An interactive web application for ToxPi

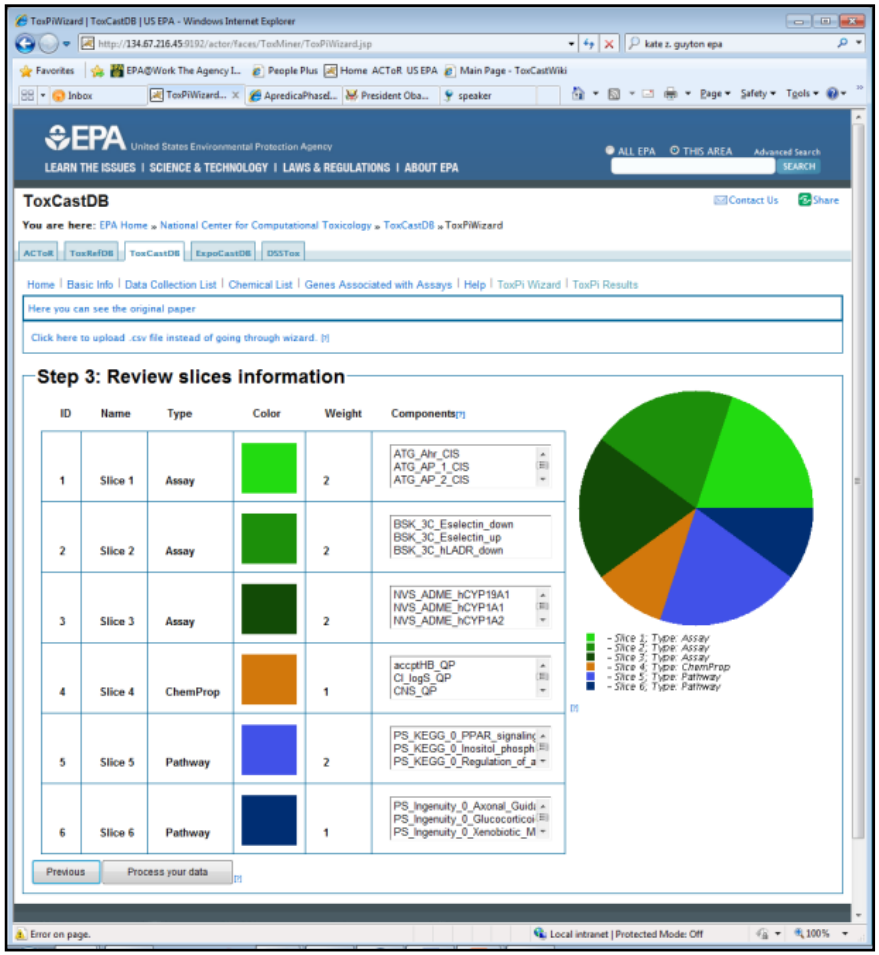
David Reif, PhD

Office of Research and Development
National Center for Computational Toxicology

Putting ToxPi in the hands of the experts

Diverse prioritization tasks are best handled by domain experts.

An interactive, web application allows users to apply their own, specialized knowledge to the analysis.



Acknowledgments

Tommy Cathey[5]
David Dix[1]
Sumit Gangwal[1]
Keith Houck[1]
John Jack[1]
Richard Judson[1]
Thomas Knudsen[1]
Robert Kavlock[1]
Parth Kothiya[1]
Nicole Kleinstreuer[1]
Matt Martin[1]
Ann Richard[1]
Ivan Rusyn[4]
Nisha Sipes[1]
Myroslav Sypa[4]
Shirlee Tan[2]
Ander Wilson[3]

. . . plus many more EPA colleagues that are participating in the continued development of this work

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Office of Research and Development, U.S. EPA

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Office of Pollution Prevention, U.S. EPA

[3]Department of Statistics
North Carolina State University

[4]Department of Environmental Sciences and Engineering
University of North Carolina at Chapel Hill

[5]Lockheed Martin

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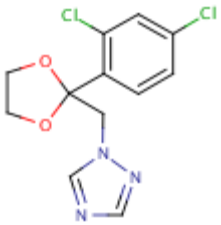
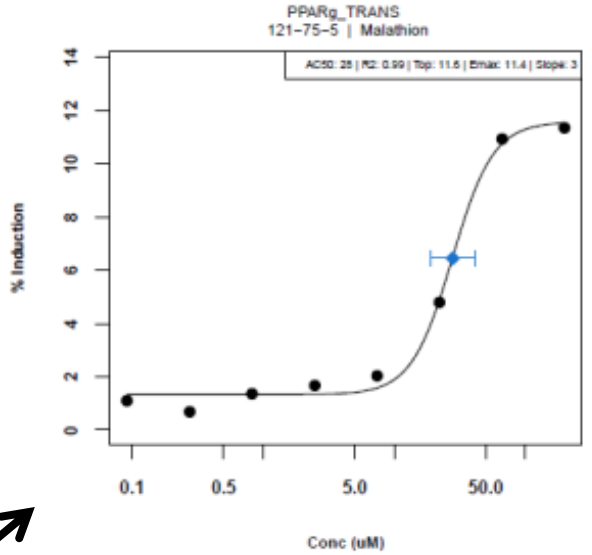
What is the problem?

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

# Chemicals	x	# Assays	=	# Results
1	x	1	=	1

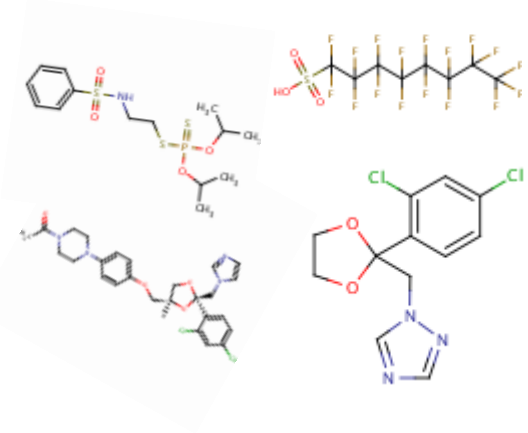


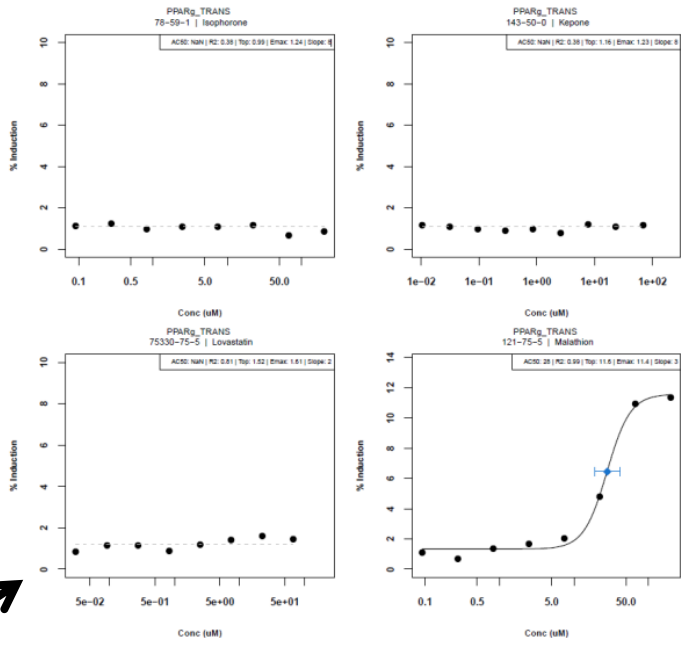


This is a manageable amount of information … but what happens as we expand the number of chemicals and assays?

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

# Chemicals	x	# Assays	=	# Results
4	x	1	=	4

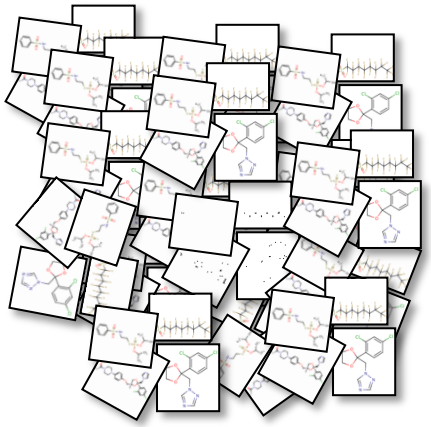


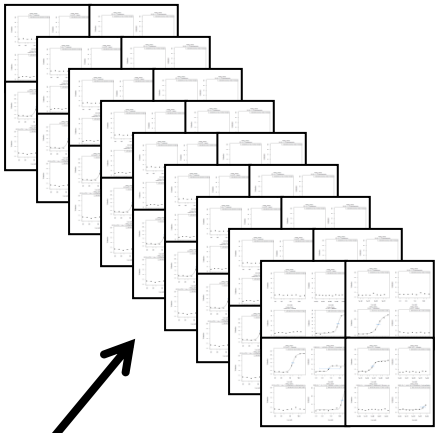


Okay … still manageable … but what happens as we expand towards the numbers needed to characterize all environmental chemicals across all relevant tests (assays)?

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….

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How do we address this giant data problem?

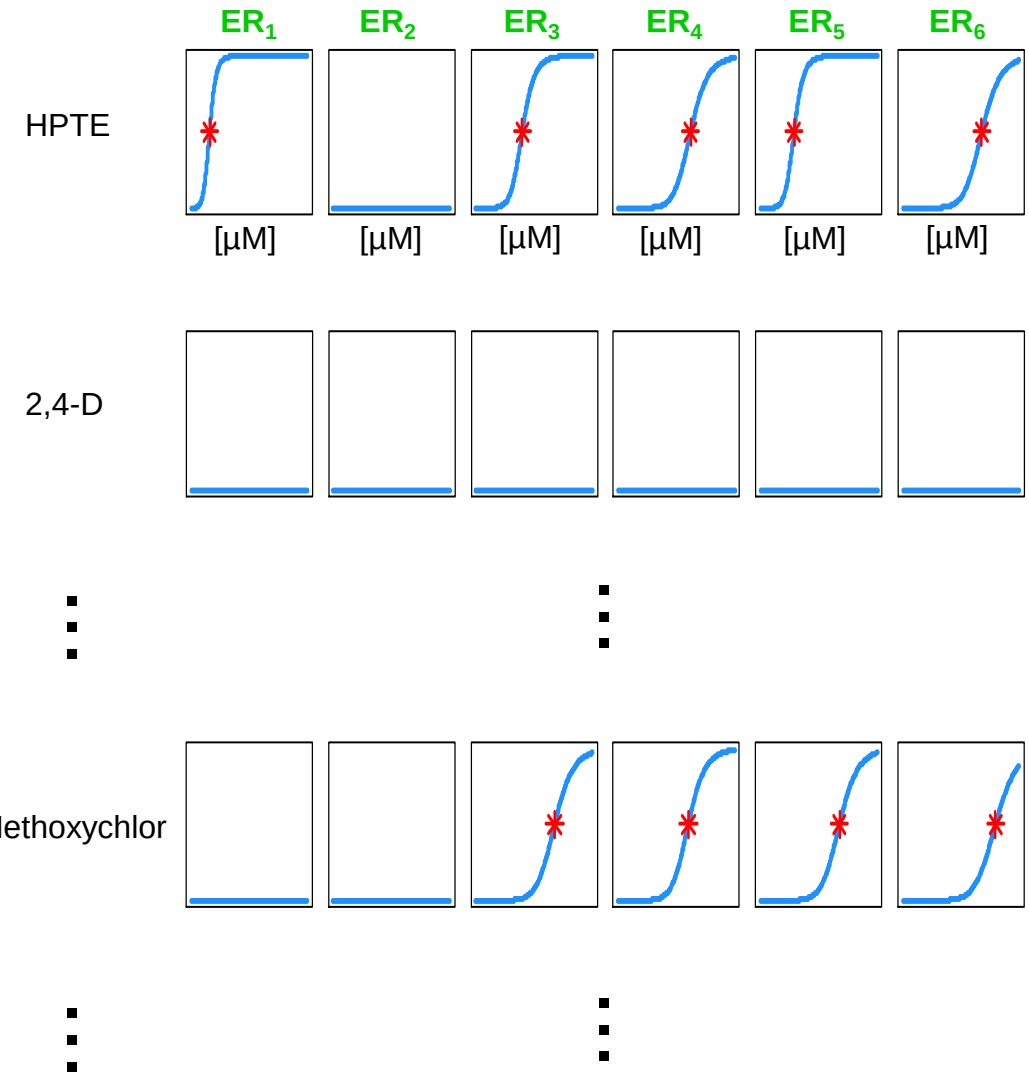
Translating multivariate results into ToxPi profiles

United States Environmental Protection Agency

1. Sum the potency across all component assays in the ER slice for each individual chemical.

2. Normalize the summed potency across all 309 chemicals.

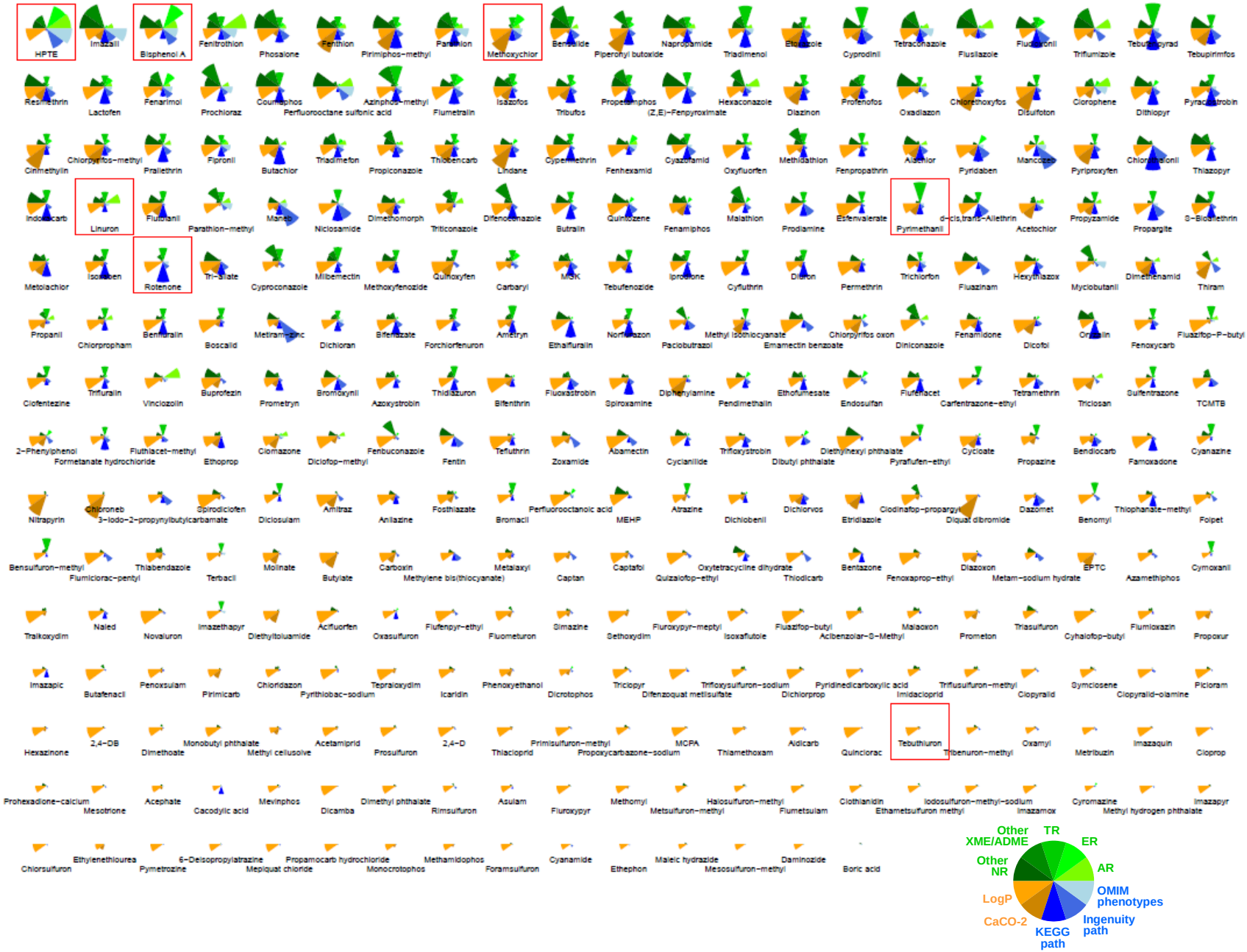
3. Plot the normalized ToxPi scores for the ER slice.



ToxPi profiles for ToxCast Phase-I chemicals

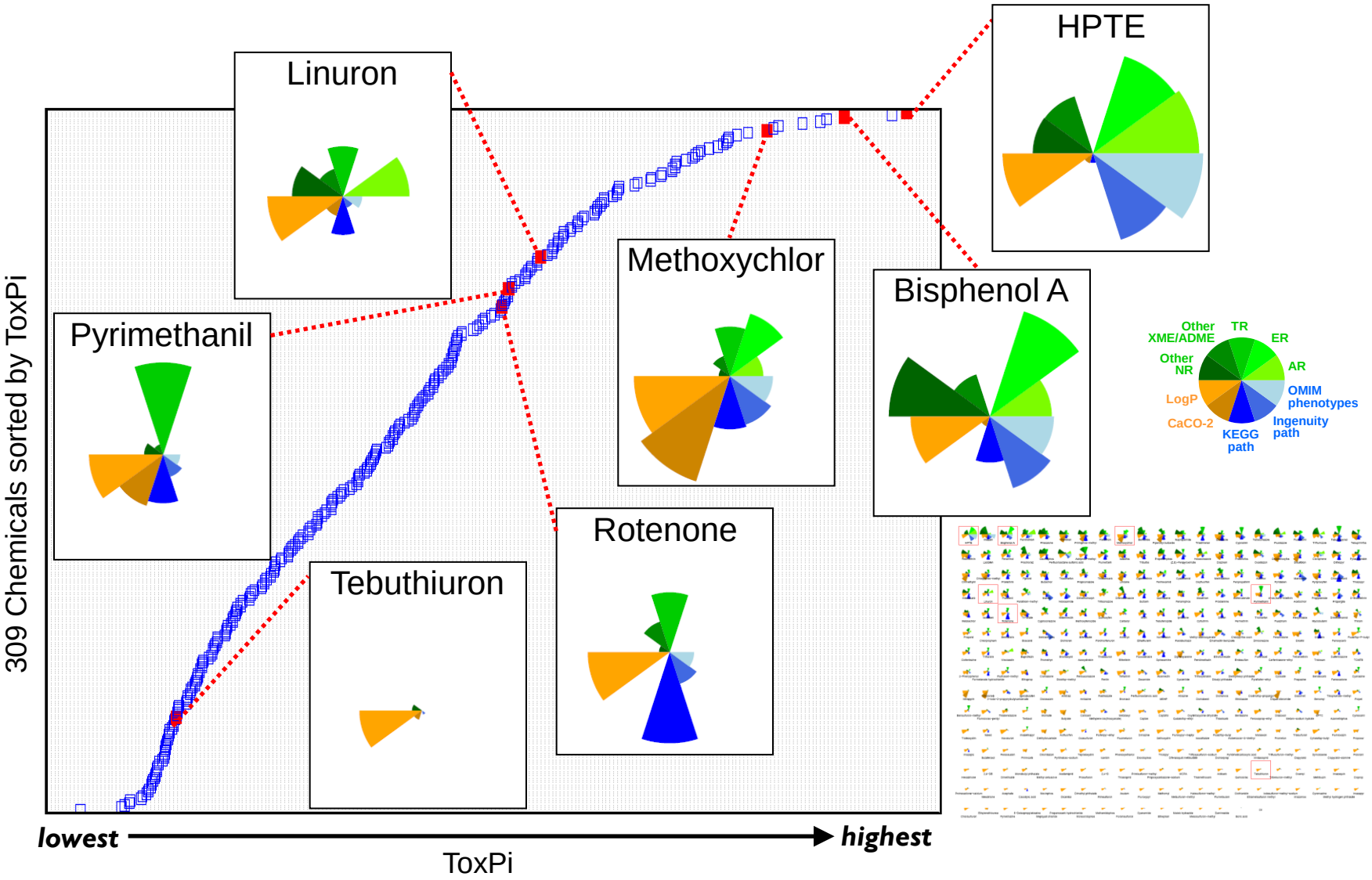
(Sorted by ToxPi; red boxes indicate "reference" chemicals)

United States Environmental Protection Agency

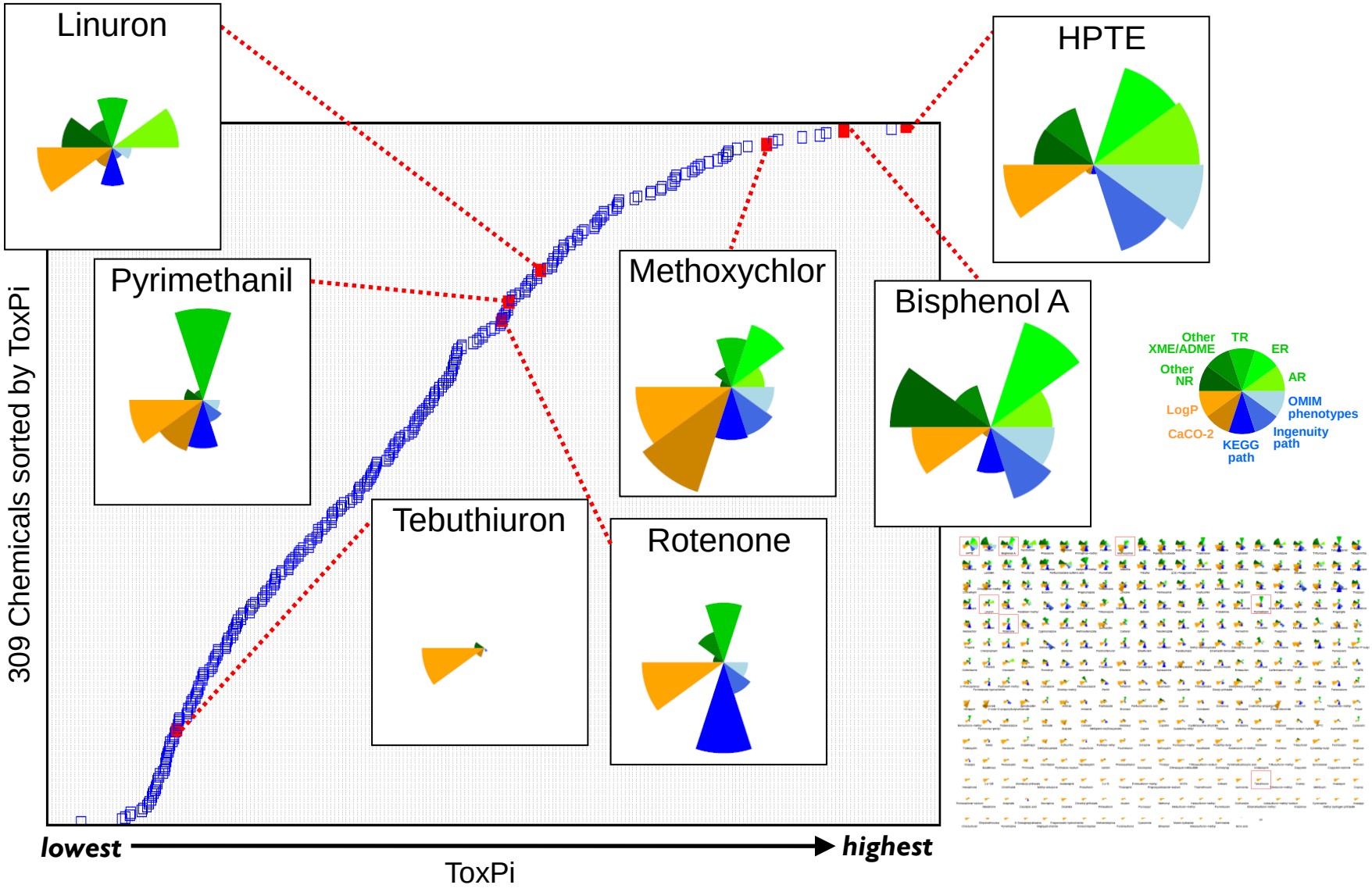


October 2011

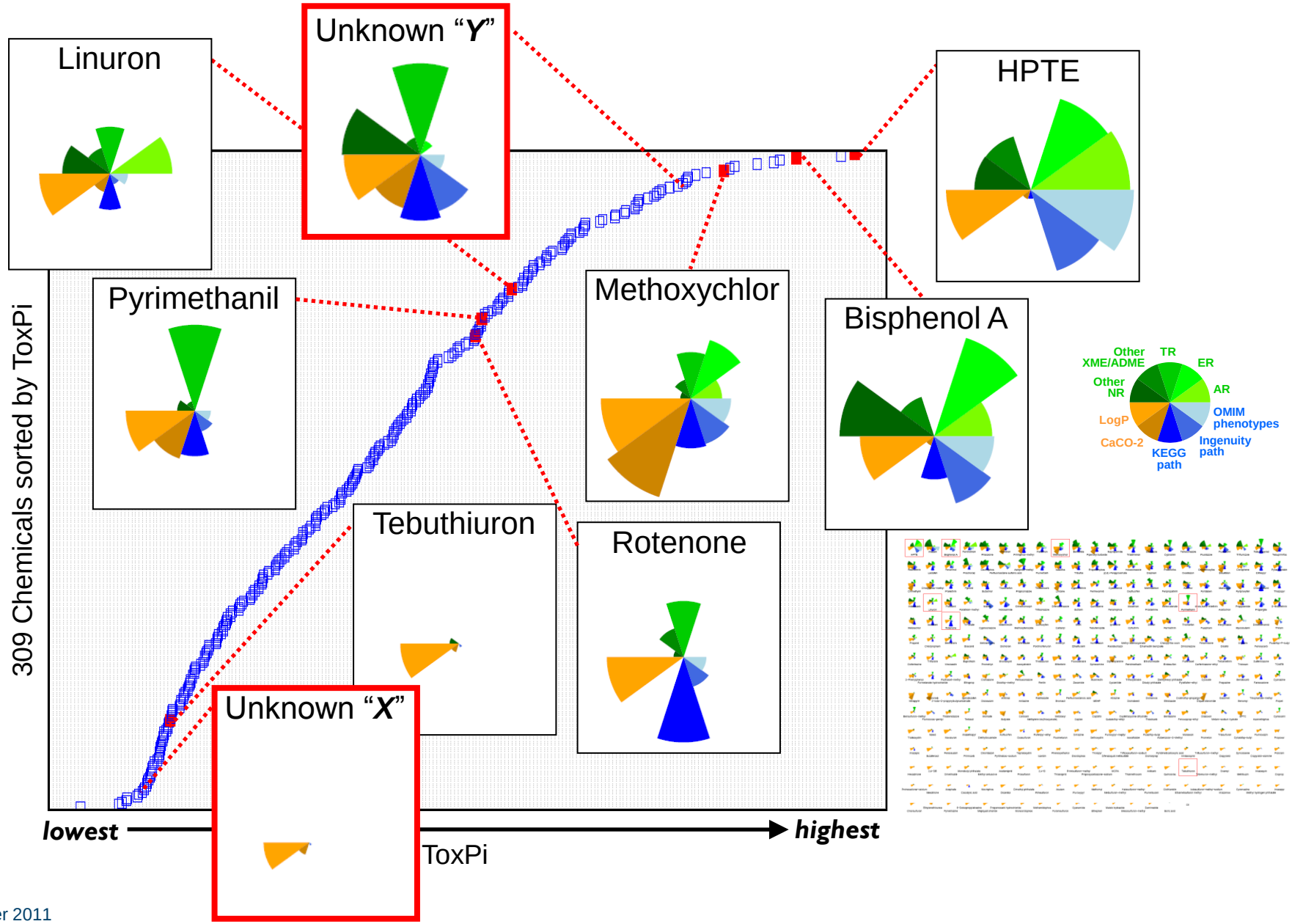
Exploring reference ("spike-in") chemicals along the sorted ToxPi distribution



Can we use these data to inform decisions about new unknown chemicals?



Can we use these data to inform decisions about new unknown chemicals?



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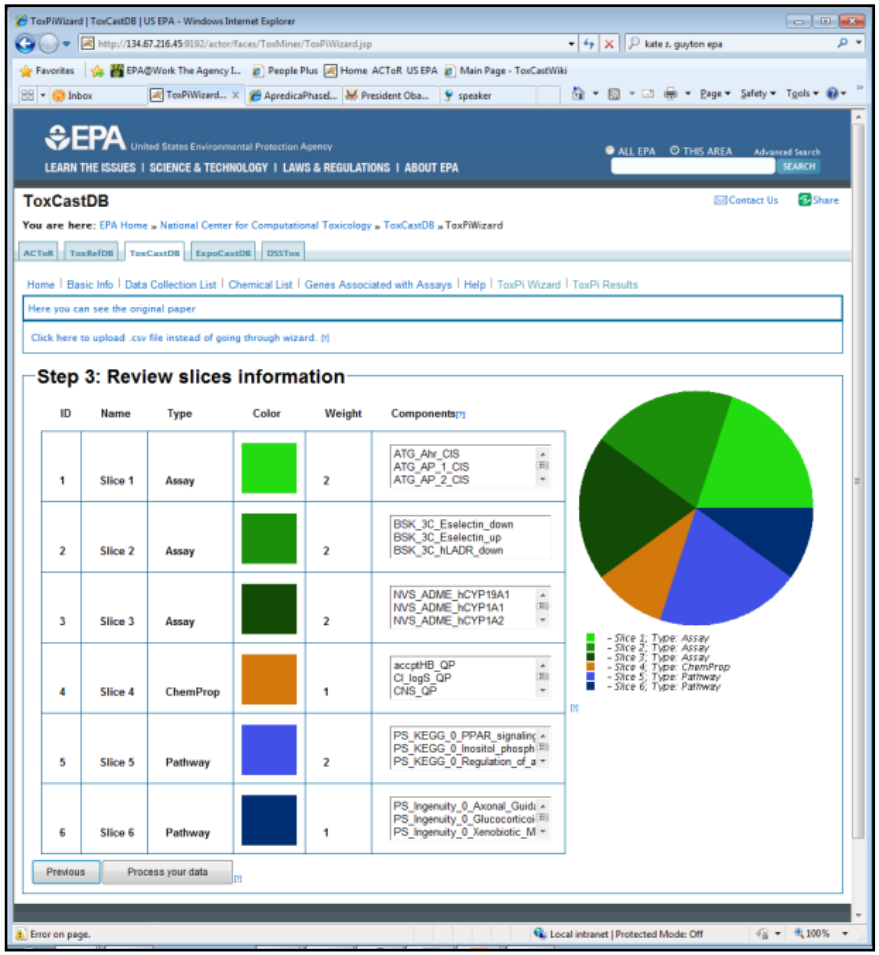
Development of a web application to allow users to develop their own ToxPi formulations

October 2011

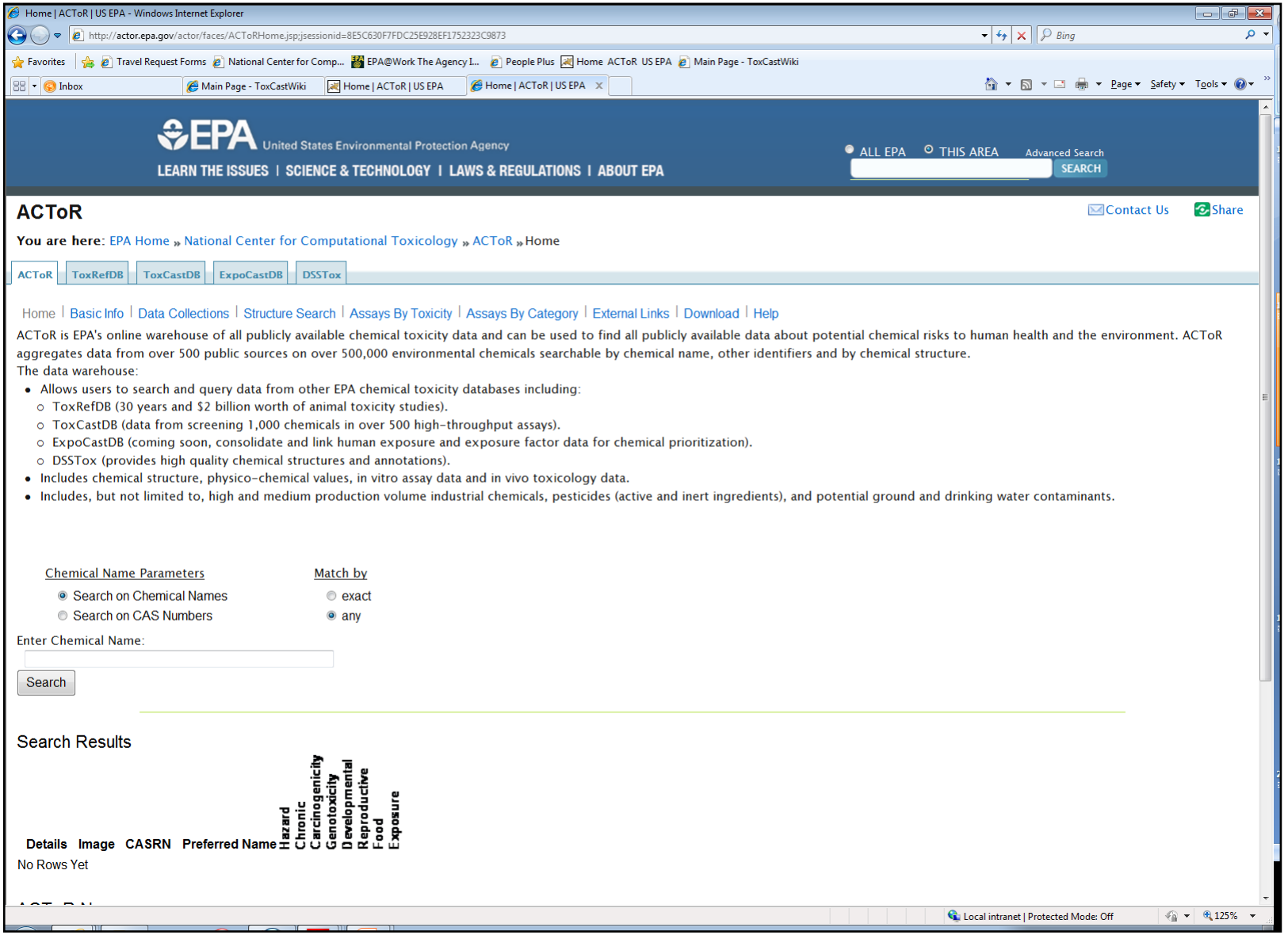
Putting ToxPi in the hands of the experts

Diverse prioritization tasks are best handled by domain experts.

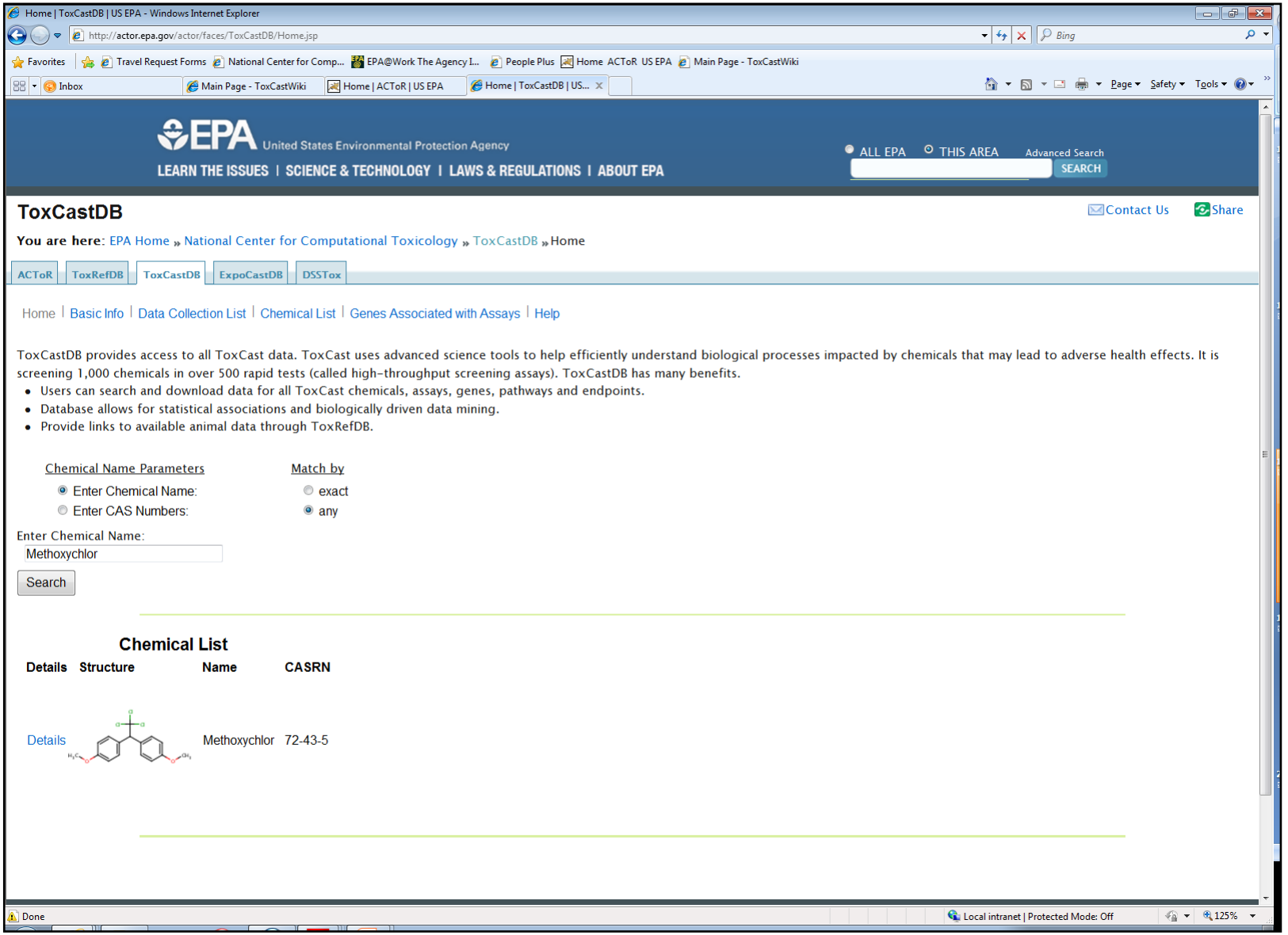
An interactive, web application allows users to apply their own, specialized knowledge to the analysis.



Building on the ACToR infrastructure: http://actor.epa.gov/actor/faces/ACToRHome.jsp

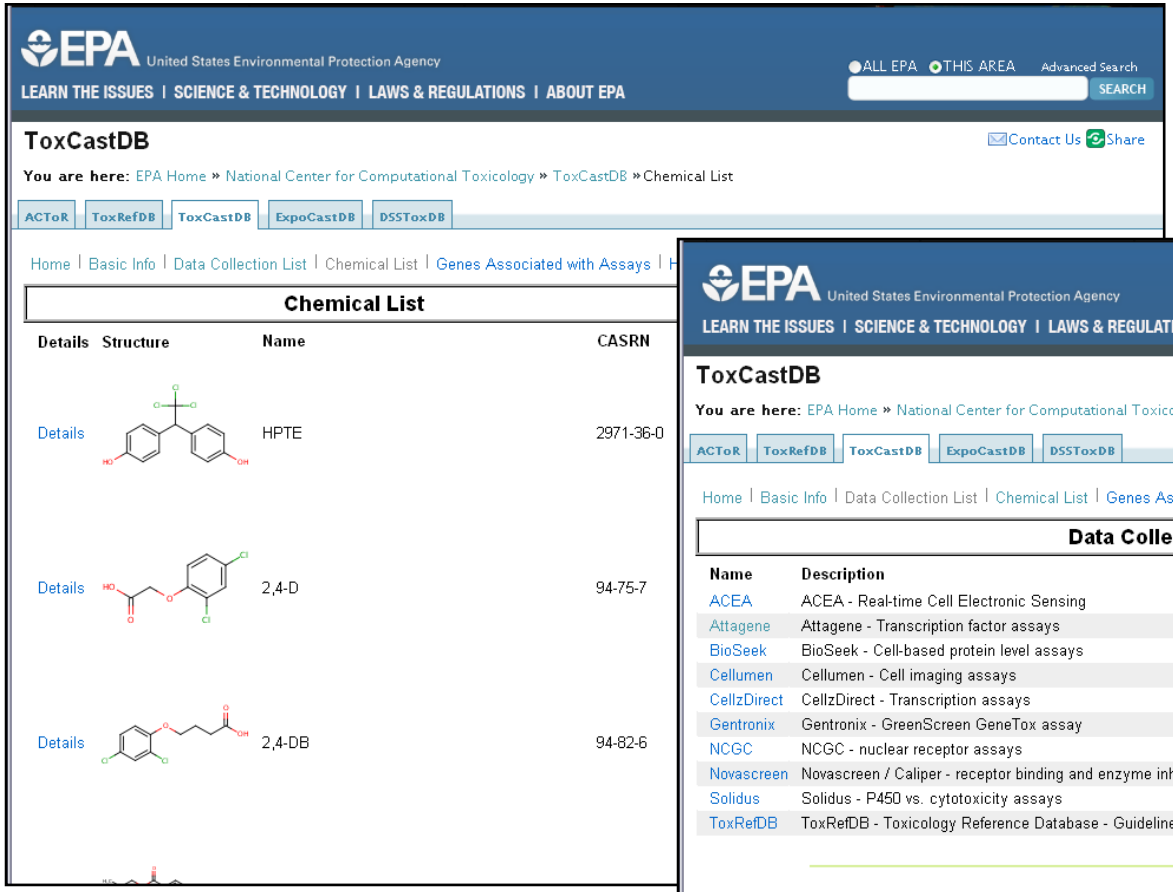


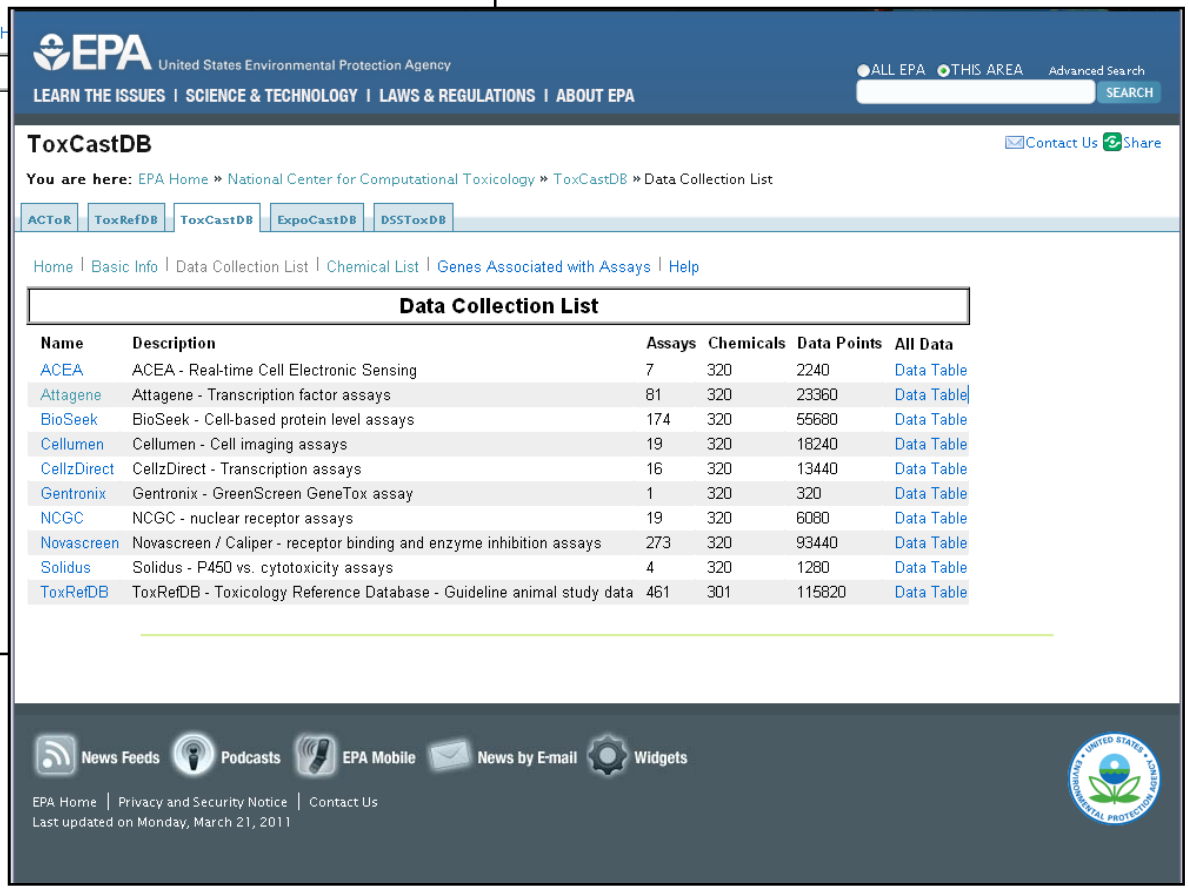
Building on the ACToR infrastructure: http://actor.epa.gov/actor/faces/ToxCastDB/Home.jsp



Building on the ACToR infrastructure: ToxCast chemicals and assays

http://actor.epa.gov/actor/faces/ToxCastDB/ChemicalList.jsp

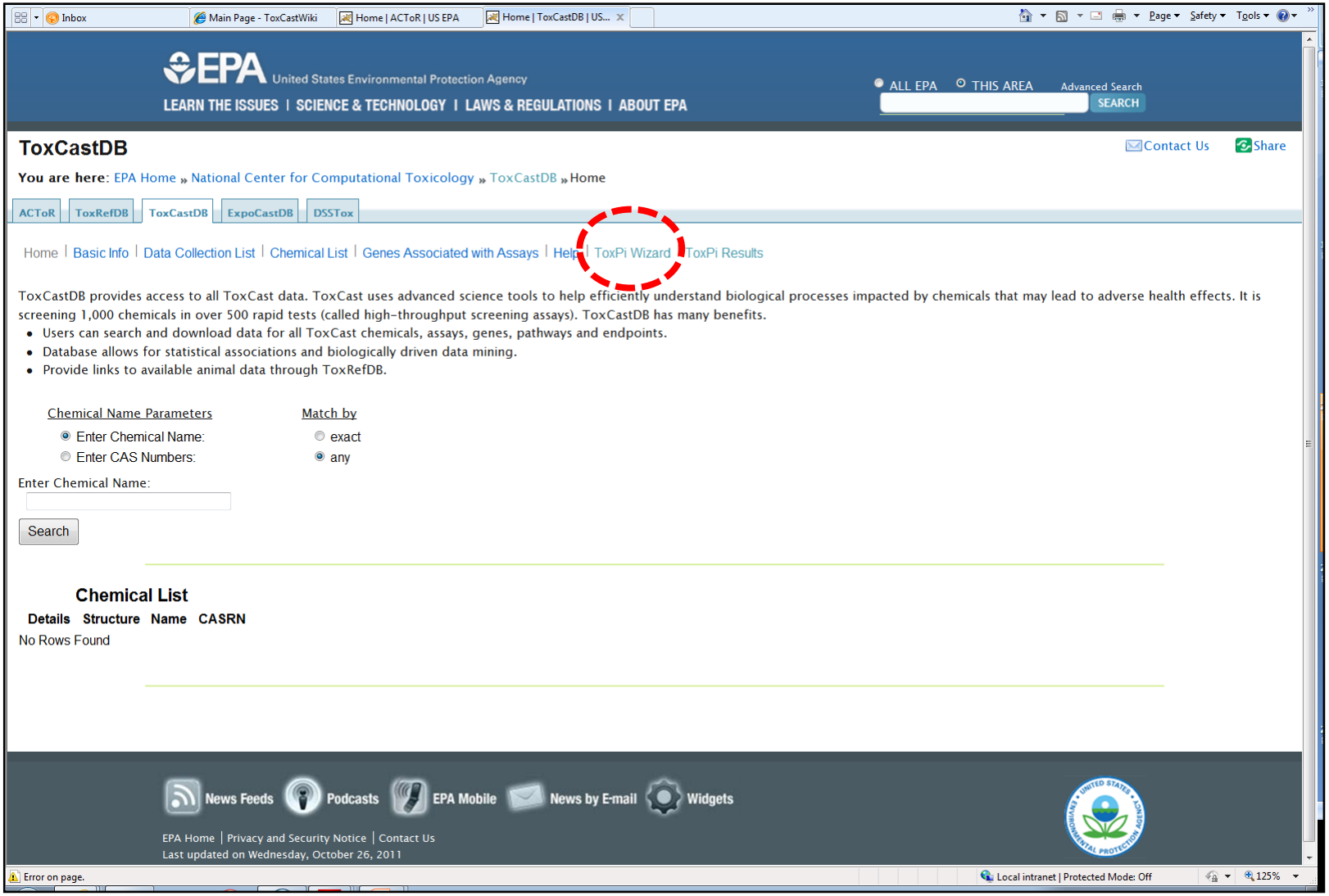




http://actor.epa.gov/actor/faces/ToxCastDB/DataCollectionList.jsp

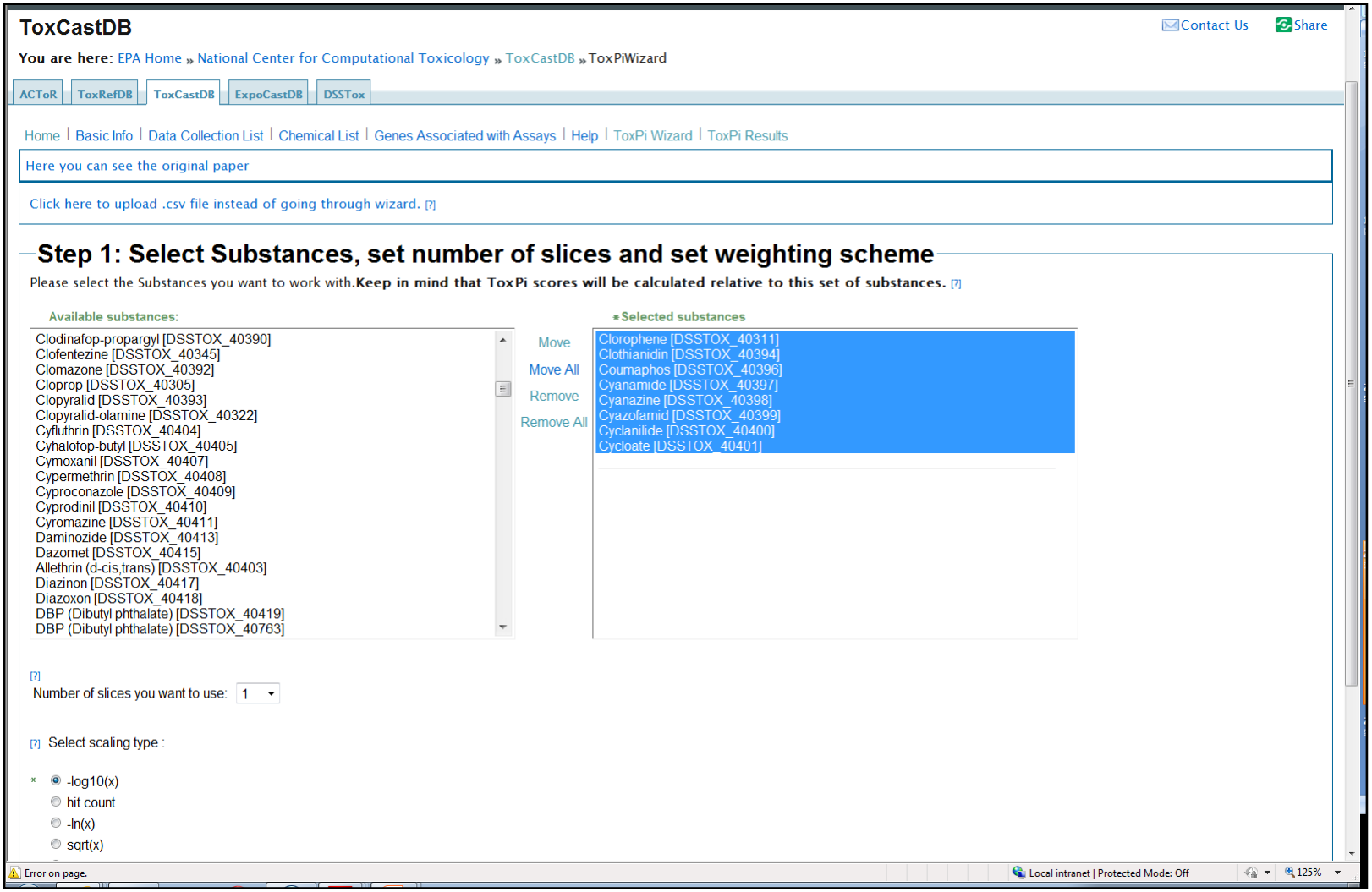
The step-by-step ToxPi wizard is implemented under the ToxCastDB tab

NOTE: The development version is undergoing final pre-release updating/testing on the EPA In***tra***net



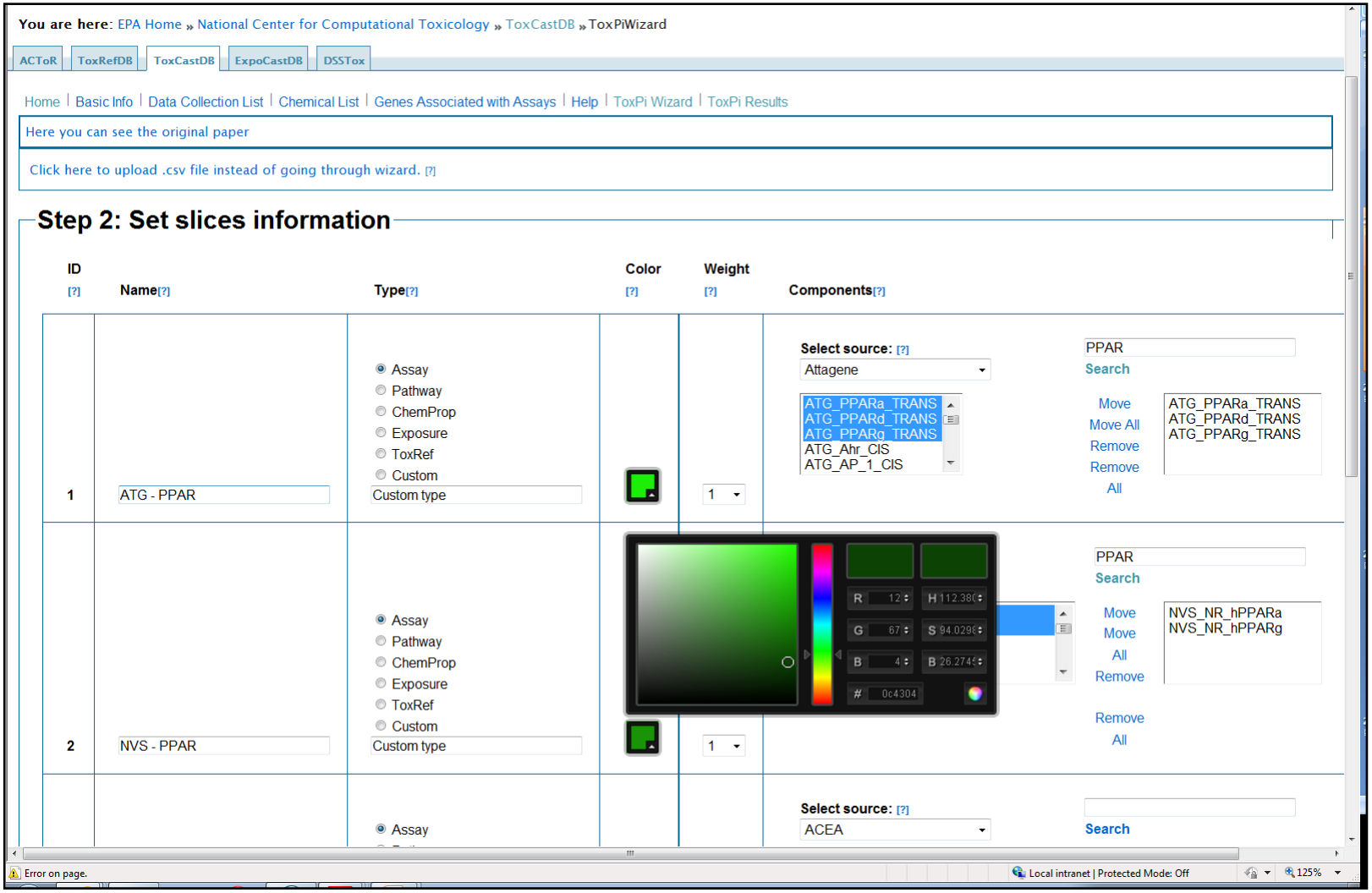
ToxPi wizard: Step 1

Options: chemicals, number of slices, data scaling



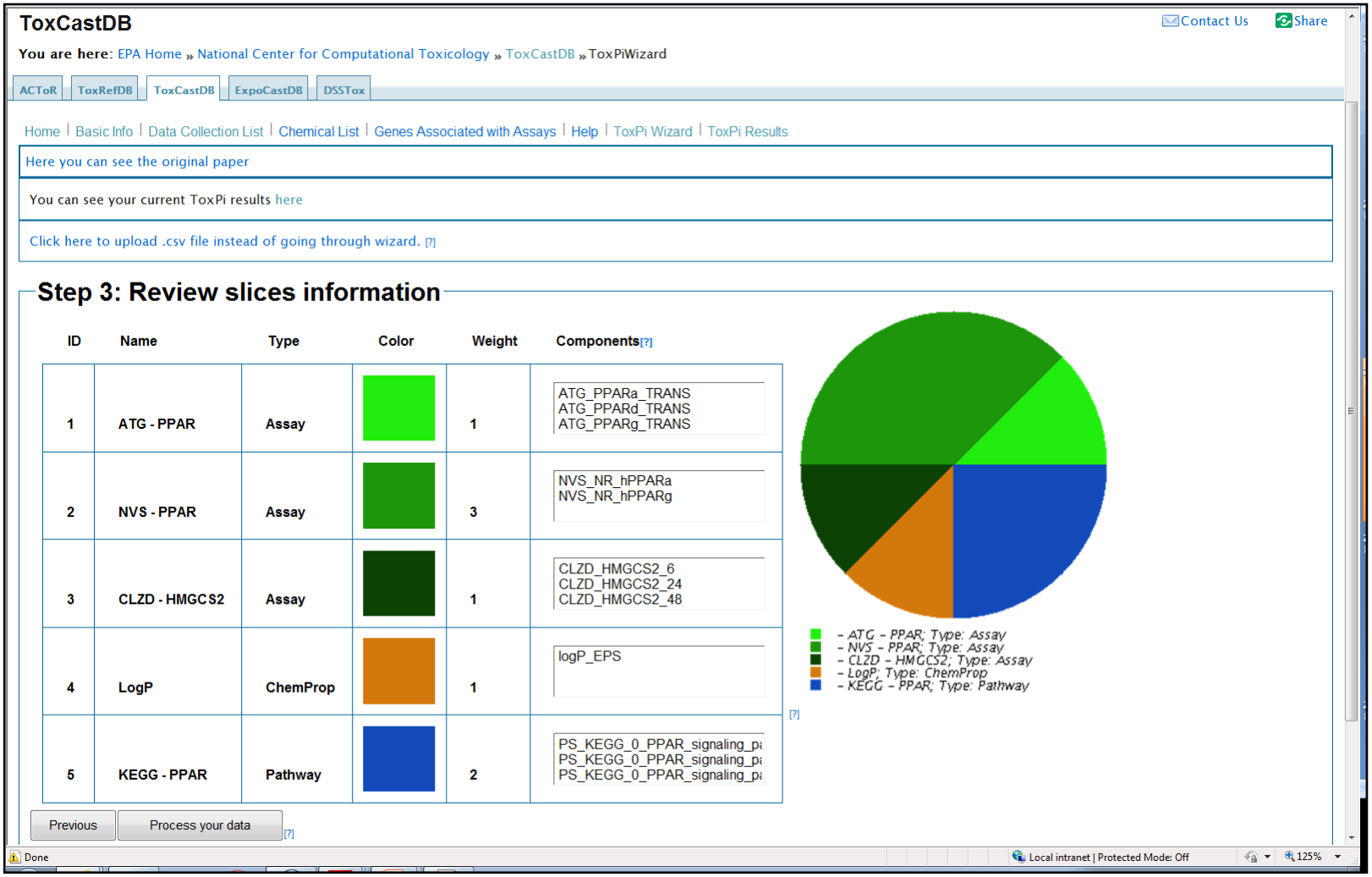
ToxPi wizard: Step 2

Options: slice type, slice components (searchable), slice weights, slice colors, return/modify previous step



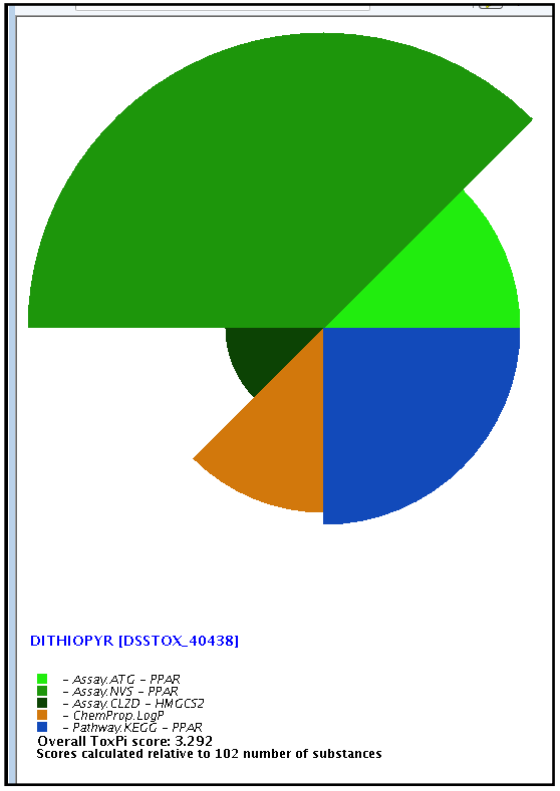
ToxPi wizard: Step 3

Options: preview ToxPi formulation, return to previous step to make changes



ToxPi wizard: Results

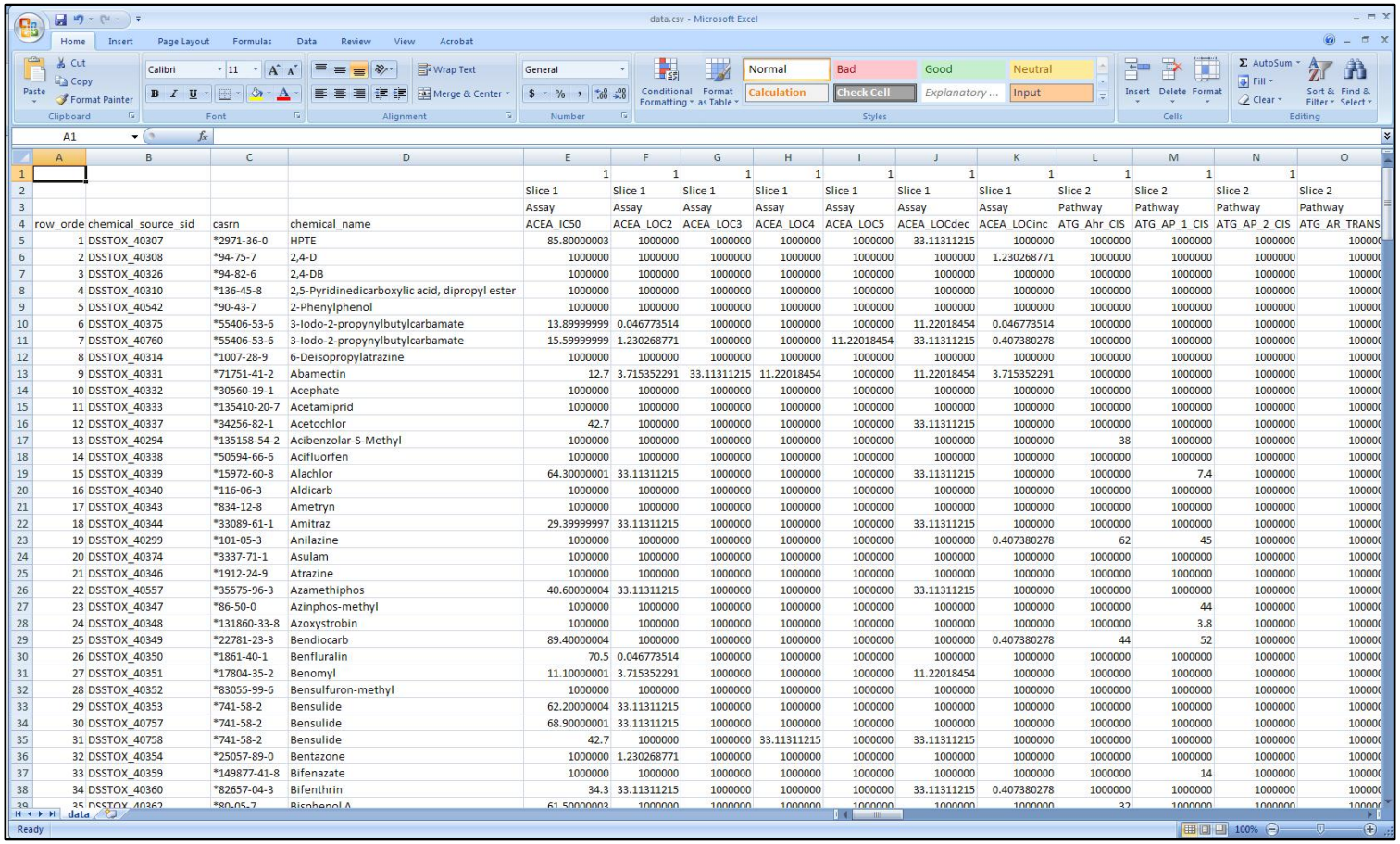
Options: dynamic sorting, modify results, highlight chemicals, download images/data/zip file(s), mouse-over to highlight particular chemicals, click to enlarge particular chemicals, return/modify previous steps



ToxPi wizard: Upload data file

Standard file format that is identical to what is provided by the downloadable results

Data upload can be used to explore data you have modified externally, produce results for data manipulations not available through the wizard, or reproduce ToxPi results



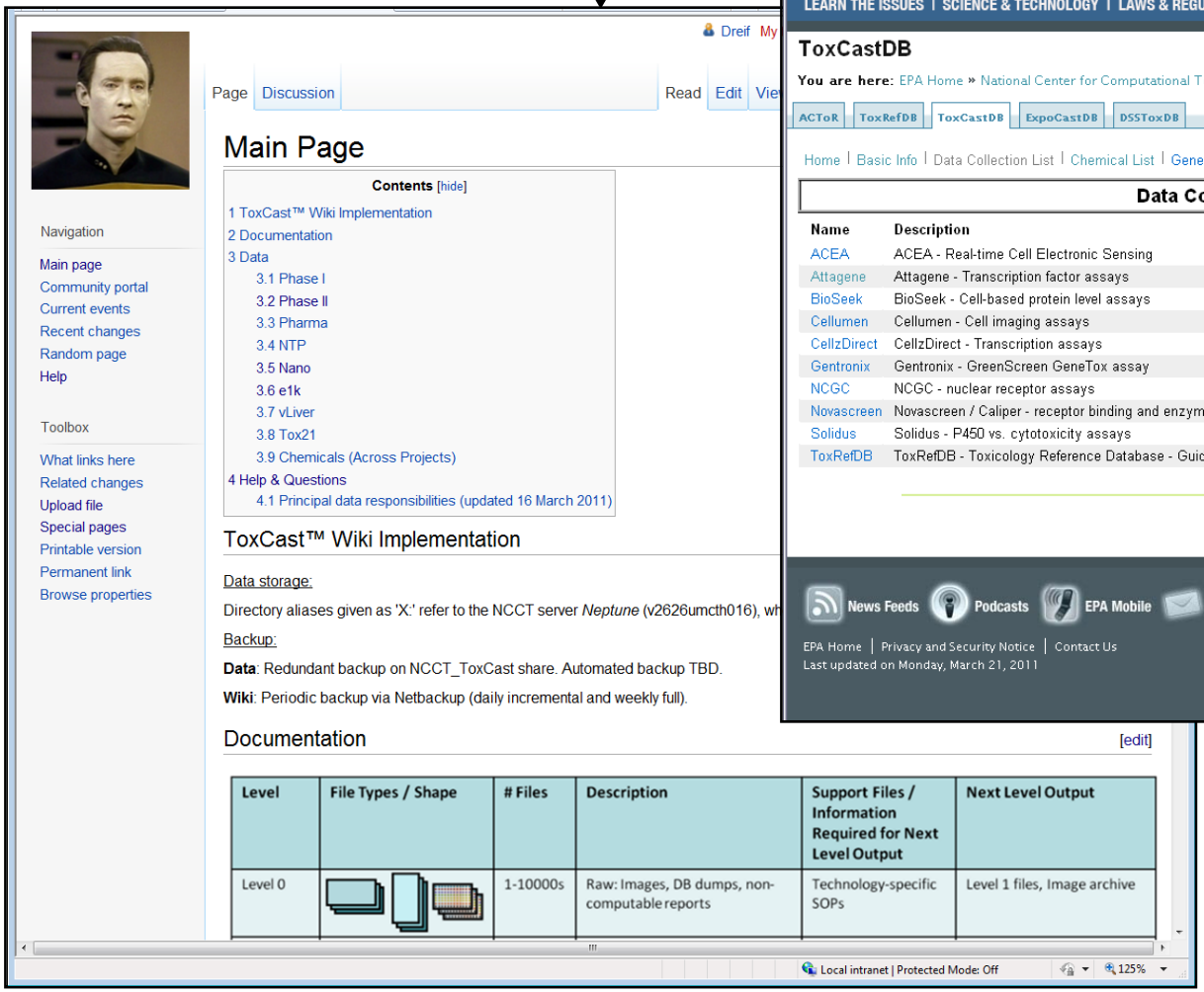
data.csv - Microsoft Excel

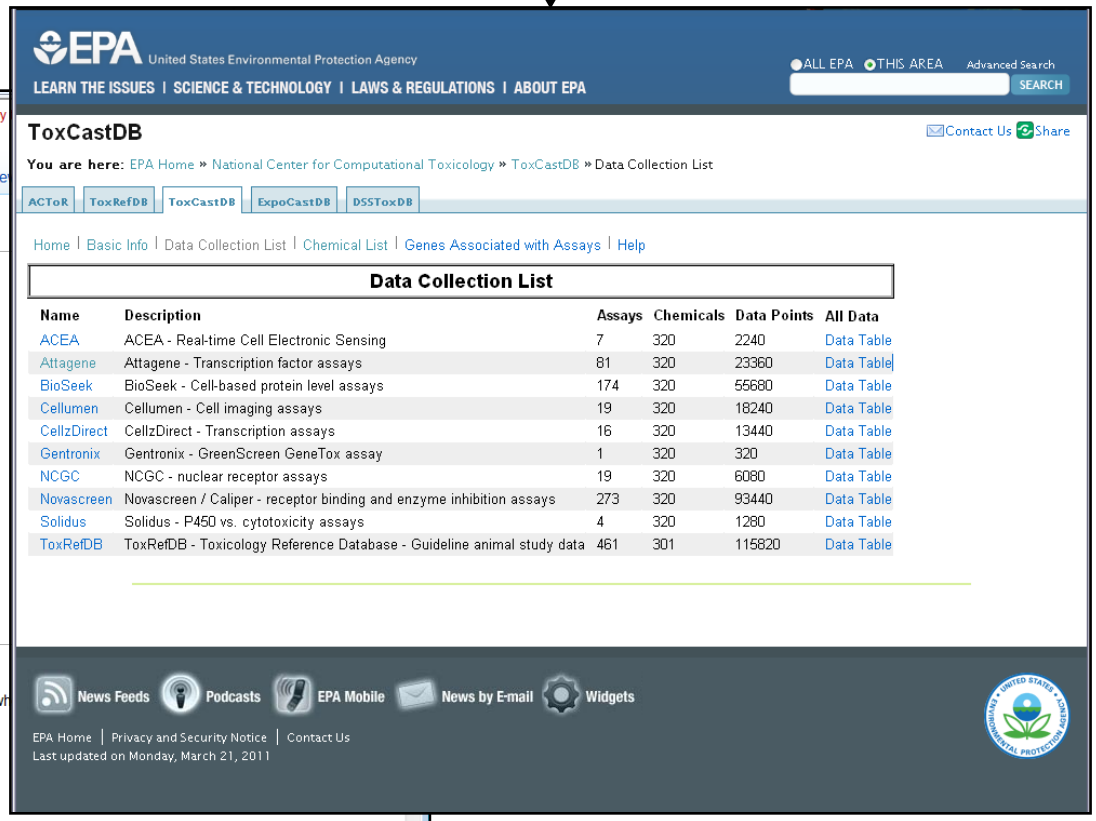
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
1					1	1	1	1	1	1	1	1	1	1	
2					Slice 1	Slice 1	Slice 1	Slice 1	Slice 1	Slice 1	Slice 1	Slice 2	Slice 2	Slice 2	Slice 2
3					Assay	Assay	Assay	Assay	Assay	Assay	Assay	Pathway	Pathway	Pathway	Pathway
4	row_orde	chemical_source_sid	casrn	chemical_name	ACEA_IC50	ACEA_LOC2	ACEA_LOC3	ACEA_LOC4	ACEA_LOC5	ACEA_LOCdec	ACEA_LOCinc	ATG_Ahr_CIS	ATG_AP_1_CIS	ATG_AP_2_CIS	ATG_AR_TRANS
5	1	DSSTOX_40307	*2971-36-0	HPTE	85.80000003	1000000	1000000	1000000	1000000	33.11311215	1000000	1000000	1000000	1000000	100000
6	2	DSSTOX_40308	*94-75-7	2,4-D	1000000	1000000	1000000	1000000	1000000	1000000	1.230268771	1000000	1000000	1000000	100000
7	3	DSSTOX_40326	*94-82-6	2,4-DB	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
8	4	DSSTOX_40310	*136-45-8	2,5-Pyridinedicarboxylic acid, dipropyl ester	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
9	5	DSSTOX_40542	*90-43-7	2-Phenylphenol	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
10	6	DSSTOX_40375	*55406-53-6	3-Iodo-2-propynylbutylcarbamate	13.89999999	0.046773514	1000000	1000000	1000000	11.22018454	0.046773514	1000000	1000000	1000000	100000
11	7	DSSTOX_40760	*55406-53-6	3-Iodo-2-propynylbutylcarbamate	15.59999999	1.230268771	1000000	1000000	11.22018454	33.11311215	0.407380278	1000000	1000000	1000000	100000
12	8	DSSTOX_40314	*1007-28-9	6-Deisopropylatrazine	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
13	9	DSSTOX_40331	*71751-41-2	Abamectin	12.7	3.715352291	33.11311215	11.22018454	1000000	11.22018454	3.715352291	1000000	1000000	1000000	100000
14	10	DSSTOX_40332	*30560-19-1	Acephate	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
15	11	DSSTOX_40333	*135410-20-7	Acetamiprid	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
16	12	DSSTOX_40337	*34256-82-1	Acetochlor	42.7	1000000	1000000	1000000	1000000	33.11311215	1000000	1000000	1000000	1000000	100000
17	13	DSSTOX_40294	*135158-54-2	Acibenzolar-S-Methyl	1000000	1000000	1000000	1000000	1000000	1000000	1000000	38	1000000	1000000	100000
18	14	DSSTOX_40338	*50594-66-6	Acifluorfen	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
19	15	DSSTOX_40339	*15972-60-8	Alachlor	64.30000001	33.11311215	1000000	1000000	1000000	33.11311215	1000000	1000000	7.4	1000000	100000
20	16	DSSTOX_40340	*116-06-3	Aldicarb	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
21	17	DSSTOX_40343	*834-12-8	Ametryn	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
22	18	DSSTOX_40344	*33089-61-1	Amitraz	29.39999997	33.11311215	1000000	1000000	1000000	33.11311215	1000000	1000000	1000000	1000000	100000
23	19	DSSTOX_40299	*101-05-3	Anilazine	1000000	1000000	1000000	1000000	1000000	1000000	0.407380278	62	45	1000000	100000
24	20	DSSTOX_40374	*3337-71-1	Asulam	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
25	21	DSSTOX_40346	*1912-24-9	Atrazine	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
26	22	DSSTOX_40557	*35575-96-3	Azamethiphos	40.60000004	33.11311215	1000000	1000000	1000000	33.11311215	1000000	1000000	1000000	1000000	100000
27	23	DSSTOX_40347	*86-50-0	Azinphos-methyl	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	44	1000000	100000
28	24	DSSTOX_40348	*131860-33-8	Azoxystrobin	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	3.8	1000000	100000
29	25	DSSTOX_40349	*22781-23-3	Bendiocarb	89.40000004	1000000	1000000	1000000	1000000	1000000	0.407380278	44	52	1000000	100000
30	26	DSSTOX_40350	*1861-40-1	Benfluralin	70.5	0.046773514	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
31	27	DSSTOX_40351	*17804-35-2	Benomyl	11.10000001	3.715352291	1000000	1000000	1000000	11.22018454	1000000	1000000	1000000	1000000	100000
32	28	DSSTOX_40352	*83055-99-6	Bensulfuron-methyl	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
33	29	DSSTOX_40353	*741-58-2	Bensulide	62.20000004	33.11311215	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
34	30	DSSTOX_40757	*741-58-2	Bensulide	68.90000001	33.11311215	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
35	31	DSSTOX_40758	*741-58-2	Bensulide	42.7	1000000	1000000	33.11311215	1000000	33.11311215	1000000	1000000	1000000	1000000	100000
36	32	DSSTOX_40354	*25057-89-0	Bentazone	1000000	1.230268771	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	100000
37	33	DSSTOX_40359	*149877-41-8	Bifenazate	1000000	1000000	1000000	1000000	1000000	1000000	1000000	1000000	14	1000000	100000
38	34	DSSTOX_40360	*82657-04-3	Bifenthrin	34.3	33.11311215	1000000	1000000	1000000	33.11311215	0.407380278	1000000	1000000	1000000	100000
39	35	DSSTOX_40362	*80-05-7	Bisphenol A	61.50000003	1000000	1000000	1000000	1000000	1000000	1000000	32	1000000	1000000	100000

All ToxCast data used in this presentation are available online via ACToR

More data on the way from multiple projects and subsequent phases of ToxCast (internal wiki)

Currently contains Phase-I results (public ACToR)





United States Environmental Protection Agency

The web application will be available soon at: http://actor.epa.gov

The internal (development) version is undergoing updates according to feedback from user testing

The ToxPi wizard will be released once these updates have been fully implemented and tested

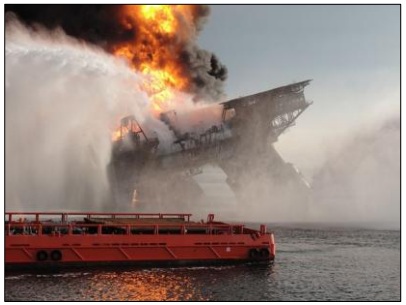
Future updates will include additional features/capabilities, as well as links to new source data

Questions?

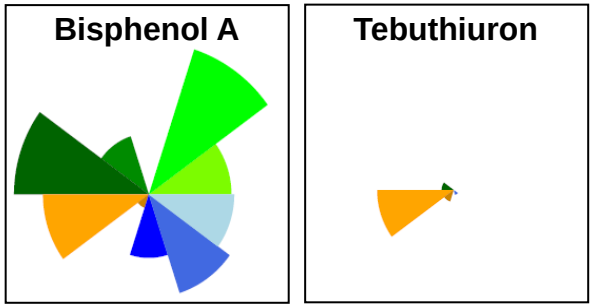
FIN

Prioritization is needed for diverse tasks

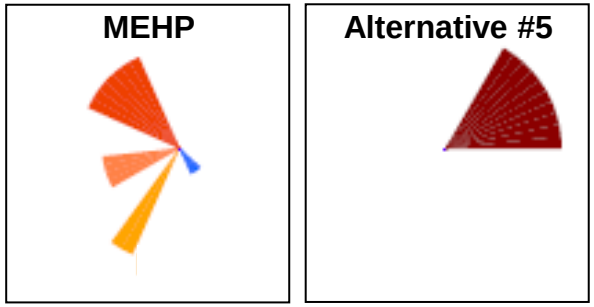
Responding to environmental emergencies: Which dispersants are safest for remediation of the Deep Water Horizon oil spill?



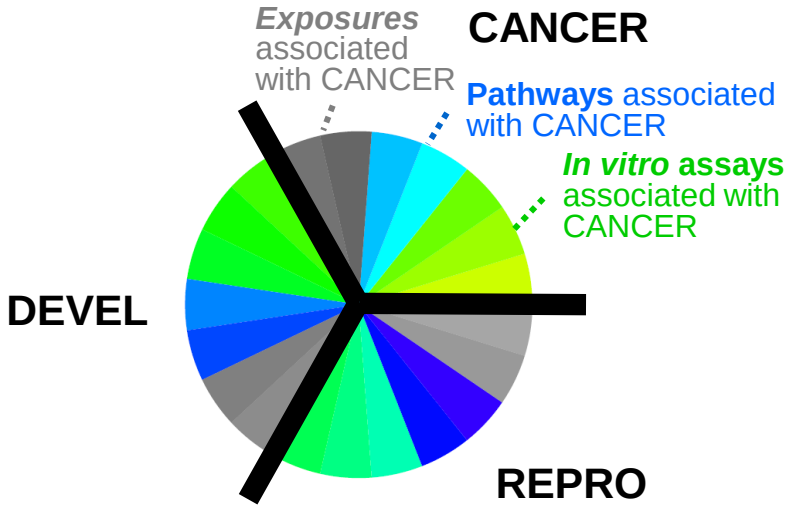
Protecting against endocrine disrupting chemicals: Supporting the Endocrine Disruptor Screening Program (EDSP)



Supporting sustainable development and Green Chemistry: Evaluating manufacturing alternatives

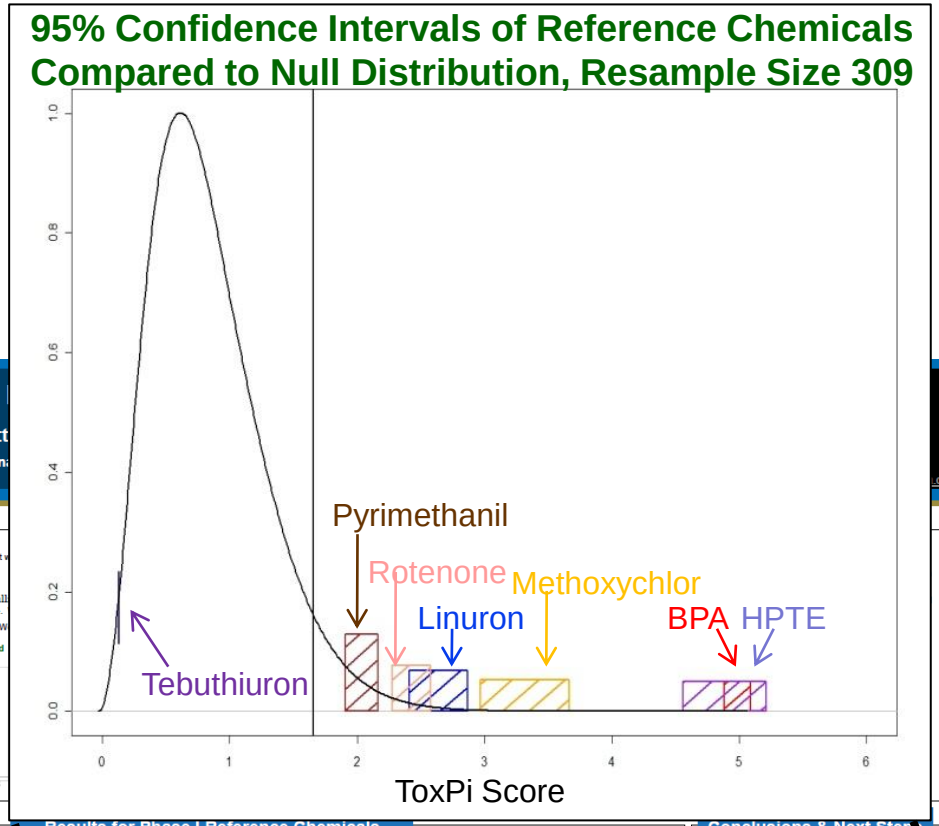


Promoting efficient, targeted testing decisions: ToxPi addressing multiple sectors of concern



Quantifying the stability of ToxPi rankings

We can make formal statements about the stability of overall rankings and specify confidence intervals for the relative activity of particular chemicals.



[Wilson et al. (2011) *Society of Toxicology Annual Meeting*]