Salicylate	Salicylate (-alkyl)	5.97	118605	2-ethylhexyl 2-hydroxybenzoate
Salicylate	Salicylate (-alkylphenyl)	4.31	118581	methylphenyl 2-hydroxybenzoate
Salicylate	Salicylate (-cyclo)	6.16	118569	3,3,5-Trimethylcyclohexyl 2-hydroxybenzoate
Salicylate	Salicylate (-phenyl)	3.82	118558	phenyl 2-hydroxybenzoate
Salicylate	Salicylate (-phenyl)	5.73	87183	4-tert-butylphenyl 2-hydroxybenzoate

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Node VII <return to Node list>

Chemicals in Node VII are hypothesized to interact with the B-site sub-pocket within the ligand binding domain of the ER (see Figure 1 and accompanying text in Hornung et al. 2014 and Katzenellenbogen et al. 2003. Pure Appl. Chem. 75, 2397-2403).

Primary Node VII: Site 'B' Specified Fragment

Sub-node: Belongs to known Active sub-class

ERES Chemical Group	Sub-group	log Kow	CASRN	Chemical Name
Aldehydes	Aldehydes [LogKow<2.3]	1.82	104552	cinnamaldehyde
Aldehydes	Aldehydes [LogKow<2.3]	2.26	104870	4-methylbenzaldehyde
Aldehydes	Aldehydes [LogKow = 4.82]	4.82	101860	alpha-hexyl cinnamaldehyde
Alkoxyanilines	4-Alkoxyanilines (2.1<LogKow<3.7)	2.14	4469801	4-propoxyaniline
Alkoxyanilines	4-Alkoxyanilines (2.1<LogKow<3.7)	2.63	4344552	4-butoxyaniline
Alkoxyanilines	4-Alkoxyanilines (2.1<LogKow<3.7)	3.12	39905505	4-pentyloxyaniline
Alkoxyanilines	4-Alkoxyanilines (2.1<LogKow<3.7)	3.61	39905572	4-hexyloxyaniline
Alkylanilines	4-Alkylanilines [LogKow<1.6]	1.08	62533	aniline
Alkylanilines	4-Alkylanilines [1.6<LogKow<5.1]	1.62	106490	4-methylaniline
Alkylanilines	4-Alkylanilines [1.6<LogKow<5.1]	2.11	589162	4-ethylaniline
Alkylanilines	4-Alkylanilines [1.6<LogKow<5.1]	2.61	2696846	4-n-propylaniline
Alkylanilines	4-Alkylanilines [1.6<LogKow<5.1]	2.99	769926	4-tert-butylaniline
Alkylanilines	4-Alkylanilines [1.6<LogKow<5.1]	3.10	104132	4-n-butylaniline
Alkylanilines	4-Alkylanilines [1.6<LogKow<5.1]	3.59	33228443	4-n-amylaniline
Alkylanilines	4-Alkylanilines [1.6<LogKow<5.1]	4.08	33228454	4-n-hexylaniline
Alkylanilines	4-Alkylanilines [1.6<LogKow<5.1]	5.06	16245797	4-n-octylaniline
Alkylanilines- other	2-n-Alkylanilines [LogKow = 2.11]	2.11	578541	2-ethylaniline
Alkylanilines- other	Multi-Subst. Alkylanilines [2.1<LogKow<4.0]	2.17	95783	2,5-dimethylaniline
Alkylanilines- other	Multi-Subst. Alkylanilines [2.1<LogKow<4.0]	3.99	24544045	2,6-diisopropylaniline
Alkylcyclohexanols	4-Alkylcyclohexanols [LogKow<2.6]	1.64	108930	cyclohexanol
Alkylcyclohexanols	4-Alkylcyclohexanols [LogKow<2.6]	2.55	4534741	4-ethylcyclohexanol
Alkylcyclohexanols	4-Alkylcyclohexanols [3.4<LogKow<5.6]	3.42	98522	4-tert-butylcyclohexanol (mixture of isomers)
Alkylcyclohexanols	4-Alkylcyclohexanols [3.4<LogKow<5.6]	3.53	70568604	4-n-butylcyclohexanol
Alkylcyclohexanols	4-Alkylcyclohexanols [3.4<LogKow<5.6]	3.91	5349519	4-tert-amyl cyclohexanol
Alkylcyclohexanols	4-Cycloalkylcyclohexanols [3.4<LogKow<5.6]	4.32	2433149	4-cyclohexyl cyclohexanol
Alkylcyclohexanols	4-Cycloalkylcyclohexanols [3.4<LogKow<5.6]	5.50	66068846	4-(5,5,6-trimethylbicyclo [2.2.1]hept-2-yl)-cyclohexanol
Alkylcyclohexanols	Bicycloalkylcyclohexanols (Exact Match) [RBA>0.00001%]	2.85	1632731	Fenchyl alcohol
Alkylcyclohexanols	2,5-Alkylcyclohexanols (Exact Match) [RBA>0.00001%]	3.38	1490046	2-isopropyl-5-methylcyclohexanol
Alkylcyclohexanols	1-Alkylcyclohexanols (Exact Match) [RBA<0.00001%]	3.07	5445249	1-n-propyl cyclohexanol
Alkylcyclohexanones	4-Alkylcyclohexanone [LogKow<1.2]	1.13	108941	cyclohexanone
Alkylcyclohexanones	4-Alkylcyclohexanones [2.5<LogKow<3.9]	2.53	40649363	4-propyl cyclohexanone
Alkylcyclohexanones	4-Alkylcyclohexanones [2.5<LogKow<3.9]	2.91	98533	4-tert-butyl cyclohexanone
Alkylcyclohexanones	4-Alkylcyclohexanones [2.5<LogKow<3.9]	3.40	16587716	4-tert-pentyl cyclohexanone
Alkylcyclohexanones	4-Alkylcyclohexanones [2.5<LogKow<3.9]	3.51	61203836	4-n-pentyl cyclohexanone
Alkylcyclohexanones	4-Cycloalkylcyclohexanones [2.5<LogKow<3.9]	3.81	92682	4-cyclohexyl cyclohexanone
Alkylcyclohexanones	2-Alkylcyclohexanones (Exact Match) [RBA>0.00001%]	2.94	14765301	2-sec-butyl cyclohexanone
Alkylcyclohexanones	Bicycloalkylcyclohexanones (Exact Match) [RBA<0.00001%]	3.04	76222	(+/-)-Camphor
Aminobenzoates	Aminobenzoates [LogKow<1.3]	0.96	150130	4-Aminobenzoic acid
Aminobenzoates	Aminobenzoates (Exact Match) [RBA>0.00001%]	1.80	94097	4-Aminobenzoic acid, ethyl ester
Aminobenzoates	Aminobenzoates (Exact Match) [RBA>0.00001%]	2.76	87252	2-Aminobenzoic acid, ethyl ester

ERES Chemical Group	Sub-group	log Kow	CASRN	Chemical Name
Benzoic Acid, methyl or ethyl ester (ring CH3).	Benzoic Acid, methyl ester (ring CH3)	2.38	89714	methyl-2-methylbenzoate
Benzoic Acid, methyl or ethyl ester (ring CH3).	Benzoic Acid, ethyl ester (ring CH3)	2.87	87241	ethyl-2-methylbenzoate
Benzoic Acid, methyl or ethyl ester (ring CH3).	Benzoic Acid, ethyl ester (ring CH3)	2.87	94086	ethyl-4-methylbenzoate
Benzoic Acid, methyl or ethyl ester (ring CH3).	Benzoic Acid, (ring tri-CH3)	2.42	480637	2,4,6-trimethylbenzoic acid
Benzoic Acid, methyl or ethyl ester (ring CH3).	Benzoic Acid, methyl ester (ring tri-CH3)	3.47	2282840	2,4,6-trimethylbenzoic acid, methyl ester
Benzoic Acid, methyl or ethyl ester (ring CH3).	Benzoic Acid, ethyl ester (ring tri-CH3)	3.96	1754558	2,4,6-trimethylbenzoic acid, ethyl ester

ERES Chemical Group	Sub-group	log Kow	CASRN	Chemical Name
Chloroanilines	Chloroanilines [LogKow<2.3]	1.72	106478	4-Chloroaniline
Chloroanilines	Chloroanilines [2.3<LogKow<3.1]	2.37	626437	3,5-Dichloroaniline
Chloroanilines	Chloroanilines [2.3<LogKow<3.1]	3.01	634935	2,4,6-Trichloroaniline
Ketones	Ketones [LogKow<3.5]	2.85	93083	2'-Acetonaphthone
Ketones	Ketones [LogKow<3.5]	3.44	92911	4-Acetylbiphenyl
Ketones	Ketones [4.2<LogKow<5.0]	4.21	23696857	Damascenone
Ketones	Ketones [4.2<LogKow<5.0]	4.84	127515	alpha-Isomethyl ionone
Ketones	Ketones [4.2<LogKow<5.0]	4.84	1335462	Methyl-Ionone
Ketones	Ketones [4.2<LogKow<5.0]	5.02	32388559	Methyl cedryl ketone
Mixed Anilines	Mixed Anilines [LogKow<1.3]	-0.84	51058	2-Diethylaminoethyl-4 aminobenzoate hydrochloride
Mixed Anilines	Mixed Anilines [LogKow<1.3]	0.16	95807	2,4-Diaminotoluene
Mixed Anilines	Mixed Anilines [LogKow<1.3]	1.28	371404	4-Fluoroaniline
Mixed Anilines	Mixed Anilines (Exact Match) [RBA>0.00001%]	2.04	98168	3-(Trifluoromethyl) aniline
Mixed Anilines	Mixed Anilines (Exact Match) [RBA>0.00001%]	4.29	97563	4-o-Tolylazo-o-toluidine
Phenones	Phenones (Branched) [2.5<LogKow<4.9]	2.58	611701	isopropyl phenyl ketone
Phenones	Phenones (Branched) [2.5<LogKow<4.9]	3.04	938169	tert-butyl phenyl ketone
Phenones	Phenones (Branched) [2.5<LogKow<4.9]	3.07	582627	isobutyl phenyl ketone
Phenones	Phenones (Branched) [2.5<LogKow<4.9]	4.84	2844099	2,2,5-trimethyl-1-phenyl-hex-4-en-1-one
Phenones	Phenones (Cyclo) [Exact Match RBA>0.00001%]	2.67	1137424	4-hydroxy benzophenone
Phenones	Phenones (Cyclo) [Exact Match RBA>0.00001%]	2.71	91010	benzhydrol
Phenones	Phenones (Cyclo) [Exact Match RBA>0.00001%]	2.96	5407987	cyclobutyl phenyl ketone
Phenones	Phenones (Cyclo) [Exact Match RBA>0.00001%]	3.15	119619	benzophenone
Phenones	Phenones (Cyclo) [Exact Match RBA<0.00001%]	3.38	451401	benzyl phenyl ketone
Phenones	Phenones (Cyclo) [Exact Match RBA>0.00001%]	3.76	97231215	cyclohexyl(2,4-dihydroxyphenyl)ketone
Phenones	Phenones (Cyclo) [Exact Match RBA<0.00001%]	3.94	712505	cyclohexyl phenyl ketone
Phenones	Phenones (Cyclo) [Exact Match RBA>0.00001%]	3.76	945493	cyclohexyl phenylmethanol
Phthalates	Phthalates 1.6<LogKow<6.6	1.66	131113	di-methylphthalate
Phthalates	Phthalates 1.6<LogKow<6.6	2.65	84662	di-ethylphthalate
Phthalates	Phthalates 1.6<LogKow<6.6	3.36	131179	di-allylphthalate
Phthalates	Phthalates 1.6<LogKow<6.6	3.48	605458	di-isopropylphthalate
Phthalates	Phthalates 1.6<LogKow<6.6	4.61	84742	di-n-butylphthalate
Phthalates	Phthalates 1.6<LogKow<6.6	4.84	85687	benzylbutylphthalate
Phthalates	Phthalates 1.6<LogKow<6.6	6.57	84753	di-n-hexylphthalate
Phthalates	Phthalates LogKow>6.6	8.39	117817	bis(2-ethylhexyl) phthalate
Phthalates	Phthalates LogKow>6.6	8.54	117840	di-n-octylphthalate
Phthalates	Iso-Phthalates	4.10	744456	diphenylisophthalate
Phthalates	Tri-Benzoates	11.59	3319311	1,2,4-benzenetricarboxylic acid, tris(2-ethylhexyl)ester

Node VIII <return to Node list>

Primary Node VIII: Mixed Organics

Sub-node: Not a known Active sub-class

Chemical Group	Sub-group	log Kow	CASRN	Chemical Name
Mixed Organics	Mixed Organics [LogKow<1.3]	-3.28	496468	Glycoluril
Mixed Organics	Mixed Organics [LogKow<1.3]	-1.88	50817	L-(+)-Ascorbic Acid
Mixed Organics	Mixed Organics [LogKow<1.3]	-1.31	520456	Dehydroacetic acid
Mixed Organics	Mixed Organics [LogKow<1.3]	-0.45	98920	niacinamide
Mixed Organics	Mixed Organics [LogKow<1.3]	-0.19	118718	3-hydroxy-2-methyl-4-pyrone
Mixed Organics	Mixed Organics [LogKow<1.3]	-0.08	51200874	4,4-Dimethyloxazolidine
Mixed Organics	Mixed Organics [LogKow<1.3]	0.15	1477550	1,3-benzenedimethanamine
Mixed Organics	Mixed Organics [LogKow<1.3]	0.18	2224444	4-(2-nitrobutyl)morpholine
Mixed Organics	Mixed Organics [LogKow<1.3]	0.62	980712	Brompheniramine hydrogen maleate
Mixed Organics	Mixed Organics [LogKow<1.3]	0.63	120923	cyclopentanone
Mixed Organics	Mixed Organics [LogKow<1.3]	0.79	85264331	3,5-Dimethylpyrazole-1-methanol
Mixed Organics	Mixed Organics [LogKow<1.3]	0.94	533744	3,5-dimethyltetrahydro-1,3,5-thiadiazine-2-2-thione
Mixed Organics	Mixed Organics [LogKow<1.3]	1.04	62203321	(4-hydroxymethyl-2-phenyl-4,5-dihydro-oxazol-4-yl)-methanol
Mixed Organics	Mixed Organics [LogKow<1.3]	1.10	122996	2-phenoxyethanol
Mixed Organics	Mixed Organics [LogKow<1.3]	1.13	1005670	4-Butylmorpholine
Mixed Organics	Mixed Organics [LogKow<1.3]	1.15	96413	cyclopentanol
Mixed Organics	Mixed Organics [LogKow<1.3]	1.17	95147	Benzotriazole
Mixed Organics	Mixed Organics [LogKow<1.3]	1.23	1214397	6-Benzylaminopurine
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	1.38	1047161	Quinacridone
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	1.43	643798	Phthaldialdehyde
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	1.65	1131017	2-chloro-2',6'-dimethylacetanilide
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	1.68	587-65-5	2-chloro-n-phenylacetamide
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	1.83	1192525	4,5-dichloro (3H)-1,2-dithiol-2-one
Mixed Organics	Mixed Organics (Exact Match) [RBA>0.00001%]	2.05	120729	Indole
Mixed Organics	Mixed Organics (Exact Match) [RBA>0.00001%]	2.40	4712554	Diphenyl phosphite
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	2.51	120467	1,3-diphenyl-1,3-propanedione
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	2.62	78591	isophorone
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	3.00	3634831	1,3-bis(isocyanatomethyl) benzene
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	3.13	470677	1,4-Cineole
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	3.22	91441	7-Diethylamino 4-methylcoumarin
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	3.37	103639	(2-Bromoethyl)benzene
Mixed Organics	Mixed Organics (Exact Match) [RBA>0.00001%]	3.62	60168889	Fenarimol
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	3.87	91532	Ethoxyquin
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	4.03	20018091	Diiodomethyl-p-tolysulfone
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	4.13	67747095	Prochloraz
Mixed Organics	Mixed Organics (Exact Match) [RBA>0.00001%]	4.61	199584388	1-methoxy-4-tert-pentylcyclohexane
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	5.27	2481949	4-(Diethylamino) azobenzene
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	6.00	137666	6-O-Palmitoyl-L-ascorbic acid
Mixed Organics	Mixed Organics (Exact Match) [RBA>0.00001%]	6.26	1222055	Galaxolide
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	6.63	509342	Rhodamine B Base
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	7.51	95385	1h-imidazole-1-ethanol, 2-(8-heptadecenyl)-4,5-dihydro-
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]	7.99	6358301	Pigment violet 23

Chemical Group	Sub-group	log Kow	CASRN	Chemical Name
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Carboxy Esters	1.80	886862	ethyl 3-aminobenzoate, methane sulfonate
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Carboxy Esters	1.95	6626842	dimethyl benzylidenemalonate
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Carboxy Esters	2.42	5437456	Benzyl bromoacetate
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Carboxy Esters	2.77	120569	ethanol, 2,2'-(1,2-ethanediylbis(oxy))bis-, dibenzoate
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Carboxy Esters	3.42	1504-69-4	Ethyl trans-4-ethoxy-cinnamate
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Carboxy Esters	3.61	27138314	Dipropylene glycol dibenzoate
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Carboxy Esters	3.86	125122	Isobornyl acetate
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Carboxy Esters	4.82	135590919	Mefenpyr-diethyl
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Carboxy Esters	5.66	163520330	Isoxadifen-ethyl
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Carboxy Esters	6.75	127253	Methyl abietate

Chemical Group	Sub-group	log Kow	CASRN	Chemical Name
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Cyclopentanol/Cyclopentanone	1.92	4694126	2,4,4-trimethylcyclopentanone
Mixed Organics	Mixed Organics (Exact Match) [RBA>0.00001%]-Cyclopentanol/Cyclopentanone	2.98	24851987	dihydrojasmonic acid methyl ester
Mixed Organics	Mixed Organics (Exact Match) [RBA>0.00001%]-Cyclopentanol/Cyclopentanone	3.34	196206367	3-tert-butyl-2-methylcyclopentanol

Chemical Group	Sub-group	log Kow	CASRN	Chemical Name
Mixed Organics	Mixed Organics (Exact Match) [RBA>0.00001%]-Ketones	2.81	6285058	4'-chloropropiophenone
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Nitro Aromatics	1.63	100254	1,4-Dinitrobenzene
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Nitro Aromatics	2.49	705602	1-phenyl-2-nitropropene
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Nitro Aromatics	2.80	52806538	Hydroxy flutamide
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Nitro Aromatics	3.51	13311847	Flutamide
Mixed Organics	Mixed Organics (Exact Match) [RBA<0.00001%]-Siloxanes	5.09	556672	Octamethylcyclotetrasiloxane

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