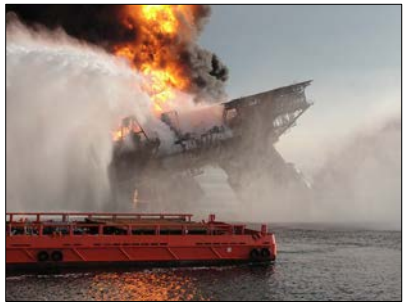
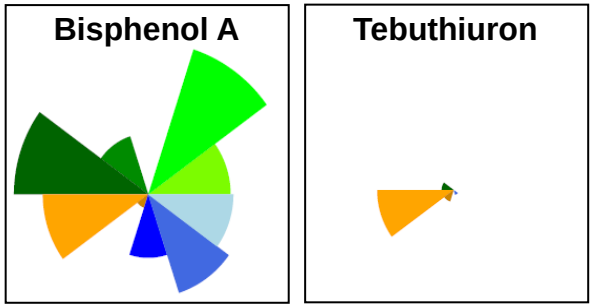
Prioritization and profiling are needed for diverse tasks

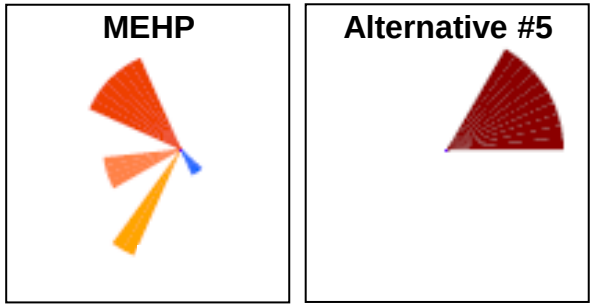
Responding to environmental emergencies: Which dispersants are safest for remediation of the Deep Water Horizon oil spill?



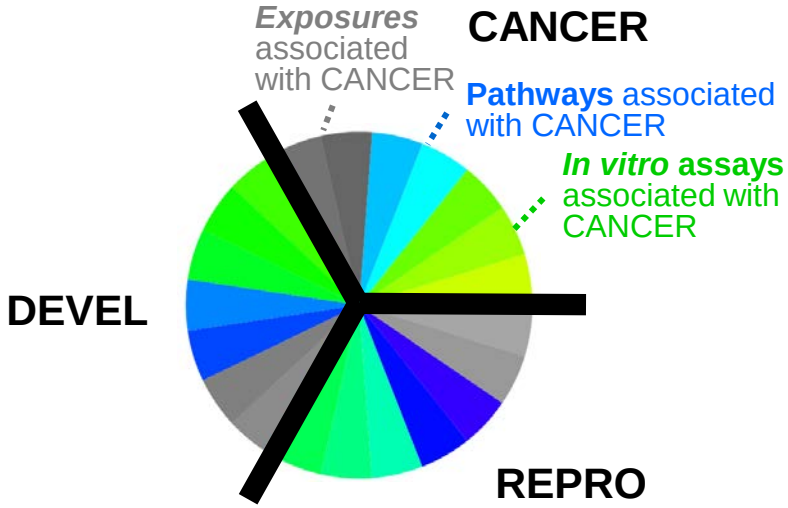
Protecting against endocrine disrupting chemicals: Supporting the Endocrine Disruptor Screening Program (EDSP)



Supporting sustainable development and Green Chemistry: Profiling manufacturing alternatives

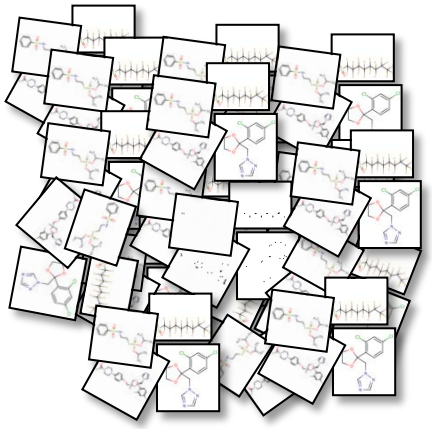


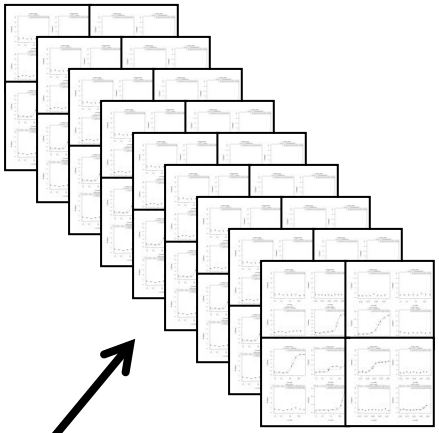
Promoting efficient, targeted testing decisions: ToxPi addressing multiple sectors of concern



Now that we have all these HTS data, how do we make sense of it?

# Chemicals	x	# Assays	=	# Results
100,000s	x	100s	=	10,000,000s





This is a problem….

Rationale for an integrated chemical prioritization scheme

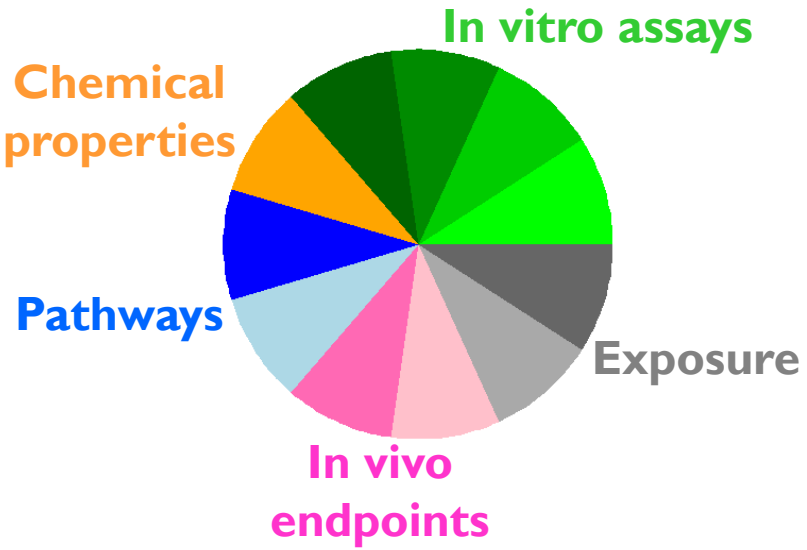
What do we know?

What are the sources of our knowledge?

Can we integrate information from disparate sources?

Does certain knowledge carry more importance?

Can we compare chemicals on an even playing field?



→ A numerical index that can be used for ranking (instead of absolute thresholds) is more flexible for different prioritization tasks and can better accommodate new data, new chemicals, data adjustments, etc.

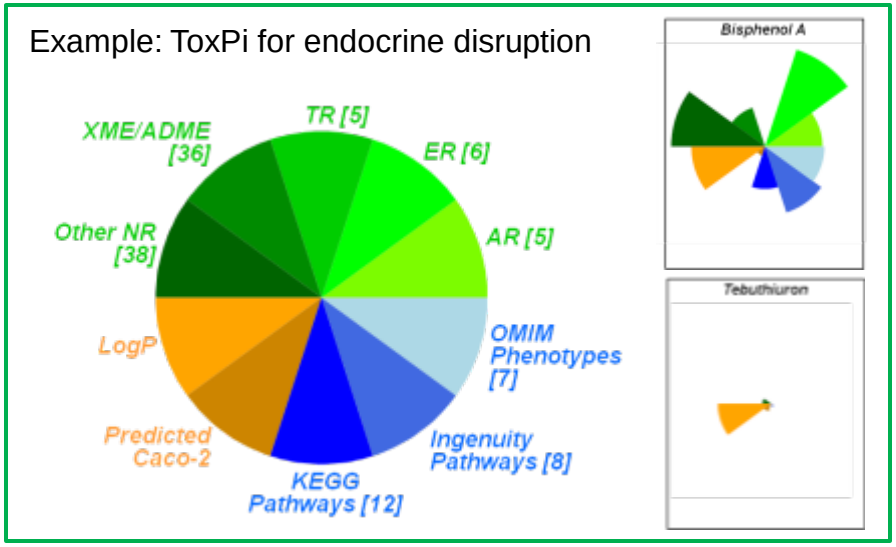
The Toxicological Prioritization Index (ToxPi)

Organizes what we know about chemicals: in vitro, in vivo, pathways and exposure

Integrates critical information from disparate sources

Flexible tool for ranking chemicals based on weight-of-evidence for different prioritization tasks

Provides visual profile of each evidence source



SOURCE: Reif et al. 2010, Env Hlth Persp 118: 1714-1720

Stand-alone ToxPi GUI tool: Putting ToxPi in the hands of the experts

Diverse prioritization tasks are best handled by domain experts.

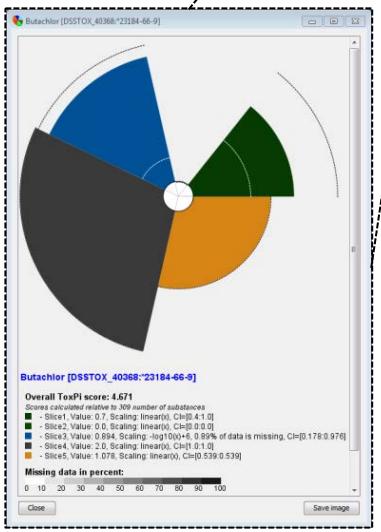
An interactive, GUI (Graphical User Interface) application allows users to apply their own, specialized knowledge to the analysis.

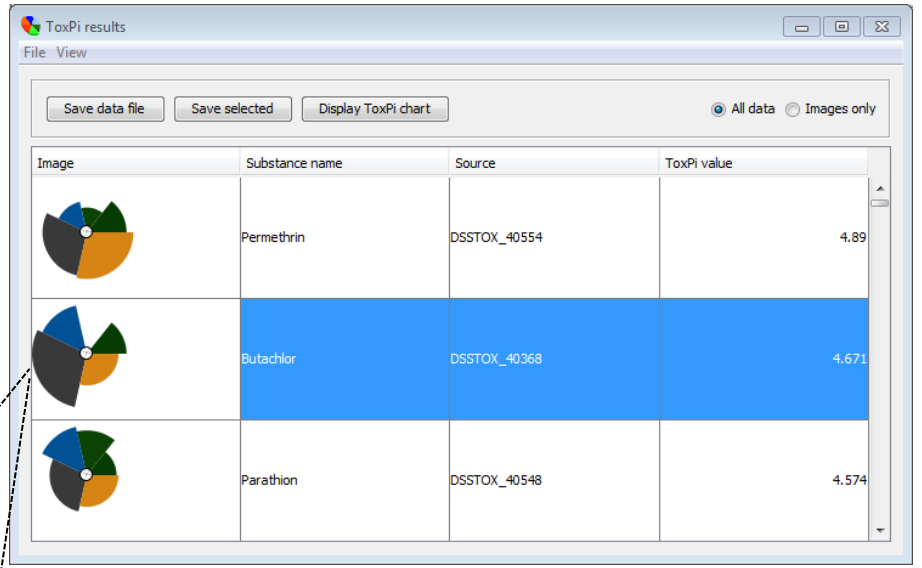
A manuscript describing the software and its intended use has been submitted for journal peer-review

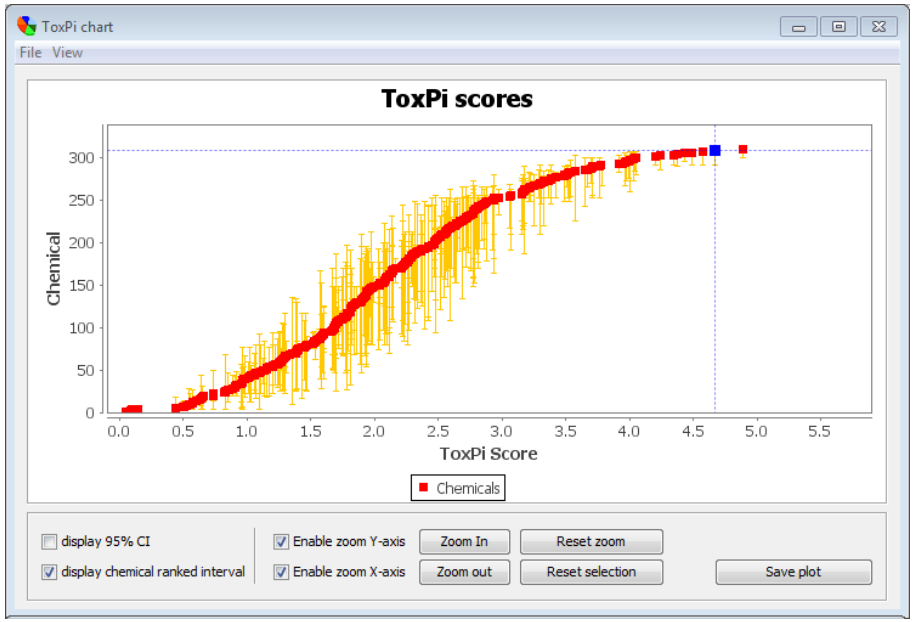
The software, user manual, and example data are available at:
http://comptox.unc.edu/toxpi.php
http://epa.gov/ncct/ToxPi/

Download software

Download user manual

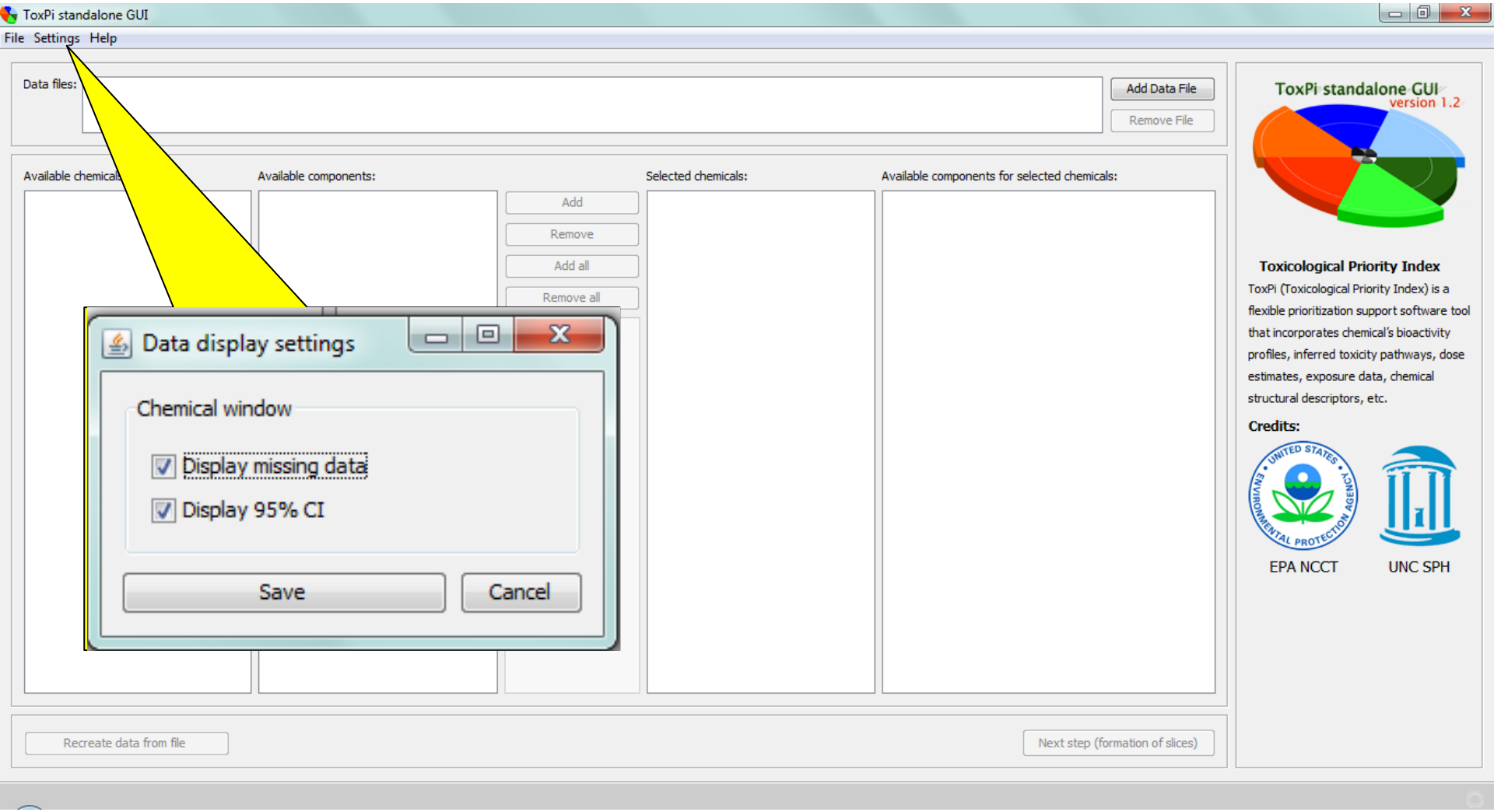






Collaboration with *Carolina Center for Computational Toxicology*

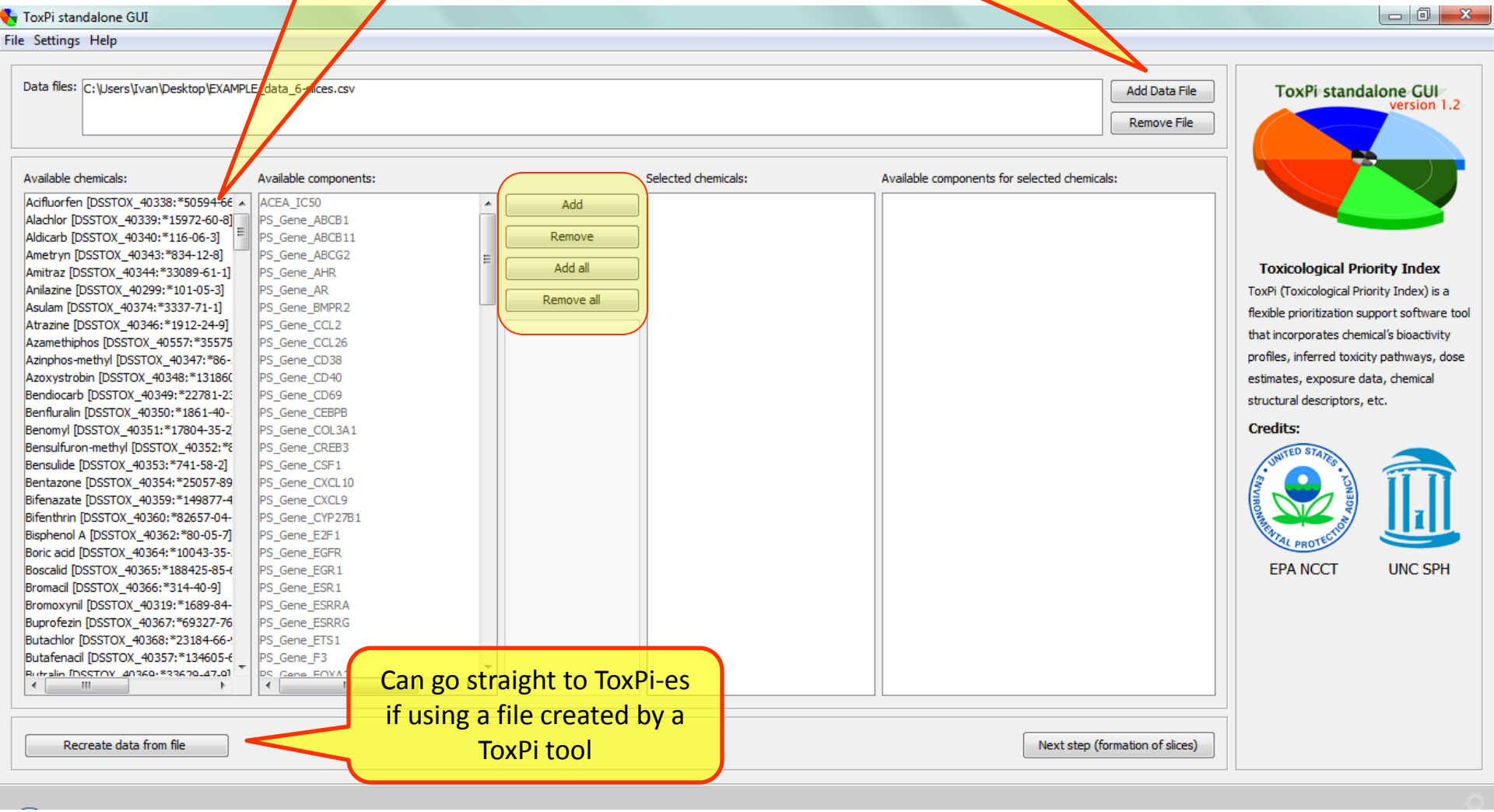
ToxPi stand-alone GUI: Front page [add data file(s), select chemicals]



ToxPi stand-alone GUI: Front page [add data file(s), select chemicals]

Select one
(or many/all) chemical(s)
(left mouse click+Ctrl/Shift)

Add/remove data file(s):
If multiple files added, the intersect of components will be shown for selected chemicals



Can go straight to ToxPi-es if using a file created by a ToxPi tool

ToxPi standalone GUI

File Settings Help

Data files: C:\Users\Iva

Available chemicals:

Acifluorfen [DSSTOX_4
Alachlor [DSSTOX_4033
Aldicarb [DSSTOX_4034
Ametryn [DSSTOX_403
Amitraz [DSSTOX_4034
Anilazine [DSSTOX_402
Asulam [DSSTOX_4037
Atrazine [DSSTOX_403
Azamethiphos [DSSTOX
Azinphos-methyl [DSST
Azoxystrobin [DSSTOX_
Bendiocarb [DSSTOX_4
Benfluralin [DSSTOX_40
Benomyl [DSSTOX_403
Bensulfuron-methyl [DS
Bensulide [DSSTOX_40
Bentazone [DSSTOX_40
Bifenazate [DSSTOX_40
Bifenthrin [DSSTOX_40
Bisphenol A [DSSTOX_4
Boric acid [DSSTOX_40
Boscalid [DSSTOX_4036
Bromacil [DSSTOX_4036
Bromoxynil [DSSTOX_4
Buprofezin [DSSTOX_40
Butachlor [DSSTOX_40
Butafenacil [DSSTOX_4
Butralin [DSSTOX_4036

Recreate data fi

Performing bootstrapping.

ToxPi results

File View

Save data file | Save selected | Save selected image | Save all image | Display ToxPi chart | All data | Images only

Image	Substance name	Source	ToxPi value
	Fipronil	DSSTOX_40466	3.747
	Phosalone	DSSTOX_40555	3.688
	Etoxazole	DSSTOX_40452	3.559
	Indoxacarb	DSSTOX_40496	3.459
			

GUI
sion 1.2

ndex
dex) is a
oftware tool
bactivity
ways, dose
mical

C SPH

ToxPi results

File View

Save data file | Save selected | Save selected image | Save all image | Display ToxPi chart | All data | Images only


Fipronil


Phosalone


Etoxazole


Indoxacarb


Tebupirimfos


Hexaconazole


Imazalil


Bisphenol A


Fluoxastrobin


Cypermethrin

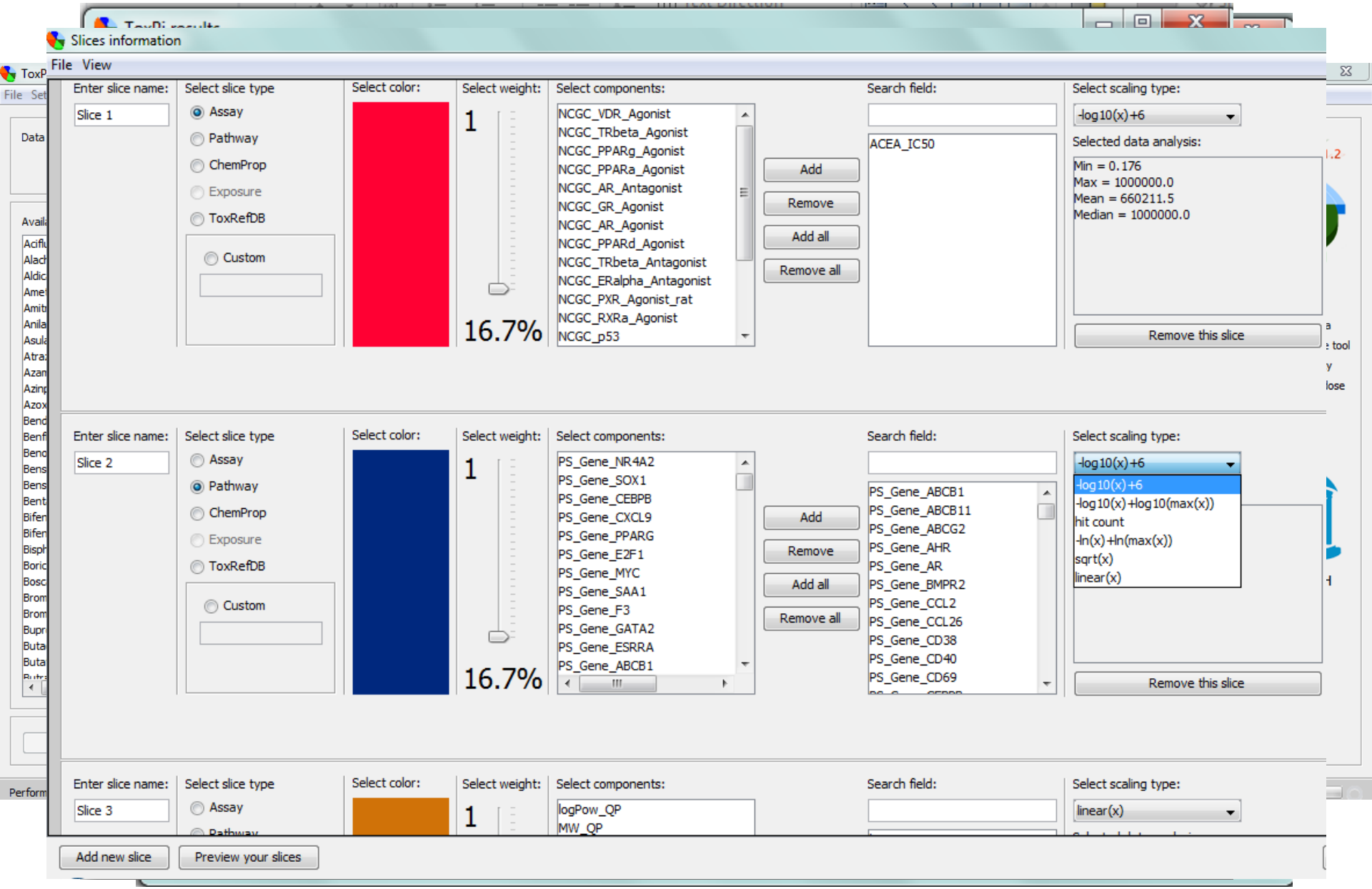

Methoxychlor


Oryzalin

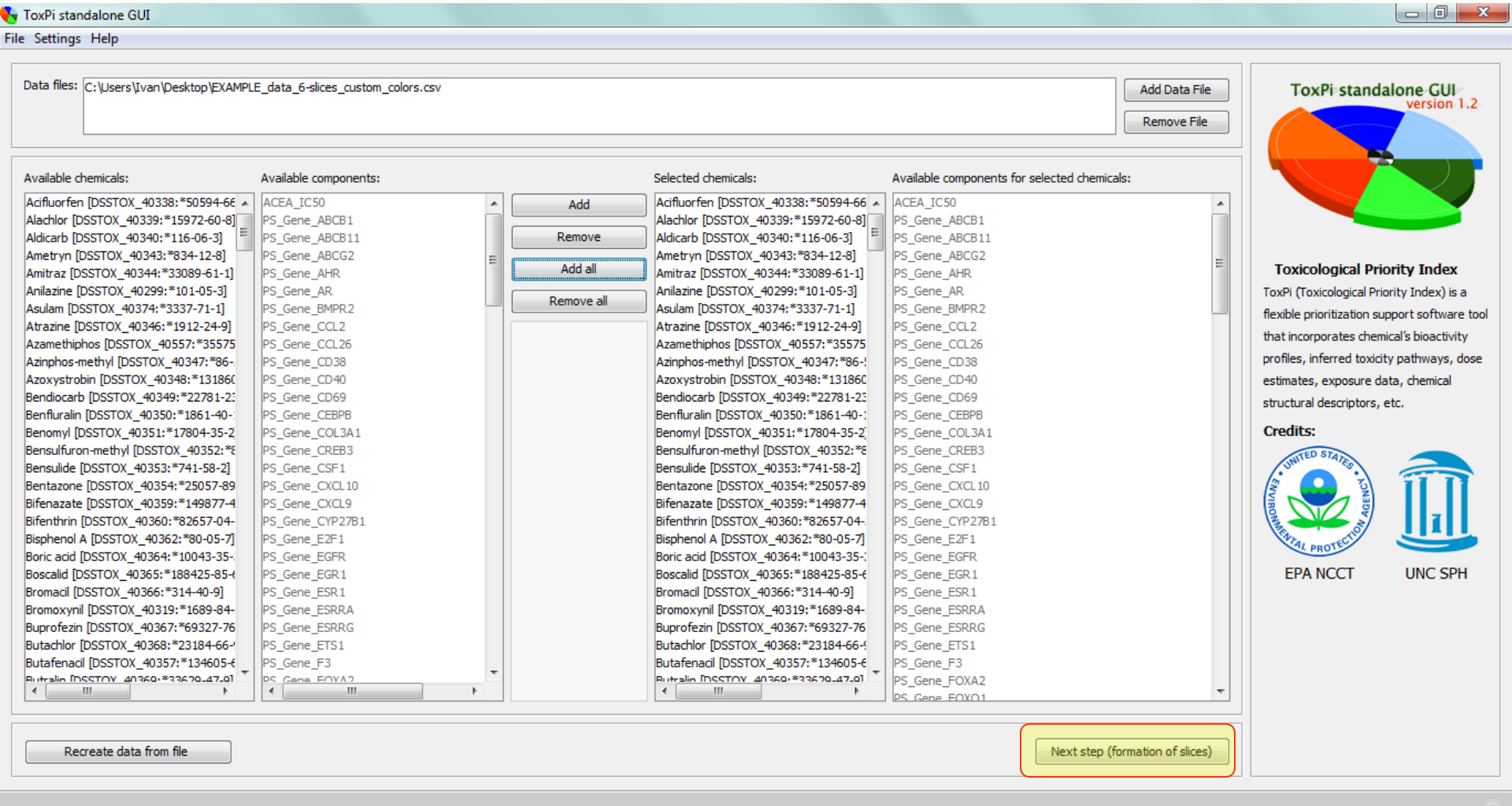

Fenpyroximate (-Z,E)

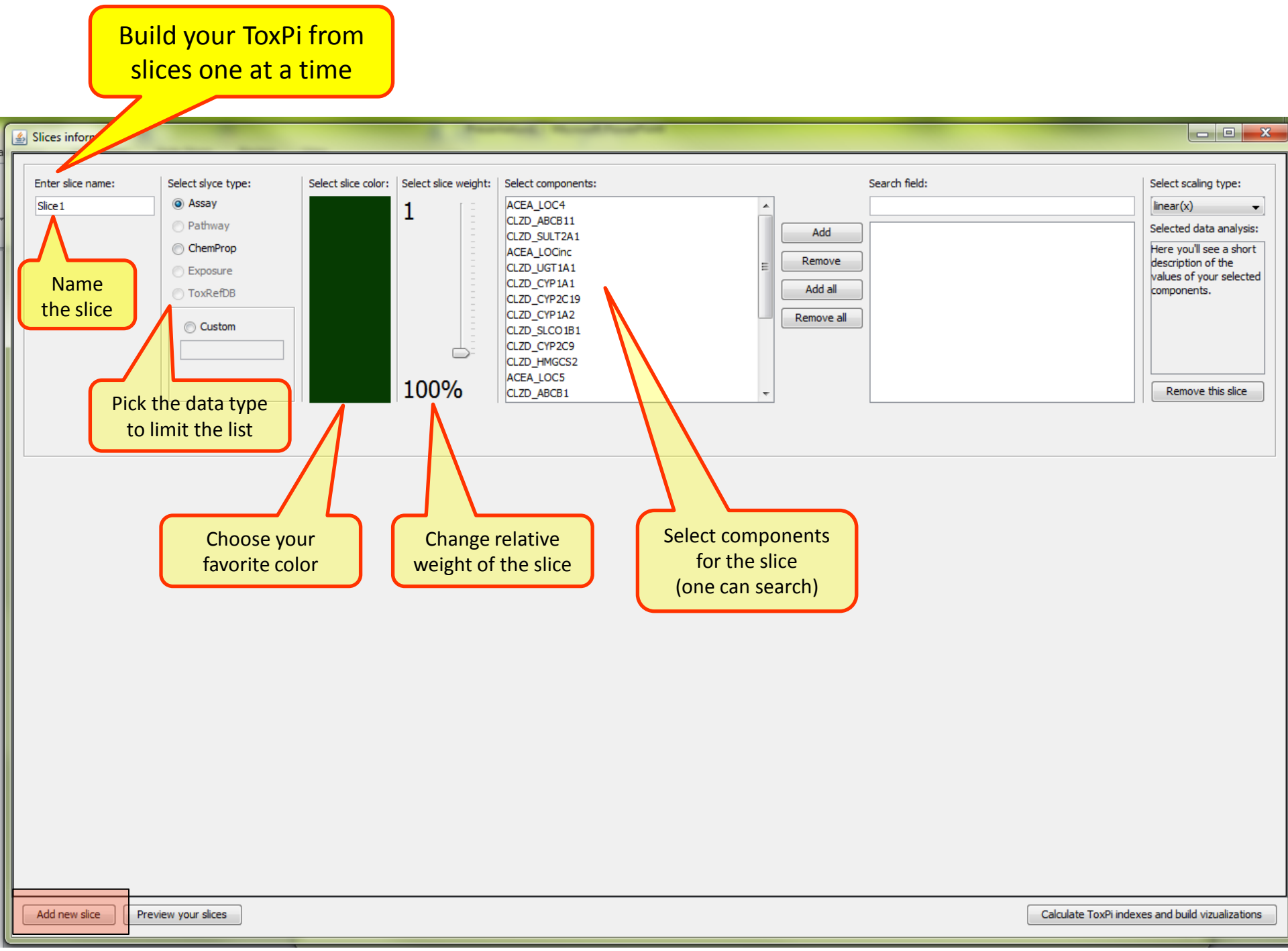

Propargite

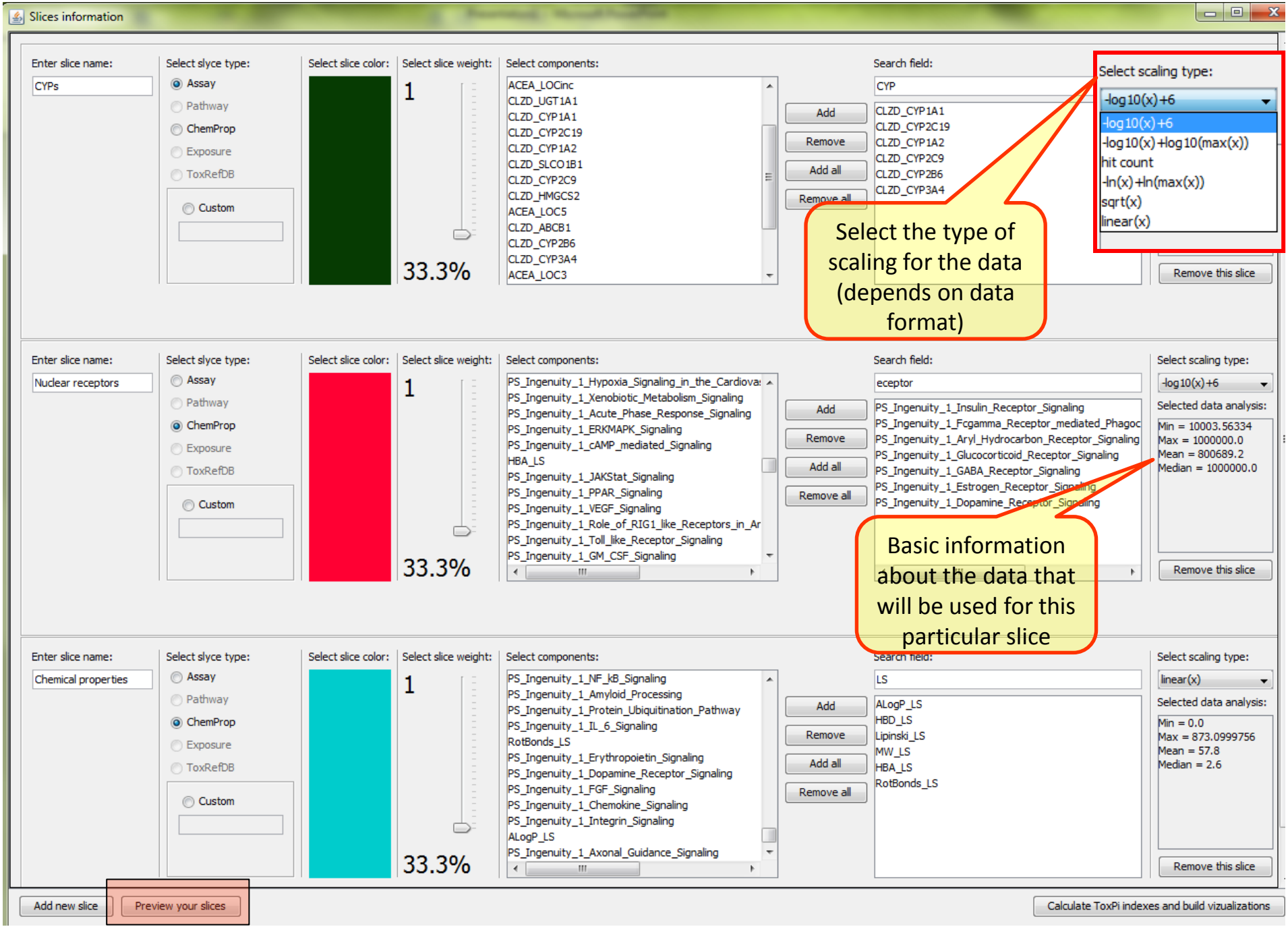

Pyridaben

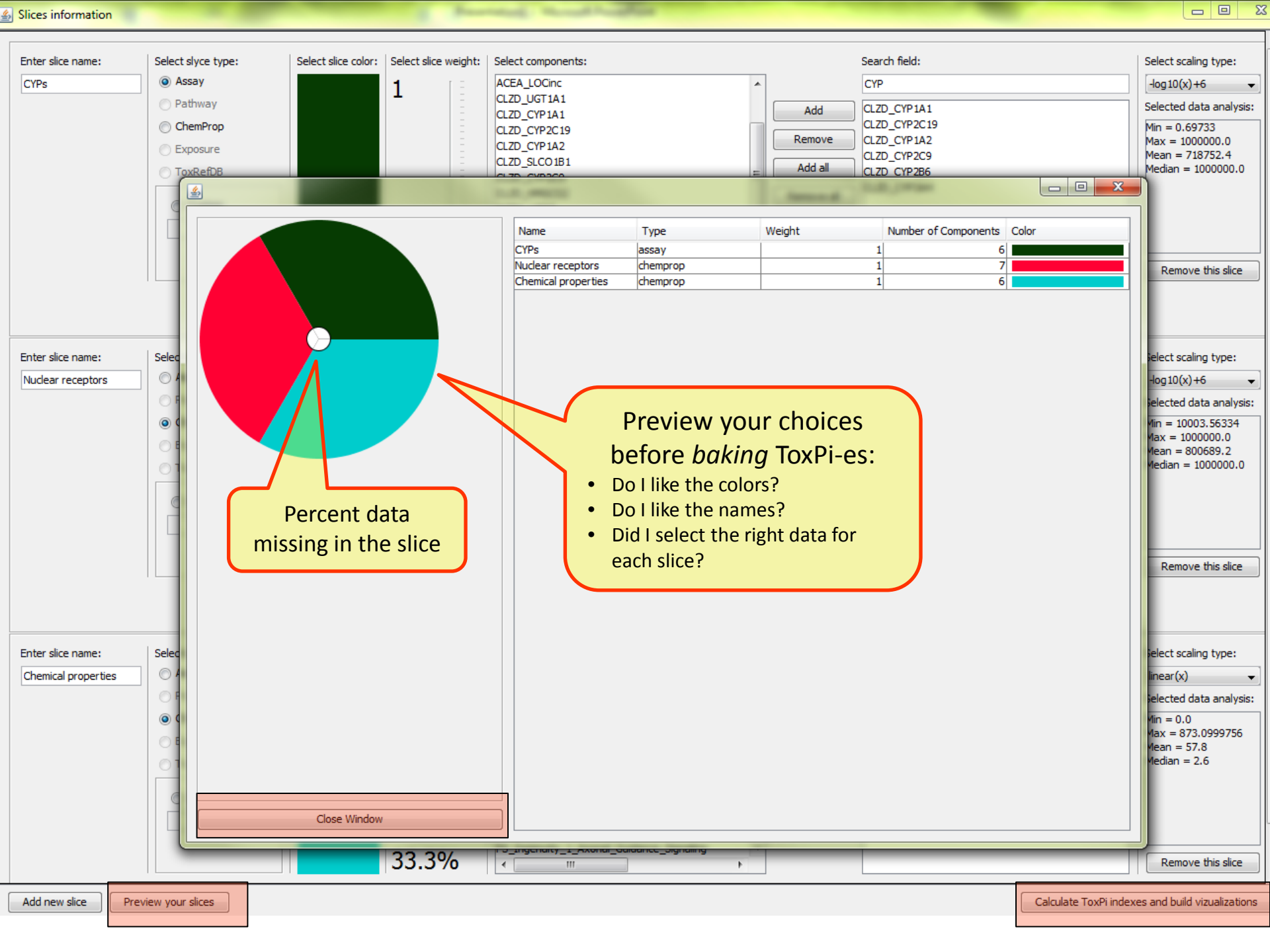

Slices information
File View
Enter slice name:
Slice 1
Select slice type
Assay
Pathway
ChemProp
Exposure
ToxRefDB
Custom
Select color:
Select weight:
1
16.7%
Select components:
NCGC_VDR_Agonist
NCGC_TRbeta_Agonist
NCGC_PPARg_Agonist
NCGC_PPARa_Agonist
NCGC_AR_Antagonist
NCGC_GR_Agonist
NCGC_AR_Agonist
NCGC_PPARd_Agonist
NCGC_TRbeta_Antagonist
NCGC_ERalpha_Antagonist
NCGC_PXR_Agonist_rat
NCGC_RXRa_Agonist
NCGC_p53
Add
Remove
Add all
Remove all
Search field:
ACEA_IC50
Select scaling type:
-log10(x)+6
Selected data analysis:
Min = 0.176
Max = 1000000.0
Mean = 660211.5
Median = 1000000.0
Remove this slice
Enter slice name:
Slice 2
Select slice type
Assay
Pathway
ChemProp
Exposure
ToxRefDB
Custom
Select color:
Select weight:
1
16.7%
Select components:
PS_Gene_NR4A2
PS_Gene_SOX1
PS_Gene_CEBPB
PS_Gene_CXCL9
PS_Gene_PPARG
PS_Gene_E2F1
PS_Gene_MYC
PS_Gene_SAA1
PS_Gene_F3
PS_Gene_GATA2
PS_Gene_ESRRA
PS_Gene_ABCB1
Add
Remove
Add all
Remove all
Search field:
PS_Gene_ABCB1
PS_Gene_ABCB11
PS_Gene_ABCG2
PS_Gene_AHR
PS_Gene_AR
PS_Gene_BMPR2
PS_Gene_CCL2
PS_Gene_CCL26
PS_Gene_CD38
PS_Gene_CD40
PS_Gene_CD69
Select scaling type:
-log10(x)+6
-log10(x)+6
-log10(x)+log10(max(x))
hit count
-ln(x)+ln(max(x))
sqrt(x)
linear(x)
Remove this slice
Enter slice name:
Slice 3
Select slice type
Assay
Select color:
Select weight:
1
Select components:
logPow_QP
MW_QP
Search field:
Select scaling type:
linear(x)
Add new slice
Preview your slices

ToxPi stand-alone GUI: Front page [add data file(s), select chemicals]

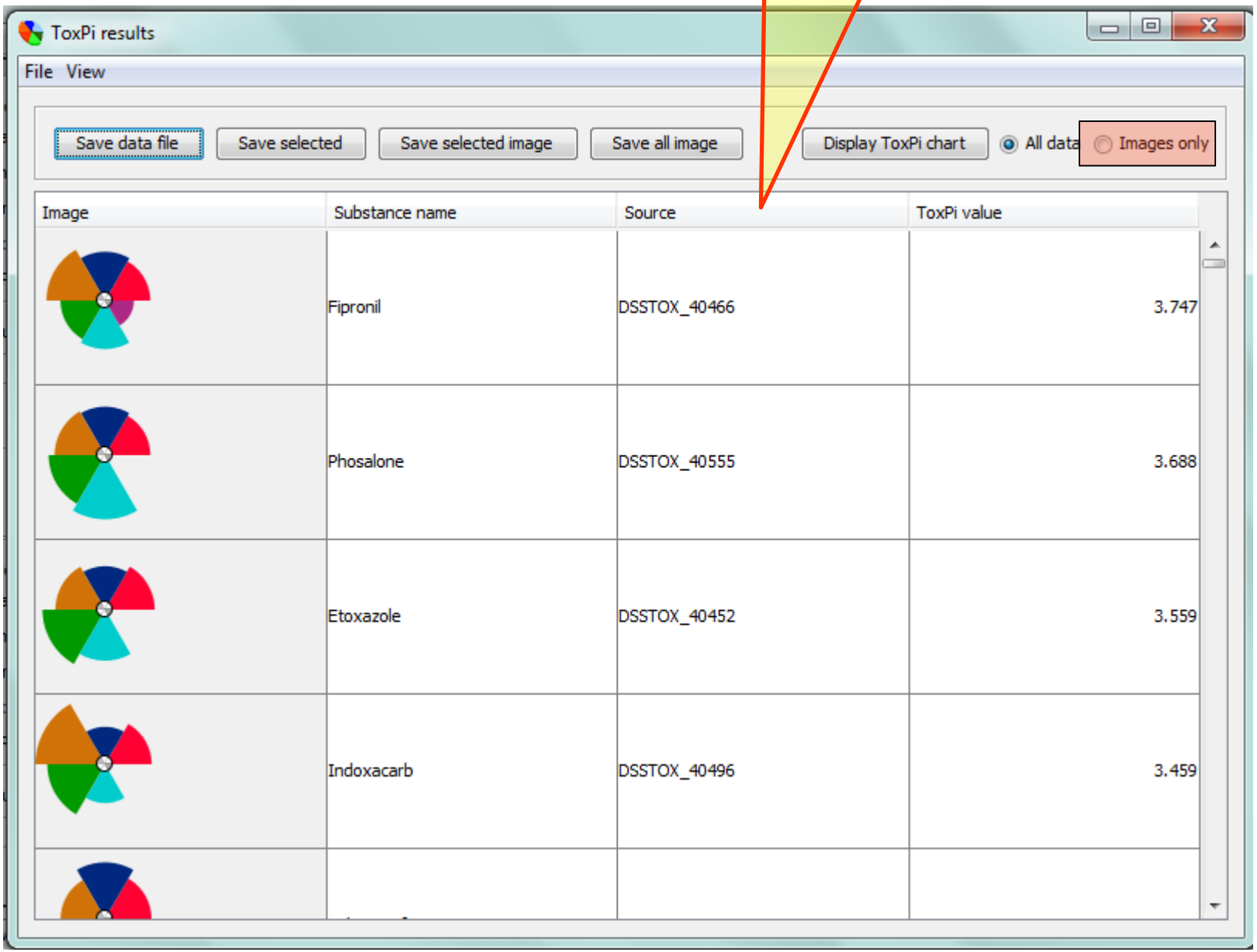



Build your ToxPi from slices one at a time
Slices inform
Enter slice name:
Slice1
Name the slice
Select slyce type:
Assay
Pathway
ChemProp
Exposure
ToxRefDB
Custom
Pick the data type to limit the list
Select slice color:
Choose your favorite color
Select slice weight:
1
100%
Change relative weight of the slice
Select components:
ACEA_LOC4
CLZD_ABCB11
CLZD_SULT2A1
ACEA_LOCinc
CLZD_UGT1A1
CLZD_CYP1A1
CLZD_CYP2C19
CLZD_CYP1A2
CLZD_SLCO1B1
CLZD_CYP2C9
CLZD_HMGCS2
ACEA_LOC5
CLZD_ABCB1
Add
Remove
Add all
Remove all
Select components for the slice (one can search)
Search field:
Select scaling type:
linear(x)
Selected data analysis:
Here you'll see a short description of the values of your selected components.
Remove this slice
Add new slice
Preview your slices
Calculate ToxPi indexes and build vizualizations


Slices information
Enter slice name:
CYPs
Select slyce type:
Assay
Pathway
ChemProp
Exposure
ToxRefDB
Custom
Select slice color:
Select slice weight:
1
33.3%
Select components:
ACEA_LOCinc
CLZD_UGT1A1
CLZD_CYP1A1
CLZD_CYP2C19
CLZD_CYP1A2
CLZD_SLCO1B1
CLZD_CYP2C9
CLZD_HMGCS2
ACEA_LOC5
CLZD_ABCB1
CLZD_CYP2B6
CLZD_CYP3A4
ACEA_LOC3
Add
Remove
Add all
Remove all
Search field:
CYP
CLZD_CYP1A1
CLZD_CYP2C19
CLZD_CYP1A2
CLZD_CYP2C9
CLZD_CYP2B6
CLZD_CYP3A4
Select scaling type:
-log10(x)+6
-log10(x)+6
-log10(x)+log10(max(x))
hit count
-ln(x)+ln(max(x))
sqrt(x)
linear(x)
Remove this slice
Select the type of scaling for the data (depends on data format)
Enter slice name:
Nuclear receptors
Select slyce type:
Assay
Pathway
ChemProp
Exposure
ToxRefDB
Custom
Select slice color:
Select slice weight:
1
33.3%
Select components:
PS_Ingenuity_1_Hypoxia_Signaling_in_the_Cardiova
PS_Ingenuity_1_Xenobiotic_Metabolism_Signaling
PS_Ingenuity_1_Acute_Phase_Response_Signaling
PS_Ingenuity_1_ERKMAPK_Signaling
PS_Ingenuity_1_cAMP_mediated_Signaling
HBA_LS
PS_Ingenuity_1_JAKStat_Signaling
PS_Ingenuity_1_PPAR_Signaling
PS_Ingenuity_1_VEGF_Signaling
PS_Ingenuity_1_Role_of_RIG1_like_Receptors_in_Ar
PS_Ingenuity_1_Toll_like_Receptor_Signaling
PS_Ingenuity_1_GM_CSF_Signaling
Add
Remove
Add all
Remove all
Search field:
eceptor
PS_Ingenuity_1_Insulin_Receptor_Signaling
PS_Ingenuity_1_Fcgamma_Receptor_mediated_Phagoc
PS_Ingenuity_1_Aryl_Hydrocarbon_Receptor_Signaling
PS_Ingenuity_1_Glucocorticoid_Receptor_Signaling
PS_Ingenuity_1_GABA_Receptor_Signaling
PS_Ingenuity_1_Estrogen_Receptor_Signaling
PS_Ingenuity_1_Dopamine_Receptor_Signaling
Select scaling type:
-log10(x)+6
Selected data analysis:
Min = 10003.56334
Max = 1000000.0
Mean = 800689.2
Median = 1000000.0
Remove this slice
Basic information about the data that will be used for this particular slice
Enter slice name:
Chemical properties
Select slyce type:
Assay
Pathway
ChemProp
Exposure
ToxRefDB
Custom
Select slice color:
Select slice weight:
1
33.3%
Select components:
PS_Ingenuity_1_NF_kB_Signaling
PS_Ingenuity_1_Amyloid_Processing
PS_Ingenuity_1_Protein_Ubiquitination_Pathway
PS_Ingenuity_1_IL_6_Signaling
RotBonds_LS
PS_Ingenuity_1_Erythropoietin_Signaling
PS_Ingenuity_1_Dopamine_Receptor_Signaling
PS_Ingenuity_1_FGF_Signaling
PS_Ingenuity_1_Chemokine_Signaling
PS_Ingenuity_1_Integrin_Signaling
ALogP_LS
PS_Ingenuity_1_Axonal_Guidance_Signaling
Add
Remove
Add all
Remove all
Search field:
LS
ALogP_LS
HBD_LS
Lipinski_LS
MW_LS
HBA_LS
RotBonds_LS
Select scaling type:
linear(x)
Selected data analysis:
Min = 0.0
Max = 873.0999756
Mean = 57.8
Median = 2.6
Remove this slice
Add new slice
Preview your slices
Calculate ToxPi indexes and build vizualizations

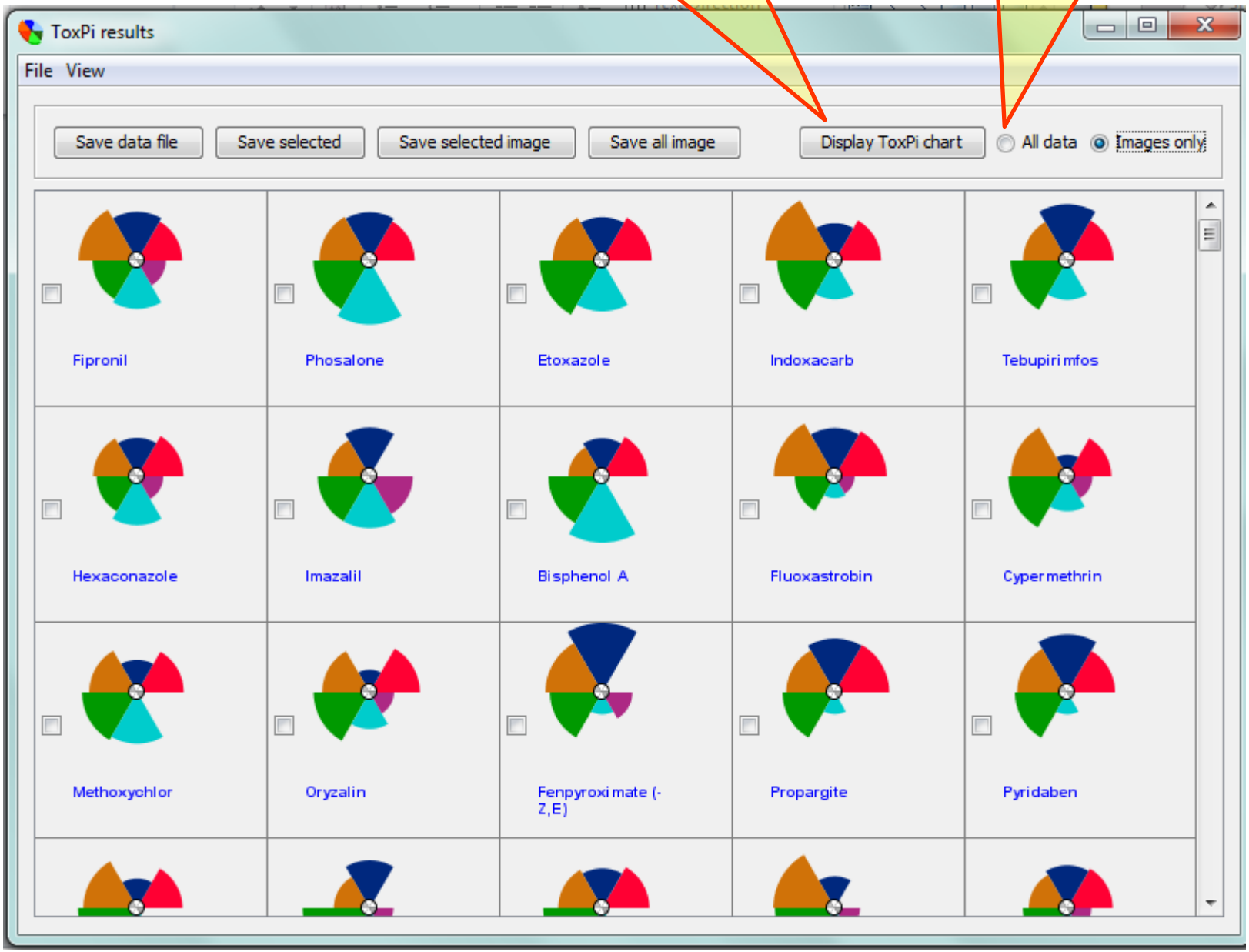

Slices information
Enter slice name:
CYPs
Select slyce type:
Assay
Pathway
ChemProp
Exposure
ToxRefDB
Select slice color:
Select slice weight:
1
Select components:
ACEA_LOCinc
CLZD_UGT1A1
CLZD_CYP1A1
CLZD_CYP2C19
CLZD_CYP1A2
CLZD_SLCO1B1
Add
Remove
Add all
Search field:
CYP
CLZD_CYP1A1
CLZD_CYP2C19
CLZD_CYP1A2
CLZD_CYP2C9
CLZD_CYP2B6
Select scaling type:
-log10(x)+6
Selected data analysis:
Min = 0.69733
Max = 1000000.0
Mean = 718752.4
Median = 1000000.0
Remove this slice
Enter slice name:
Nuclear receptors
Select scaling type:
-log10(x)+6
Selected data analysis:
Min = 10003.56334
Max = 1000000.0
Mean = 800689.2
Median = 1000000.0
Remove this slice
Enter slice name:
Chemical properties
Select scaling type:
linear(x)
Selected data analysis:
Min = 0.0
Max = 873.0999756
Mean = 57.8
Median = 2.6
Remove this slice
33.3%
Add new slice
Preview your slices
Calculate ToxPi indexes and build vizualizations
Name
Type
Weight
Number of Components
Color
CYPs
assay
1
6
Nuclear receptors
chemprop
1
7
Chemical properties
chemprop
1
6
Percent data missing in the slice
Preview your choices before *baking* ToxPi-es:
Do I like the colors?
Do I like the names?
Did I select the right data for each slice?
Close Window

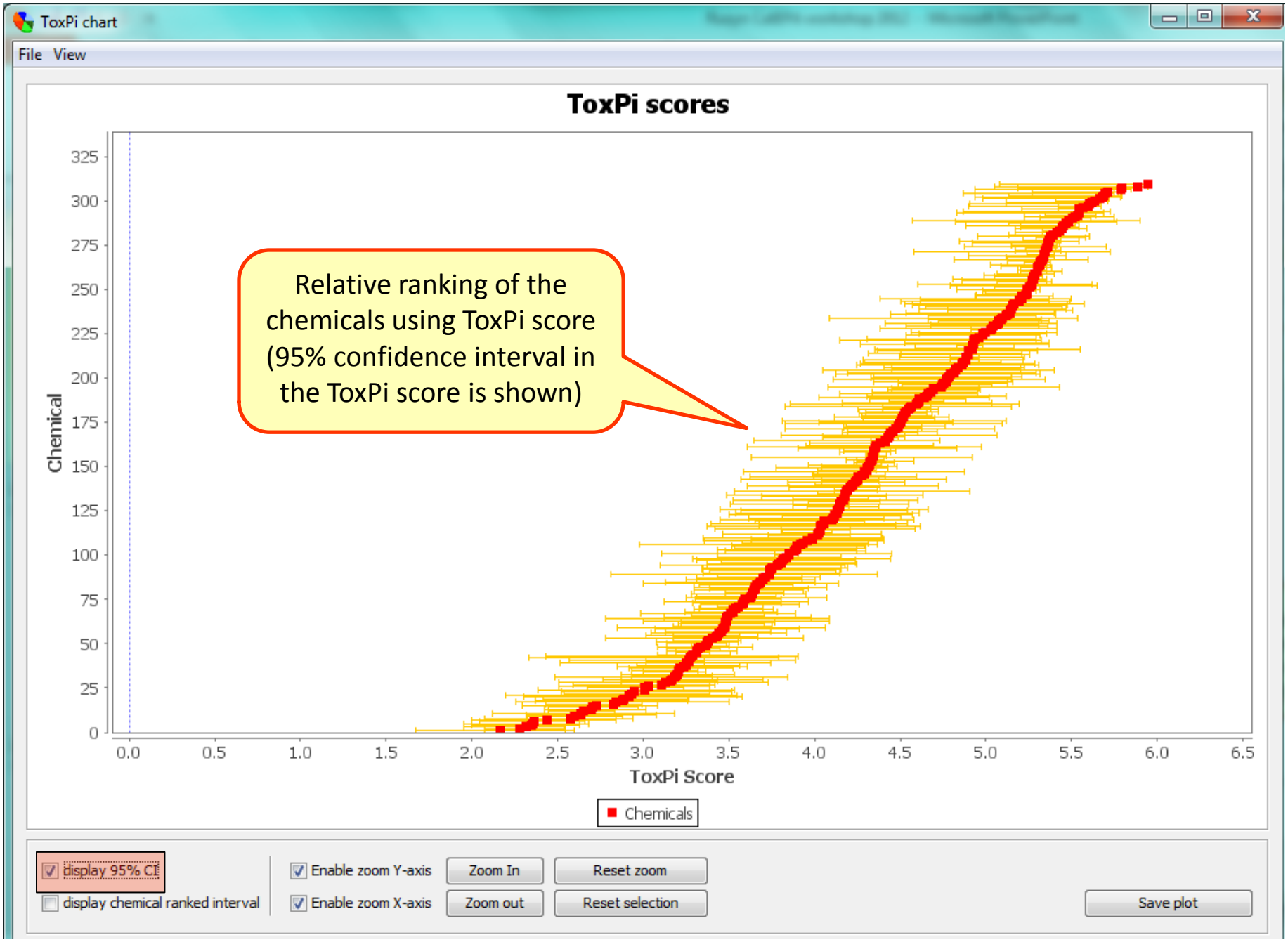
One can re-sort this table by clicking on a header of a particular column

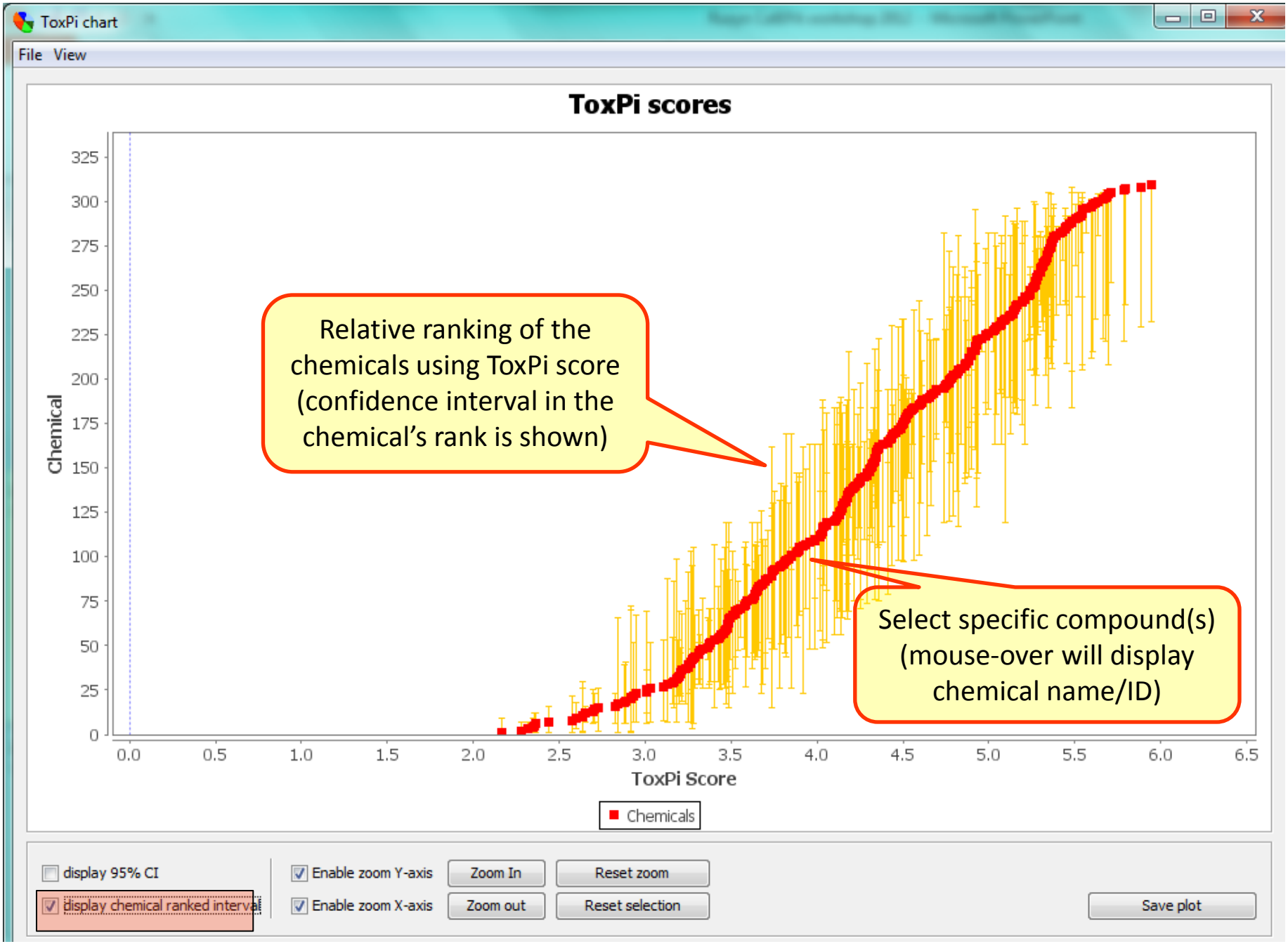


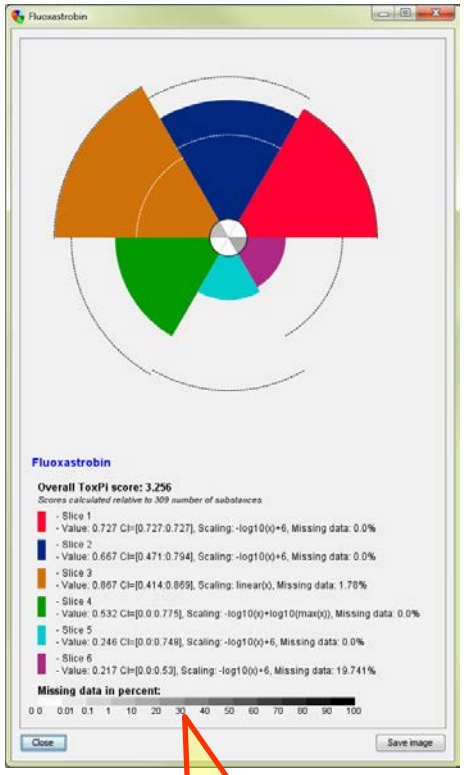
… or go to the chart of relative ranking of the chemicals by ToxPi score

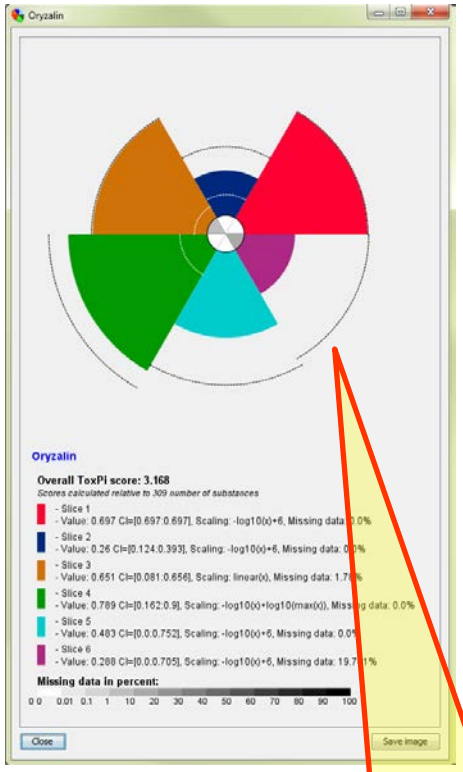
Return to the main table of the results by clicking this radio-button…

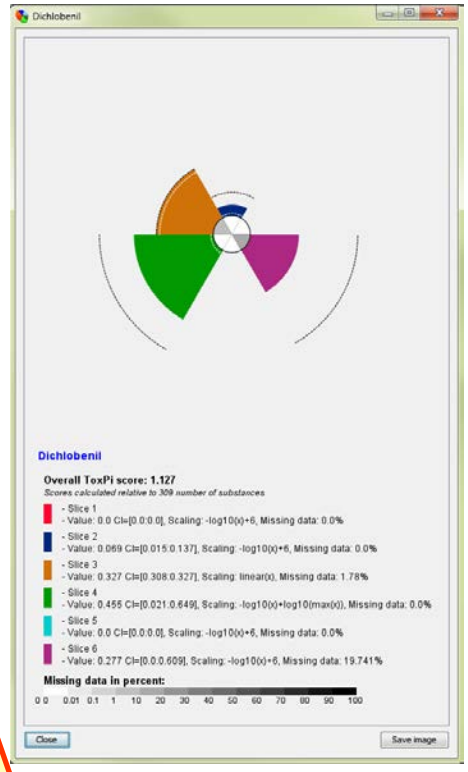


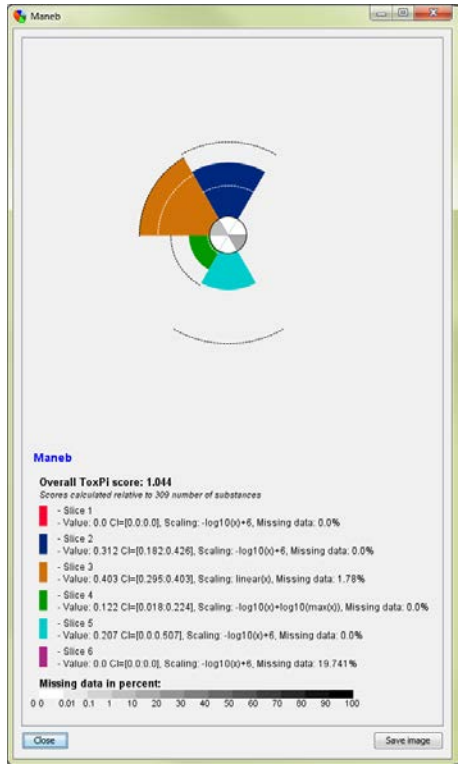

ToxPi chart
File View
ToxPi scores
Relative ranking of the chemicals using ToxPi score (95% confidence interval in the ToxPi score is shown)
Chemical
0
25
50
75
100
125
150
175
200
225
250
275
300
325
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
ToxPi Score
Chemicals
display 95% CI
display chemical ranked interval
Enable zoom Y-axis
Enable zoom X-axis
Zoom In
Zoom out
Reset zoom
Reset selection
Save plot


ToxPi chart
File View
ToxPi scores
Chemical
ToxPi Score
Chemicals
Relative ranking of the chemicals using ToxPi score (confidence interval in the chemical's rank is shown)
Select specific compound(s) (mouse-over will display chemical name/ID)
display 95% CI
display chemical ranked interval
Enable zoom Y-axis
Enable zoom X-axis
Zoom In
Zoom out
Reset zoom
Reset selection
Save plot



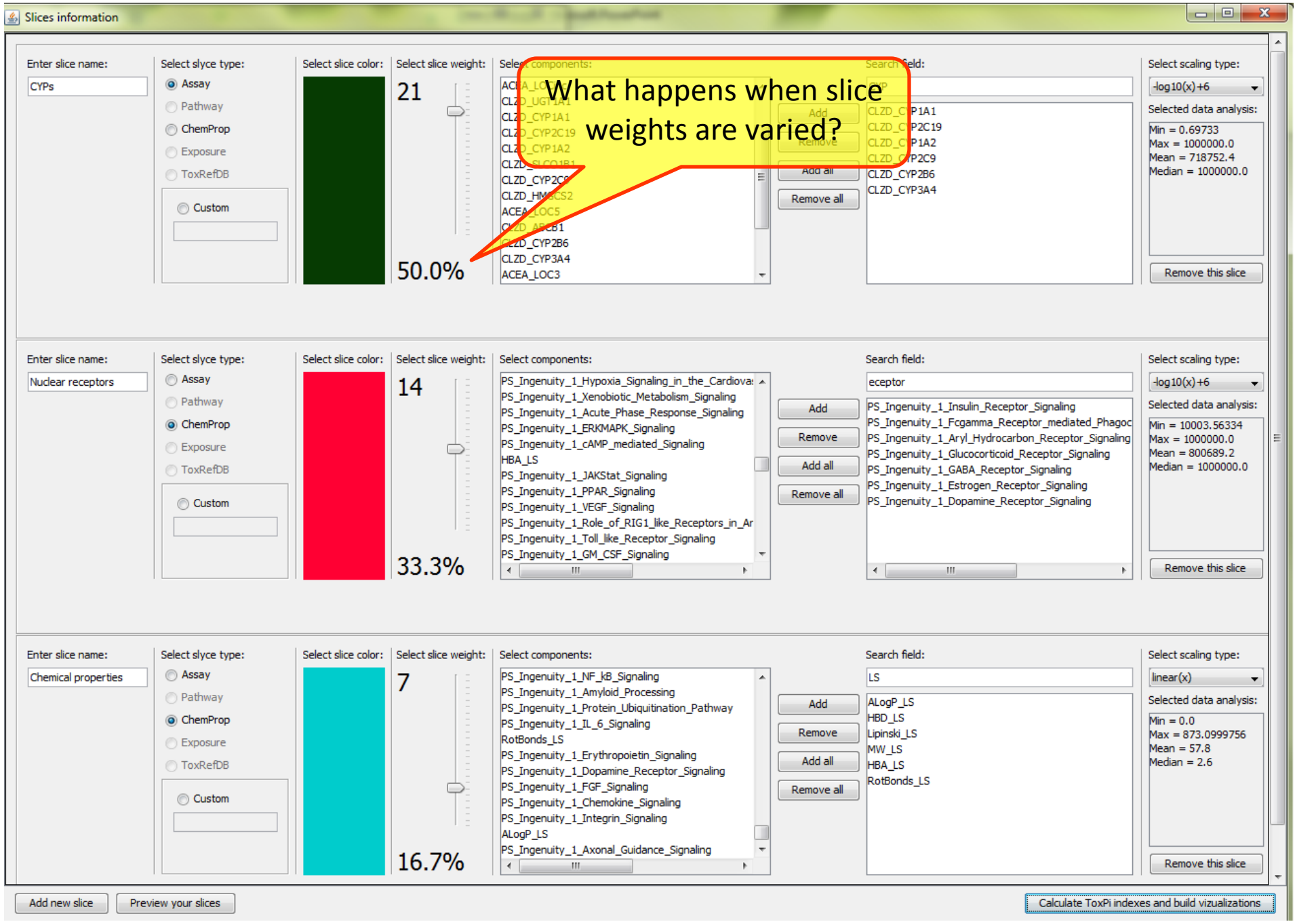




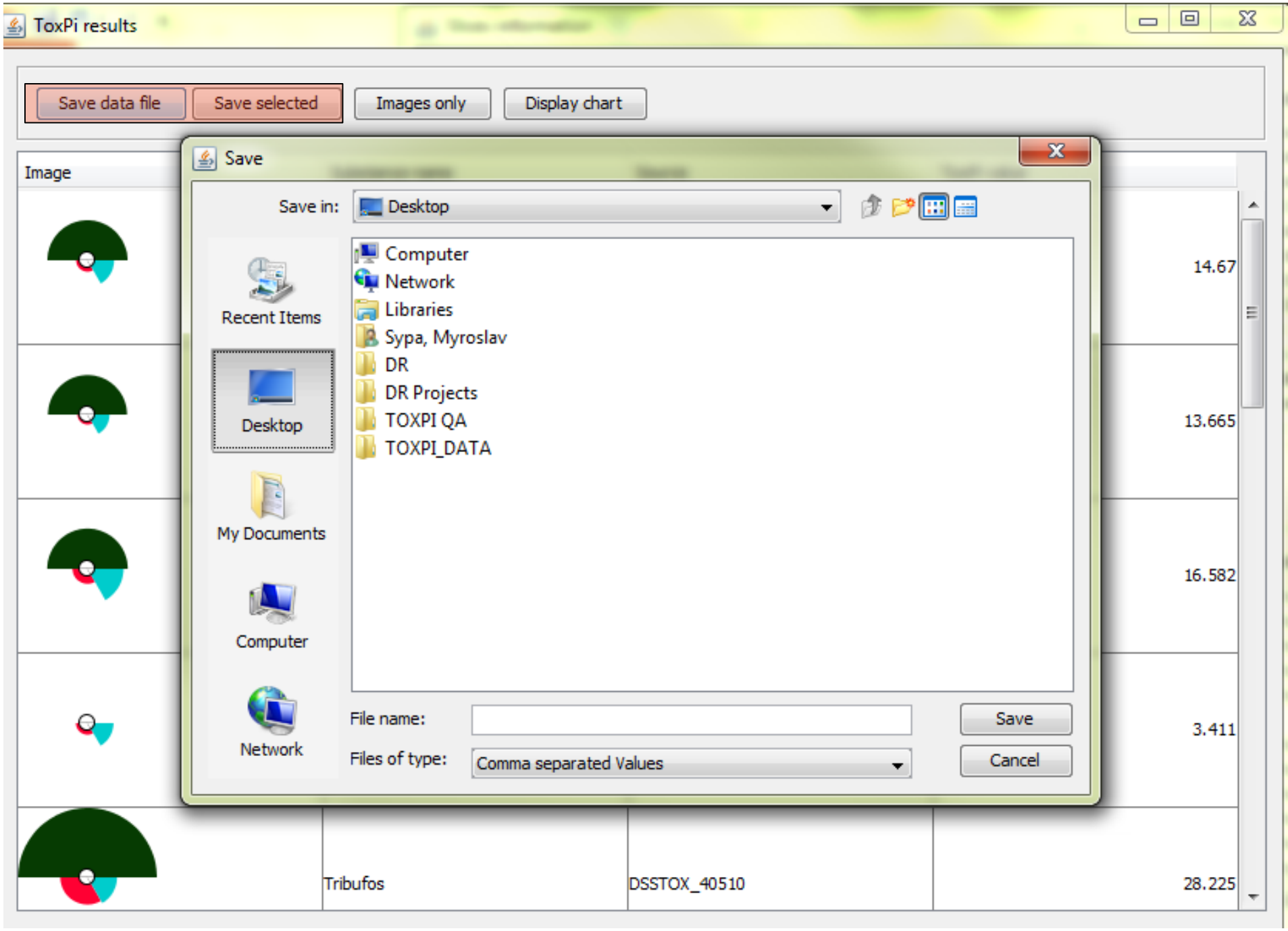


Information about each ToxPi score and image

Confidence intervals are displayed for each slice

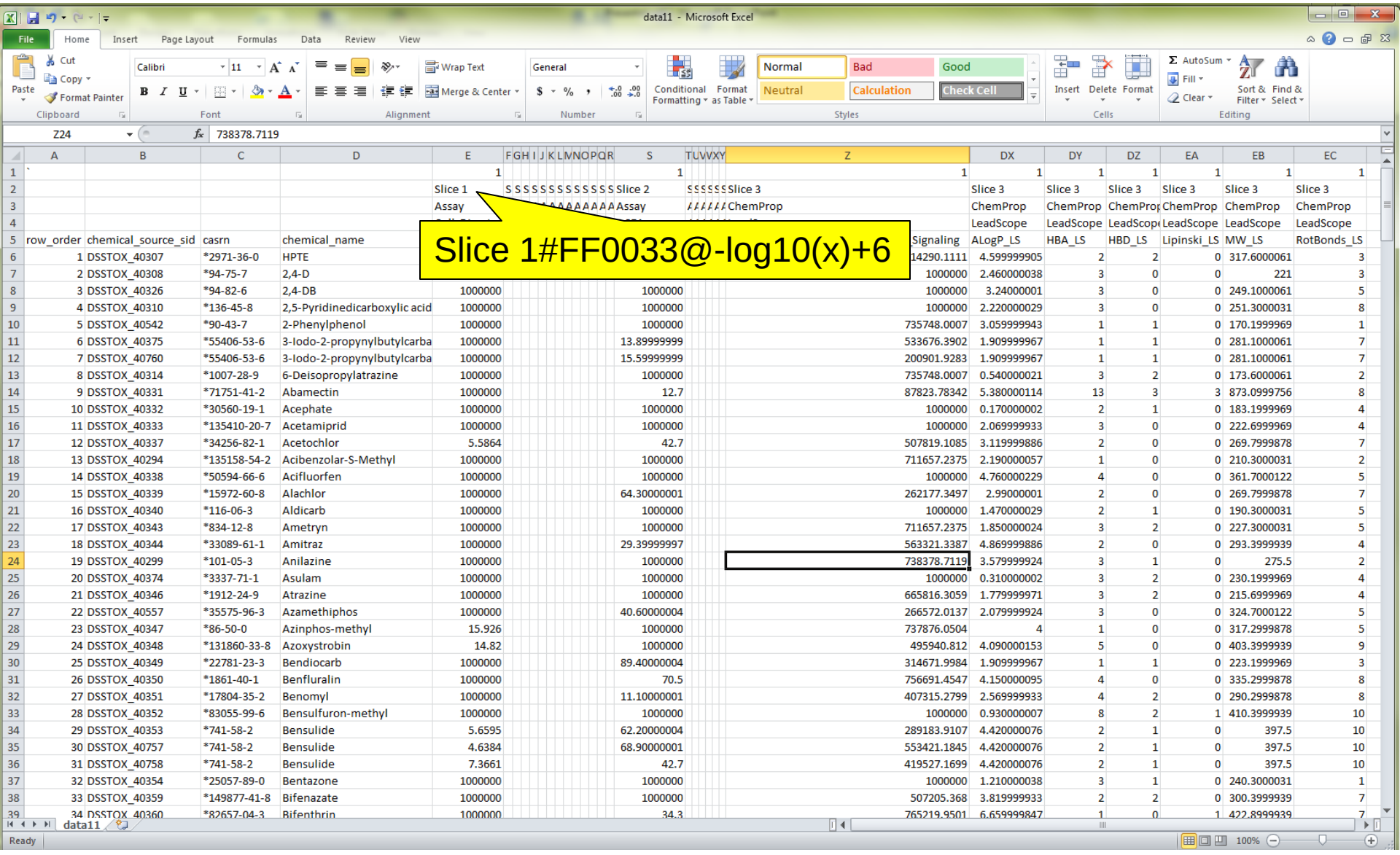

Slices information
What happens when slice weights are varied?
Enter slice name:
CYPs
Select slyce type:
Assay
Pathway
ChemProp
Exposure
ToxRefDB
Custom
Select slice color:
Select slice weight:
21
50.0%
Select components:
CLZD_CYP1A1
CLZD_CYP2C19
CLZD_CYP1A2
CLZD_CYP2B6
CLZD_CYP3A4
ACEA_LOC3
Add
Remove
Add all
Remove all
Search field:
CYP
CLZD_CYP1A1
CLZD_CYP2C19
CLZD_CYP1A2
CLZD_CYP2C9
CLZD_CYP2B6
CLZD_CYP3A4
Select scaling type:
-log10(x)+6
Selected data analysis:
Min = 0.69733
Max = 1000000.0
Mean = 718752.4
Median = 1000000.0
Remove this slice
Enter slice name:
Nuclear receptors
Select slyce type:
Assay
Pathway
ChemProp
Exposure
ToxRefDB
Custom
Select slice color:
Select slice weight:
14
33.3%
Select components:
PS_Ingenuity_1_Hypoxia_Signaling_in_the_Cardiova
PS_Ingenuity_1_Xenobiotic_Metabolism_Signaling
PS_Ingenuity_1_Acute_Phase_Response_Signaling
PS_Ingenuity_1_ERKMAPK_Signaling
PS_Ingenuity_1_cAMP_mediated_Signaling
HBA_LS
PS_Ingenuity_1_JAKStat_Signaling
PS_Ingenuity_1_PPAR_Signaling
PS_Ingenuity_1_VEGF_Signaling
PS_Ingenuity_1_Role_of_RIG1_like_Receptors_in_Ar
PS_Ingenuity_1_Toll_like_Receptor_Signaling
PS_Ingenuity_1_GM_CSF_Signaling
Add
Remove
Add all
Remove all
Search field:
eceptor
PS_Ingenuity_1_Insulin_Receptor_Signaling
PS_Ingenuity_1_Fcgamma_Receptor_mediated_Phagoc
PS_Ingenuity_1_Aryl_Hydrocarbon_Receptor_Signaling
PS_Ingenuity_1_Glucocorticoid_Receptor_Signaling
PS_Ingenuity_1_GABA_Receptor_Signaling
PS_Ingenuity_1_Estrogen_Receptor_Signaling
PS_Ingenuity_1_Dopamine_Receptor_Signaling
Select scaling type:
-log10(x)+6
Selected data analysis:
Min = 10003.56334
Max = 1000000.0
Mean = 800689.2
Median = 1000000.0
Remove this slice
Enter slice name:
Chemical properties
Select slyce type:
Assay
Pathway
ChemProp
Exposure
ToxRefDB
Custom
Select slice color:
Select slice weight:
7
16.7%
Select components:
PS_Ingenuity_1_NF_kB_Signaling
PS_Ingenuity_1_Amyloid_Processing
PS_Ingenuity_1_Protein_Ubiquitination_Pathway
PS_Ingenuity_1_IL_6_Signaling
RotBonds_LS
PS_Ingenuity_1_Erythropoietin_Signaling
PS_Ingenuity_1_Dopamine_Receptor_Signaling
PS_Ingenuity_1_FGF_Signaling
PS_Ingenuity_1_Chemokine_Signaling
PS_Ingenuity_1_Integrin_Signaling
ALogP_LS
PS_Ingenuity_1_Axonal_Guidance_Signaling
Add
Remove
Add all
Remove all
Search field:
LS
ALogP_LS
HBD_LS
Lipinski_LS
MW_LS
HBA_LS
RotBonds_LS
Select scaling type:
linear(x)
Selected data analysis:
Min = 0.0
Max = 873.0999756
Mean = 57.8
Median = 2.6
Remove this slice
Add new slice
Preview your slices
Calculate ToxPi indexes and build vizualizations


Fluoxastrobin
Overall ToxPi score: 3.256
Oryzalin
Overall ToxPi score: 3.168
Dichlobenil
Overall ToxPi score: 1.127
Maneb
Overall ToxPi score: 1.044
What happens when slice weights are varied?
Fluoxastrobin
Overall ToxPi score: 4.71
Oryzalin
Overall ToxPi score: 4.562
Dichlobenil
Overall ToxPi score: 1.127
Maneb
Overall ToxPi score: 1.044
Missing data in percent:
Close
Save image


ToxPi results
Save data file
Save selected
Images only
Display chart
Image
14.67
13.665
16.582
3.411
Tribufos
DSSTOX_40510
28.225
Save
Save in:
Desktop
Computer
Network
Libraries
Sypa, Myroslav
DR
DR Projects
TOXPI QA
TOXPI_DATA
Recent Items
Desktop
My Documents
Computer
Network
File name:
Files of type:
Comma separated Values
Save
Cancel

ToxPi stand-alone GUI: Data File Format

(build your own or bring from Web-based ToxPi)



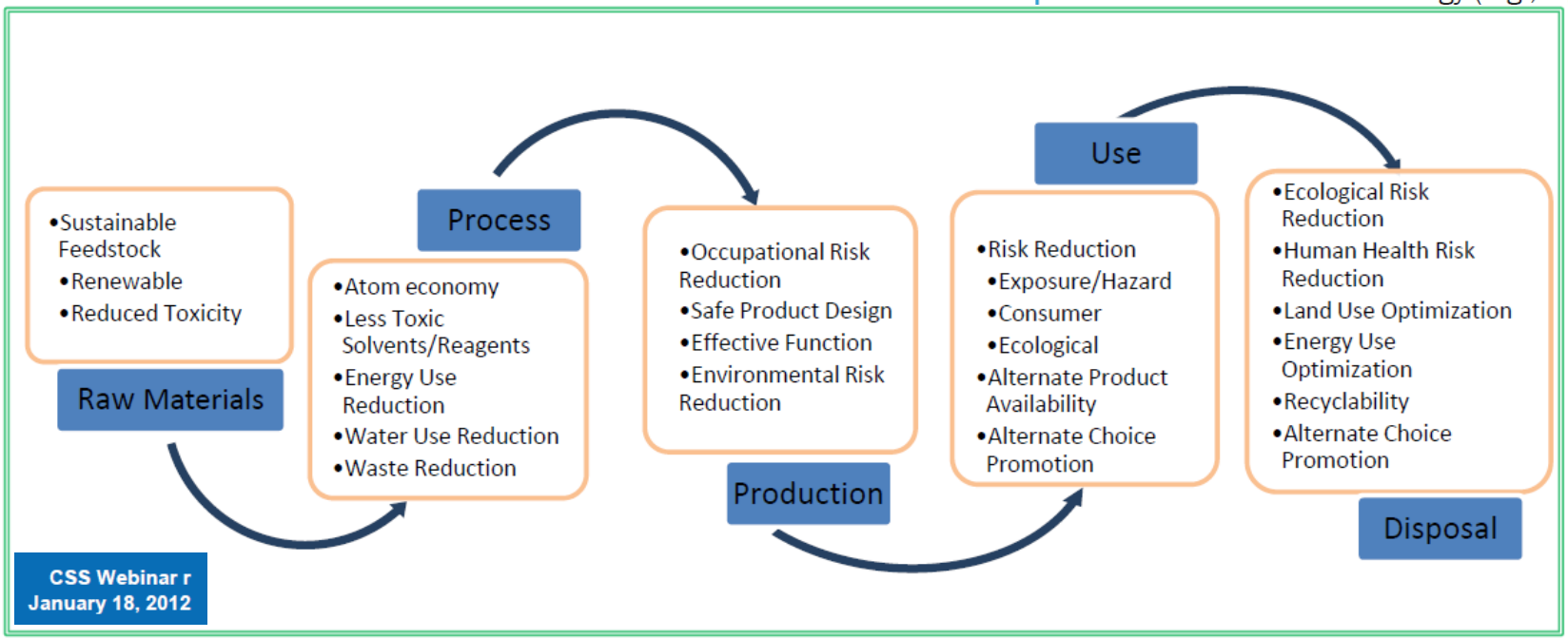
	A	B	C	D	E	S	Z	DX	DY	DZ	EA	EB	EC
1					1	1	1	1	1	1	1	1	1
2					Slice 1	Slice 2	Slice 3	Slice 3	Slice 3	Slice 3	Slice 3	Slice 3	Slice 3
3					Assay	Assay	ChemProp	ChemProp	ChemProp	ChemProp	ChemProp	ChemProp	ChemProp
4								LeadScope	LeadScope	LeadScope	LeadScope	LeadScope	LeadScope
5	row_order	chemical_source_sid	casrn	chemical_name			Signaling	ALogP_LS	HBA_LS	HBD_LS	Lipinski_LS	MW_LS	RotBonds_LS
6	1	DSSTOX_40307	*2971-36-0	HPTE			14290.1111	4.599999905	2	2	0	317.6000061	3
7	2	DSSTOX_40308	*94-75-7	2,4-D			1000000	2.460000038	3	0	0	221	3
8	3	DSSTOX_40326	*94-82-6	2,4-DB	1000000	1000000	1000000	3.24000001	3	0	0	249.1000061	5
9	4	DSSTOX_40310	*136-45-8	2,5-Pyridinedicarboxylic acid	1000000	1000000	1000000	2.220000029	3	0	0	251.3000031	8
10	5	DSSTOX_40542	*90-43-7	2-Phenylphenol	1000000	1000000	735748.0007	3.059999943	1	1	0	170.1999969	1
11	6	DSSTOX_40375	*55406-53-6	3-Iodo-2-propynylbutylcarba	1000000	13.89999999	533676.3902	1.909999967	1	1	0	281.1000061	7
12	7	DSSTOX_40760	*55406-53-6	3-Iodo-2-propynylbutylcarba	1000000	15.59999999	200901.9283	1.909999967	1	1	0	281.1000061	7
13	8	DSSTOX_40314	*1007-28-9	6-Deisopropylatrazine	1000000	1000000	735748.0007	0.540000021	3	2	0	173.6000061	2
14	9	DSSTOX_40331	*71751-41-2	Abamectin	1000000	12.7	87823.78342	5.380000114	13	3	3	873.0999756	8
15	10	DSSTOX_40332	*30560-19-1	Acephate	1000000	1000000	1000000	0.170000002	2	1	0	183.1999969	4
16	11	DSSTOX_40333	*135410-20-7	Acetamiprid	1000000	1000000	1000000	2.069999933	3	0	0	222.6999969	4
17	12	DSSTOX_40337	*34256-82-1	Acetochlor	5.5864	42.7	507819.1085	3.119999886	2	0	0	269.7999878	7
18	13	DSSTOX_40294	*135158-54-2	Acibenzolar-S-Methyl	1000000	1000000	711657.2375	2.190000057	1	0	0	210.3000031	2
19	14	DSSTOX_40338	*50594-66-6	Acifluorfen	1000000	1000000	1000000	4.760000229	4	0	0	361.7000122	5
20	15	DSSTOX_40339	*15972-60-8	Alachlor	1000000	64.30000001	262177.3497	2.99000001	2	0	0	269.7999878	7
21	16	DSSTOX_40340	*116-06-3	Aldicarb	1000000	1000000	1000000	1.470000029	2	1	0	190.3000031	5
22	17	DSSTOX_40343	*834-12-8	Ametryn	1000000	1000000	711657.2375	1.850000024	3	2	0	227.3000031	5
23	18	DSSTOX_40344	*33089-61-1	Amitraz	1000000	29.39999997	563321.3387	4.869999886	2	0	0	293.3999939	4
24	19	DSSTOX_40299	*101-05-3	Anilazine	1000000	1000000	738378.7119	3.579999924	3	1	0	275.5	2
25	20	DSSTOX_40374	*3337-71-1	Asulam	1000000	1000000	1000000	0.310000002	3	2	0	230.1999969	4
26	21	DSSTOX_40346	*1912-24-9	Atrazine	1000000	1000000	665816.3059	1.779999971	3	2	0	215.6999969	4
27	22	DSSTOX_40557	*35575-96-3	Azamethiphos	1000000	40.60000004	266572.0137	2.079999924	3	0	0	324.7000122	5
28	23	DSSTOX_40347	*86-50-0	Azinphos-methyl	15.926	1000000	737876.0504	4	1	0	0	317.2999878	5
29	24	DSSTOX_40348	*131860-33-8	Azoxystrobin	14.82	1000000	495940.812	4.090000153	5	0	0	403.3999939	9
30	25	DSSTOX_40349	*22781-23-3	Bendiocarb	1000000	89.40000004	314671.9984	1.909999967	1	1	0	223.1999969	3
31	26	DSSTOX_40350	*1861-40-1	Benfluralin	1000000	70.5	756691.4547	4.150000095	4	0	0	335.2999878	8
32	27	DSSTOX_40351	*17804-35-2	Benomyl	1000000	11.10000001	407315.2799	2.569999933	4	2	0	290.2999878	8
33	28	DSSTOX_40352	*83055-99-6	Bensulfuron-methyl	1000000	1000000	1000000	0.930000007	8	2	1	410.3999939	10
34	29	DSSTOX_40353	*741-58-2	Bensulide	5.6595	62.20000004	289183.9107	4.420000076	2	1	0	397.5	10
35	30	DSSTOX_40757	*741-58-2	Bensulide	4.6384	68.90000001	553421.1845	4.420000076	2	1	0	397.5	10
36	31	DSSTOX_40758	*741-58-2	Bensulide	7.3661	42.7	419527.1699	4.420000076	2	1	0	397.5	10
37	32	DSSTOX_40354	*25057-89-0	Bentazone	1000000	1000000	1000000	1.210000038	3	1	0	240.3000031	1
38	33	DSSTOX_40359	*149877-41-8	Bifenazate	1000000	1000000	507205.368	3.819999933	2	2	0	300.3999939	7
39	34	DSSTOX_40360	*82657-04-3	Bifenthrin	1000000	34.3	765219.9501	6.659999847	1	0	1	422.8999939	7

EMERGING SCIENCE FOR ENVIRONMENTAL HEALTH DECISIONS

Applying 21st Century Toxicology to Green Chemical and Material Design

SEPTEMBER 20-21, 2011 ■ TUESDAY 8:30–5:00, WEDNESDAY 8:30–NOON*
HOUSE OF SWEDEN EVENT CENTER, 2900 K STREET NW, WASHINGTON, DC

The origin of this workshop topic was the Toxics and Risk Subcommittee (T&R) of the National Science and Technology Council's Committee on Environment, Natural Resources, and Sustainability. T&R is comprised of senior representatives from 16 federal agencies and seeks to coordinate federal science and technology efforts related to the identification, prevention, and mitigation of problems arising from human and non-human exposure of to potentially toxic materials. One focus is on how advances in molecular and compu-tational methods in toxicology (e.g., high-throughput
al design.
nair and sponsor
pic was advanced
he NAS and the

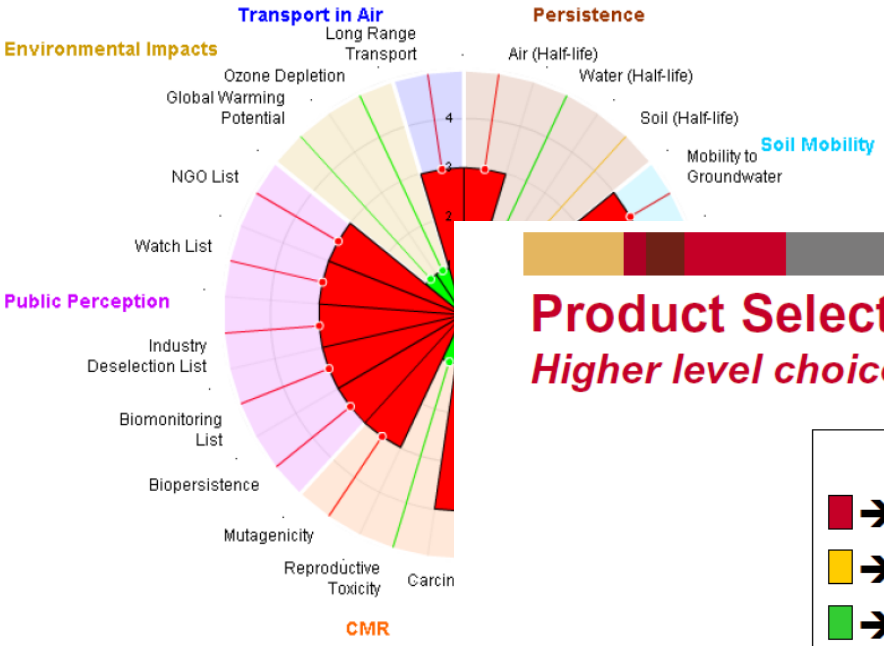


DuPont METIS Chemical Screening Visualization Tool

Potential for Concern
Indicated by Color: Red: High / Very High; Orange: Moderate; Green: Low
or
Indicated by Wedge Length: 1 = Low; 2 = Moderate; 3 = High; 4 = Very High

Mark E. Thompson, Director
DuPont Haskell Global Centers for Health and Environmental Sciences

20 September 2011



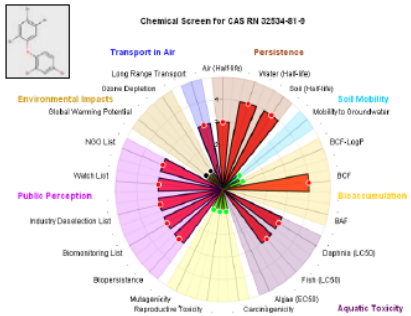
Product Selection by Inspection

Higher level choices require expert consultation

Key

- ➔Potential for High level of concern
- ➔Potential for Moderate level of concern
- ➔Potential for Low level of concern

1



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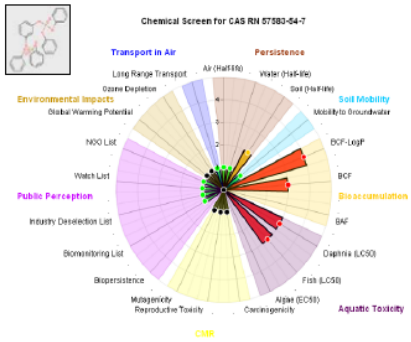

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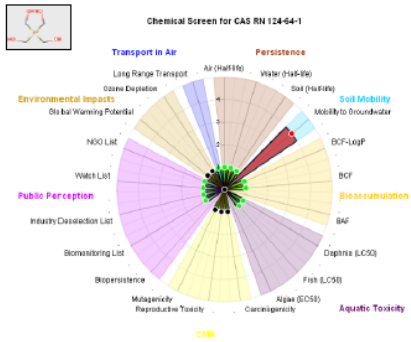

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Green Screen for Safer Chemicals

Helen Holder
Corporate Material Selection Manager
20 Sept 2011

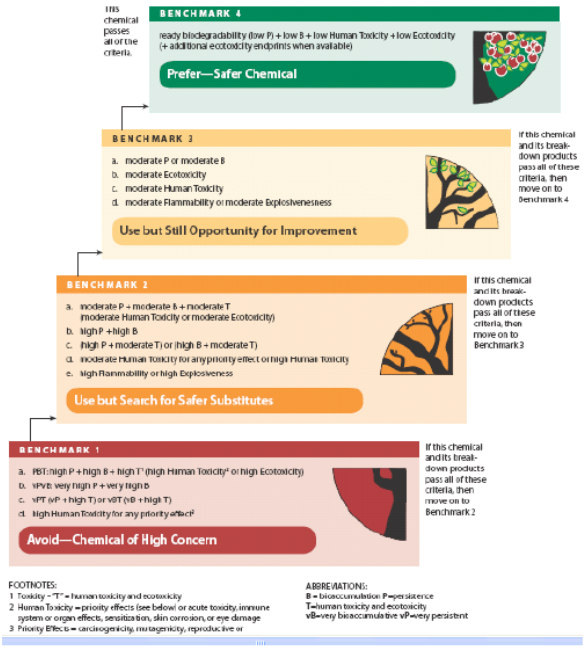
- Comparative chemical hazard assessment
  - Developed by Clean Production Action
- Rates 17 hazard topics (High, Medium, Low)
  - Considers both environment and human health
  - Addresses constituents and breakdown products
- Decision logic looks at particular combinations of scores for a final four-point benchmark score
  - Uses the most conservative scori
  - Data driven, meaningful threshol
- Compatible with risk assessr

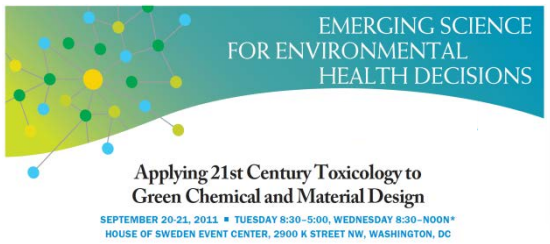
More information available

Alternatives Assessment with Green Screen Meets Business Needs

Helps us to identify alternatives that won't be restricted in the future

Helps us articulate materials goals to suppliers and chemical formulators



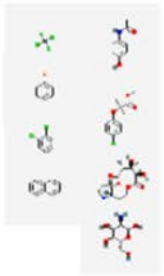


Application of ToxCast High Throughput Screening to Green Chemical Design—David Dix, *Environmental Protection Agency*

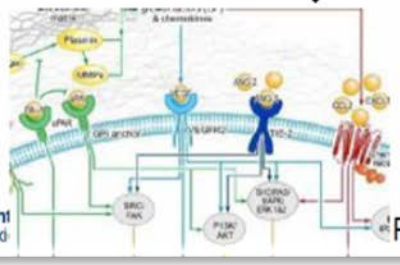
Green Chemistry and CompTox

EPA United States Environmental Protection Agency

- Less expensive, higher throughput approach to hazard prediction
- Prioritization of green alternative chemicals for further development and testing
- High throughput exposure predictions also needed

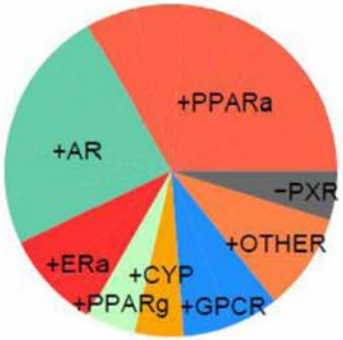


in vitro testing



Toxicity Pathways

Prioritization, Predictive and Systems Models



BPA

TGSA

Office of Research and Development
National Center for Computational Toxi

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EPA United States Environmental Protection Agency

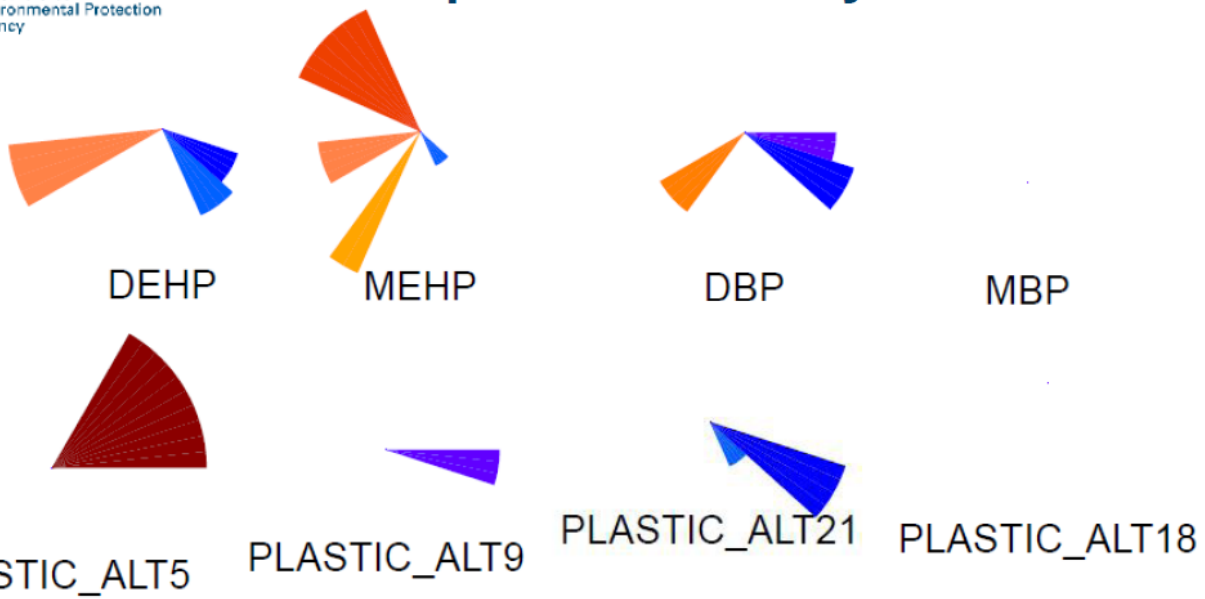
ReproTox Predictions

Biol Reprod. 2011 Aug;85(2):327-39. Epub 2011
Predictive model of rat reproductive toxicity f
Martin MT, Knudsen TB, Reif DM, Houck KA, Jud

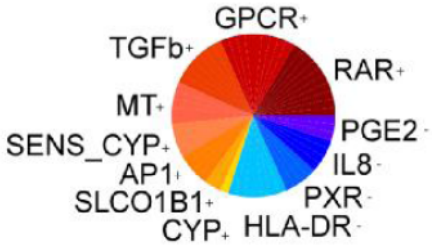
Office of Research and Development
National Center for Computational Toxicology

EPA United States Environmental Protection Agency

Developmental Toxicity Predictions



Toxicol Sci. 2011 Aug 26. [Epub ahead of print]
Predictive models of prenatal developmental toxicity from ToxCast high-throughput screening data.
Sipes NS, Martin MT, Reif DM, Kleinstreuer NC, Judson RS, Singh AV, Chandler KJ, Dix DJ, Kavlock RJ, Knudsen TB.



Office of Research and Development
National Center for Computational Toxicology

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So, what is ToxPi (potentially) good for?

- **Prioritizing chemicals for additional experiments/screening:**
  Promoting efficient, targeted testing decisions

- **Sustainable development and "Green chemistry:"**
  Decision support for selecting manufacturing alternatives

- **Facilitating arguments on "chemical similarity" through integration of diverse data streams into a single (and visually appealing) score:**
  Read-across of ToxPi profiles

- **Integrating non-biomedical data into decision-making:**
  Combining environmental exposure metrics with socio-economic and other factors for comparing different neighborhoods/communities

- **Setting priorities for chemical grouping and assessment:**
  Decision support for tiered assessment strategies
  Inclusion of novel data streams in human health risk assessments