

An interactive web application for ToxPi

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY



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.

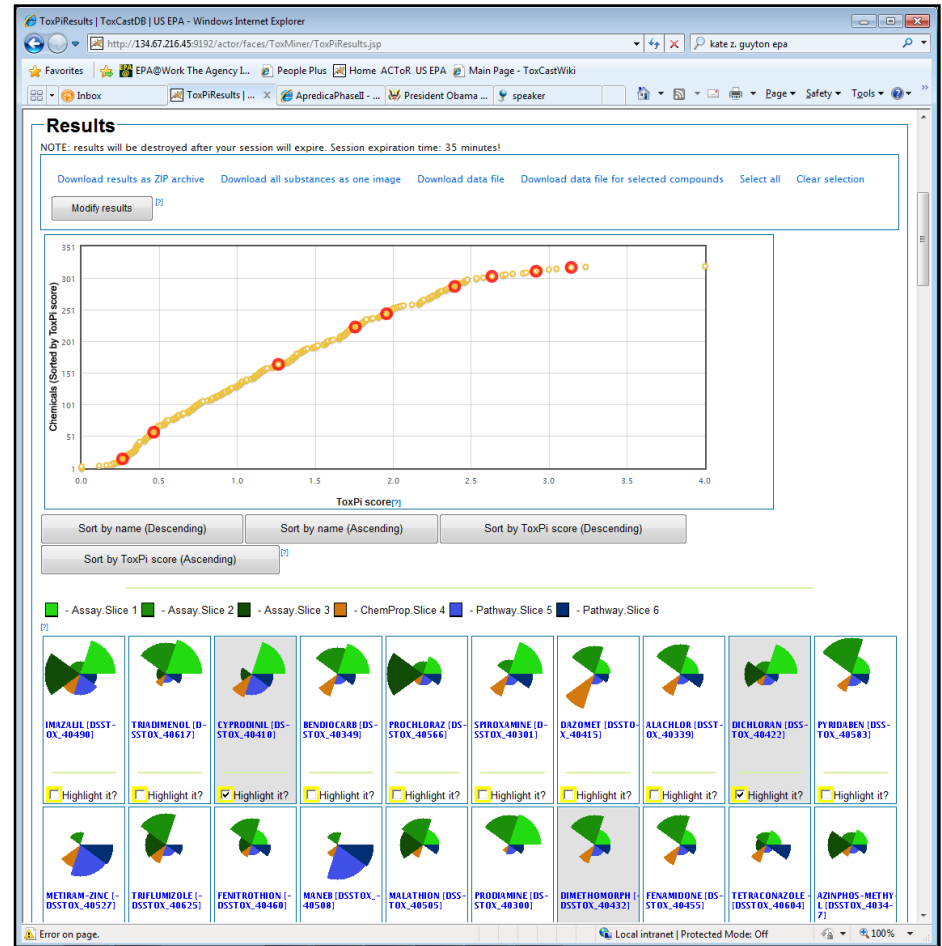


Step 3: Review slices information

ID	Name	Type	Color	Weight	Components
1	Slice 1	Assay	Light Green	2	ATG_Ahr_CIS ATG_AP_1_CIS ATG_AP_2_CIS
2	Slice 2	Assay	Dark Green	2	BSK_3C_Eselectin_down BSK_3C_Eselectin_up BSK_3C_IL6DR_down
3	Slice 3	Assay	Medium Green	2	NVS_ADME_hCYP19A1 NVS_ADME_hCYP1A1 NVS_ADME_hCYP1A2
4	Slice 4	ChemProp	Orange	1	accpHB_QP Cl_logS_QP CNS_QP
5	Slice 5	Pathway	Light Blue	2	PS_KEGG_0_PPAR_signaling PS_KEGG_0_Inositol_phosph PS_KEGG_0_Regulation_of_a
6	Slice 6	Pathway	Dark Blue	1	PS_Ingenuty_0_Axonal_Guidi PS_Ingenuty_0_Glucocorticoi PS_Ingenuty_0_Xenobiotic_M

Legend for Slices:

- Slice 1, Type: Assay (Light Green)
- Slice 2, Type: Assay (Dark Green)
- Slice 3, Type: Assay (Medium Green)
- Slice 4, Type: ChemProp (Orange)
- Slice 5, Type: Pathway (Light Blue)
- Slice 6, Type: Pathway (Dark Blue)



Results

NOTE: results will be destroyed after your session will expire. Session expiration time: 35 minutes!

Download results as ZIP archive | Download all substances as one image | Download data file | Download data file for selected compounds | Select all | Clear selection

Modify results

Chemicals (Sorted by ToxPi score)



Sort by name (Descending) | Sort by name (Ascending) | Sort by ToxPi score (Descending)

Sort by ToxPi score (Ascending)

Legend for Slices:

- Assay.Slice 1 (Light Green)
- Assay.Slice 2 (Dark Green)
- Assay.Slice 3 (Medium Green)
- ChemProp.Slice 4 (Orange)
- Pathway.Slice 5 (Light Blue)
- Pathway.Slice 6 (Dark Blue)

Chemical Name	DSSTOX ID	Highlight it?
IMAZAUL	(DSSTOX_40498)	<input type="checkbox"/>
TRIAMENOL	(DSSTOX_40617)	<input type="checkbox"/>
CYPRODINIL	(DSSTOX_40410)	<input checked="" type="checkbox"/>
BENDICARB	(DSSTOX_40349)	<input type="checkbox"/>
PROCHLORAZ	(DSSTOX_40566)	<input type="checkbox"/>
SPROXAMINE	(DSSTOX_40301)	<input type="checkbox"/>
DAZOMET	(DSSTOX_40415)	<input type="checkbox"/>
ALACHLOR	(DSSTOX_40339)	<input type="checkbox"/>
DICHLORAN	(DSSTOX_40422)	<input type="checkbox"/>
PYRIDABEN	(DSSTOX_40583)	<input type="checkbox"/>
METIRAM-ZINC	(DSSTOX_40527)	<input type="checkbox"/>
TRIFLUMZOLE	(DSSTOX_40625)	<input type="checkbox"/>
FENTROTHION	(DSSTOX_40466)	<input type="checkbox"/>
MANER	(DSSTOX_40508)	<input type="checkbox"/>
MALATHION	(DSSTOX_40595)	<input type="checkbox"/>
PRODIMAM	(DSSTOX_40300)	<input type="checkbox"/>
DIMETHOMORPH	(DSSTOX_40432)	<input type="checkbox"/>
FENAMIDONE	(DSSTOX_40455)	<input type="checkbox"/>
TETRACONAZOLE	(DSSTOX_40604)	<input checked="" type="checkbox"/>
AZINPHOS-METHY	(DSSTOX_40347)	<input type="checkbox"/>

Acknowledgments

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Office of Pollution Prevention, U.S. EPA**

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North Carolina State University**

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⁵Lockheed Martin

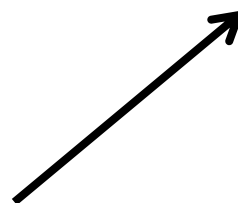
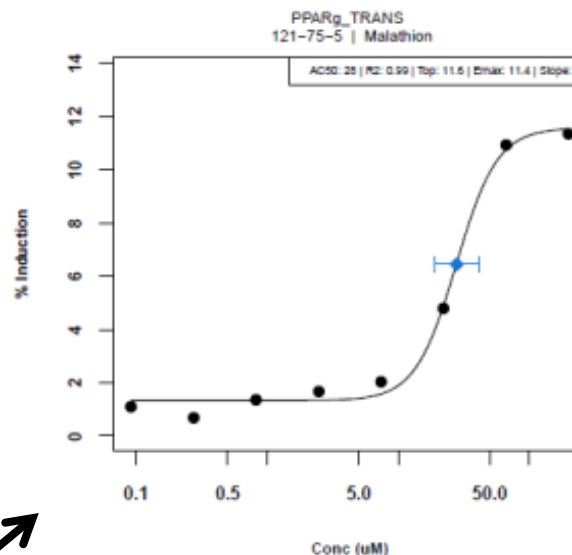
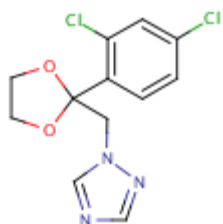
**... plus many more EPA
colleagues that are
participating in the
continued development of
this work**



What is the problem?

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

$$\begin{array}{ccccccc} \# \text{ Chemicals} & & \times & & \# \text{ Assays} & & = & & \# \text{ Results} \\ \\ 1 & & \times & & 1 & & = & & 1 \end{array}$$

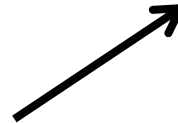
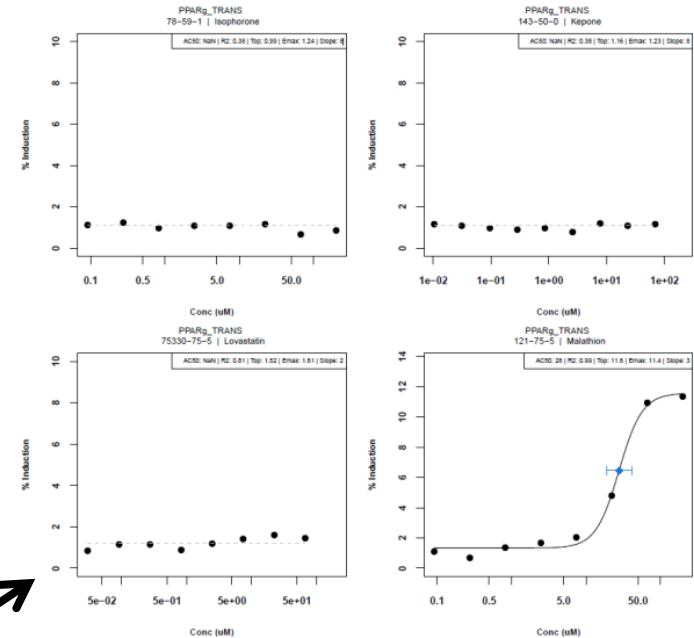
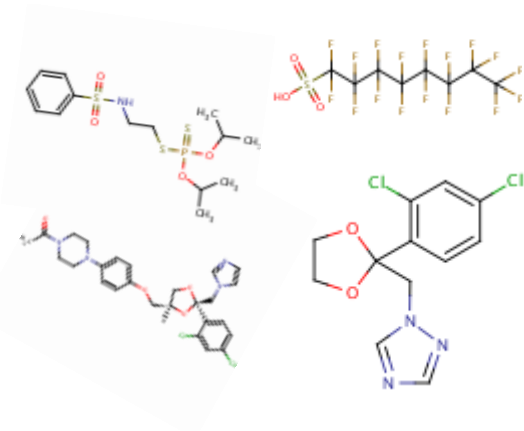


This is a manageable amount of information ... but what happens as we expand the number of chemicals and assays?

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

$$\# \text{ Chemicals} \quad \times \quad \# \text{ Assays} \quad = \quad \# \text{ Results}$$

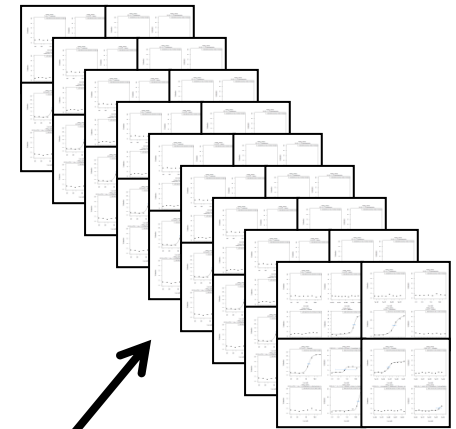
$$4 \quad \times \quad 1 \quad = \quad 4$$



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?

$$\begin{array}{ccccccc} \# \text{ Chemicals} & & \times & & \# \text{ Assays} & & = & & \# \text{ Results} \\ 100,000\text{s} & & \times & & 100\text{s} & & = & & 10,000,000\text{s} \end{array}$$



...



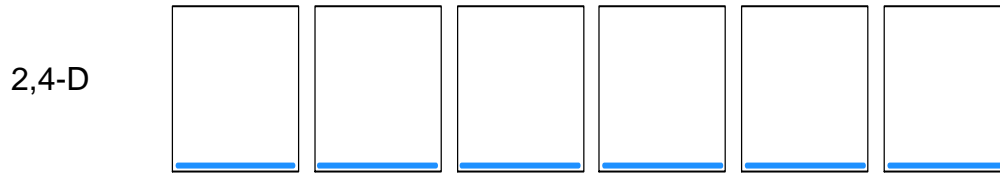
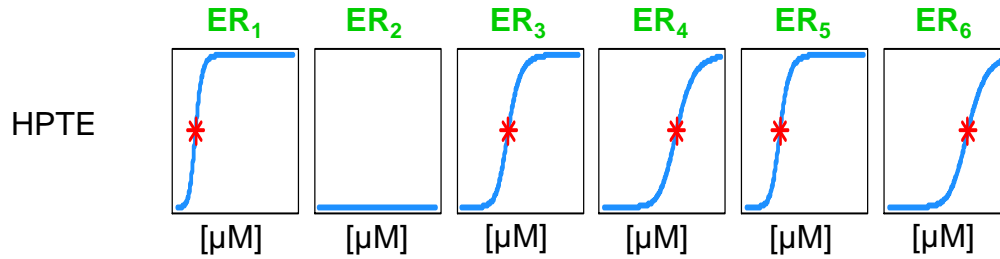
This is a problem....

...

How do we address this giant data problem?

Translating multivariate results into ToxPi profiles

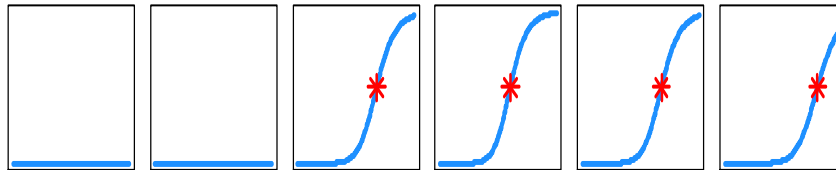
1. Sum the potency across all component assays in the ER slice for each individual chemical.



⋮

⋮

Methoxychlor



⋮

⋮

2. Normalize the summed potency across all 309 chemicals.

$$\sum_{ER} HPTE$$

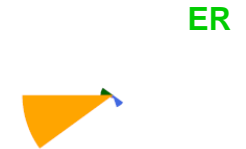
$$\sum_{ER} 2,4-D$$

⋮

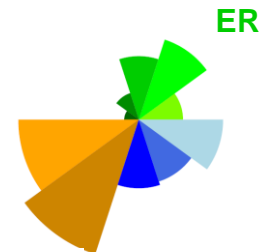
$$\sum_{ER} Methoxychlor$$

⋮

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



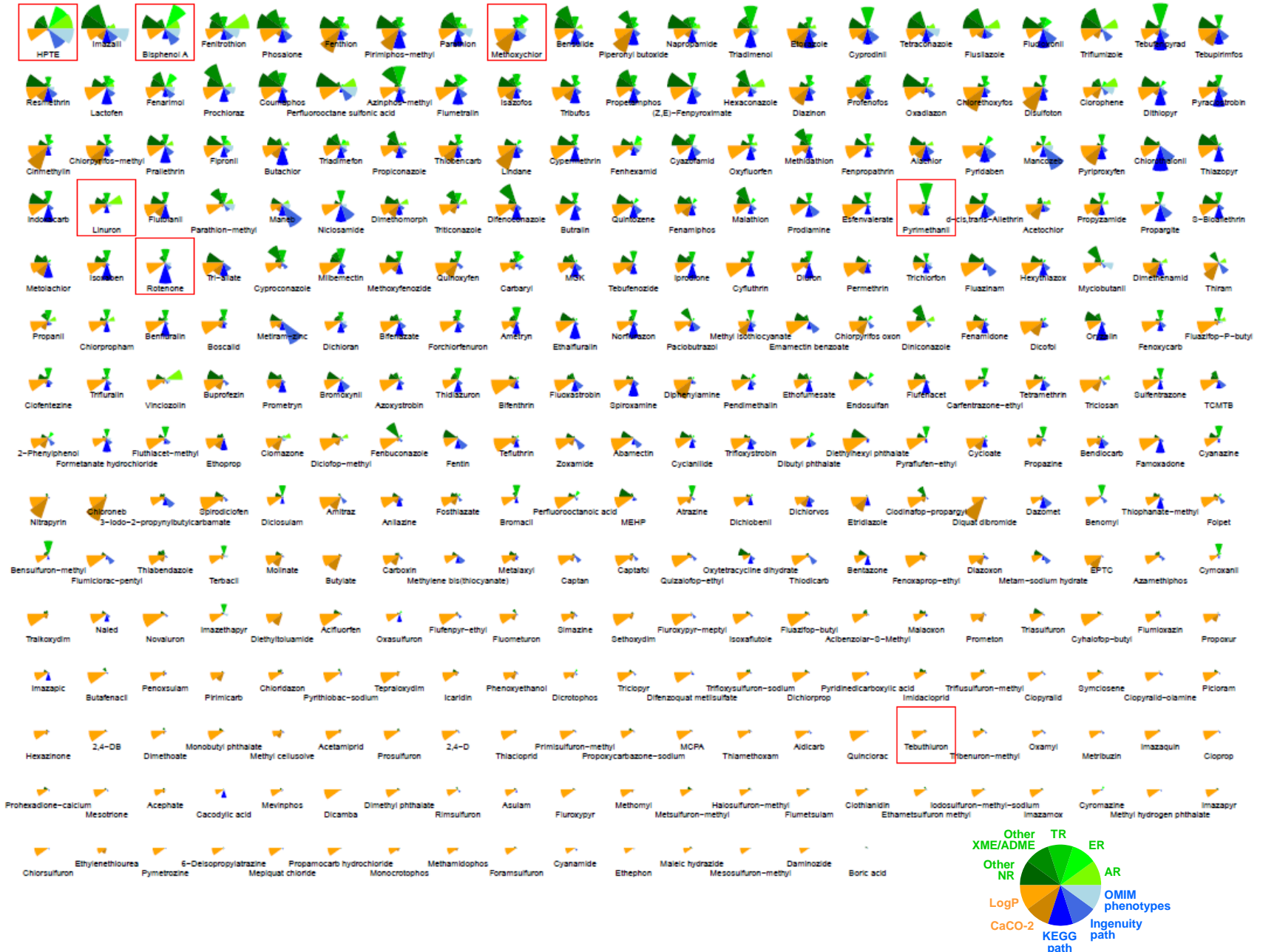
⋮



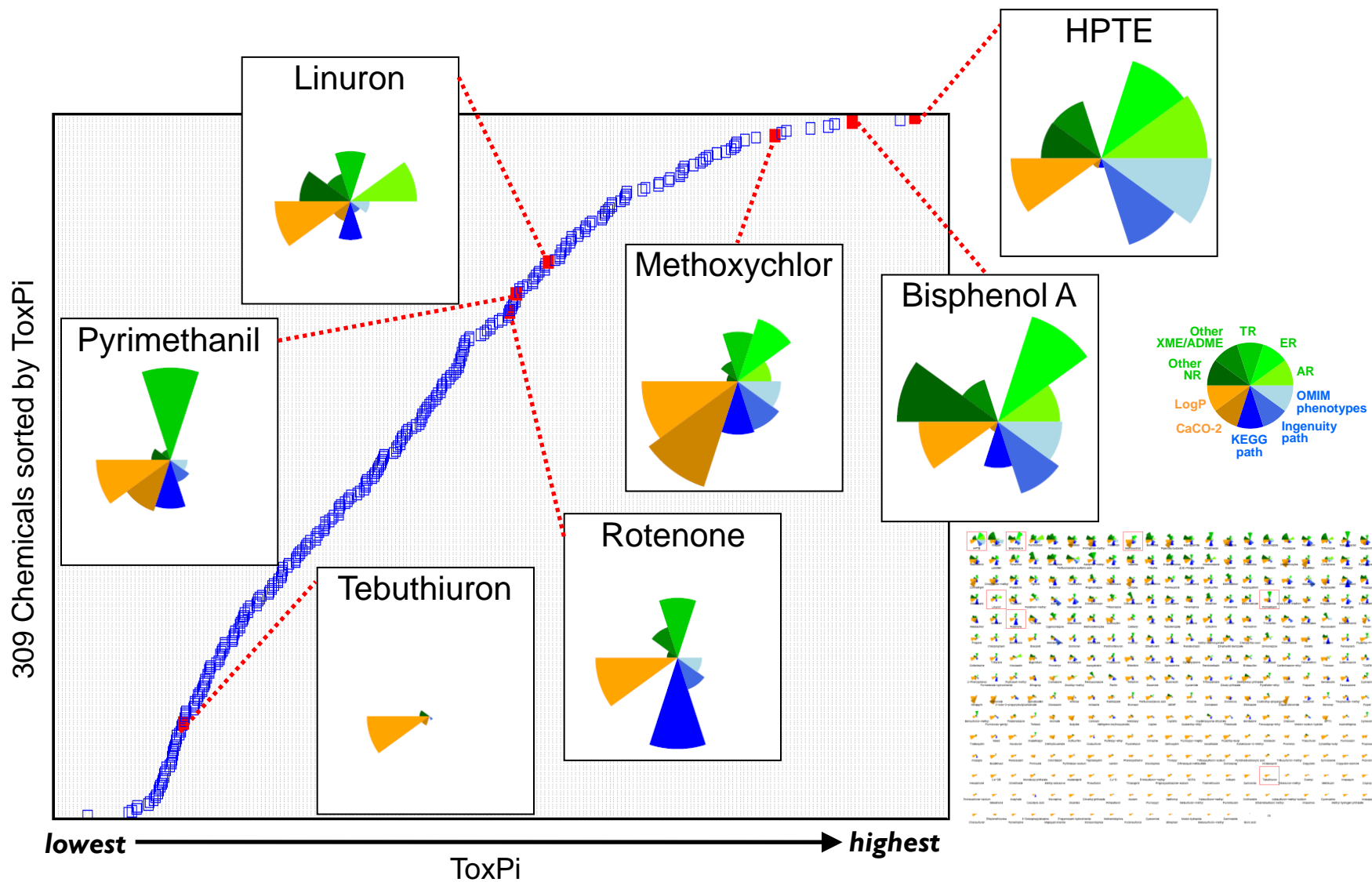
⋮

ToxPi profiles for ToxCast Phase-I chemicals

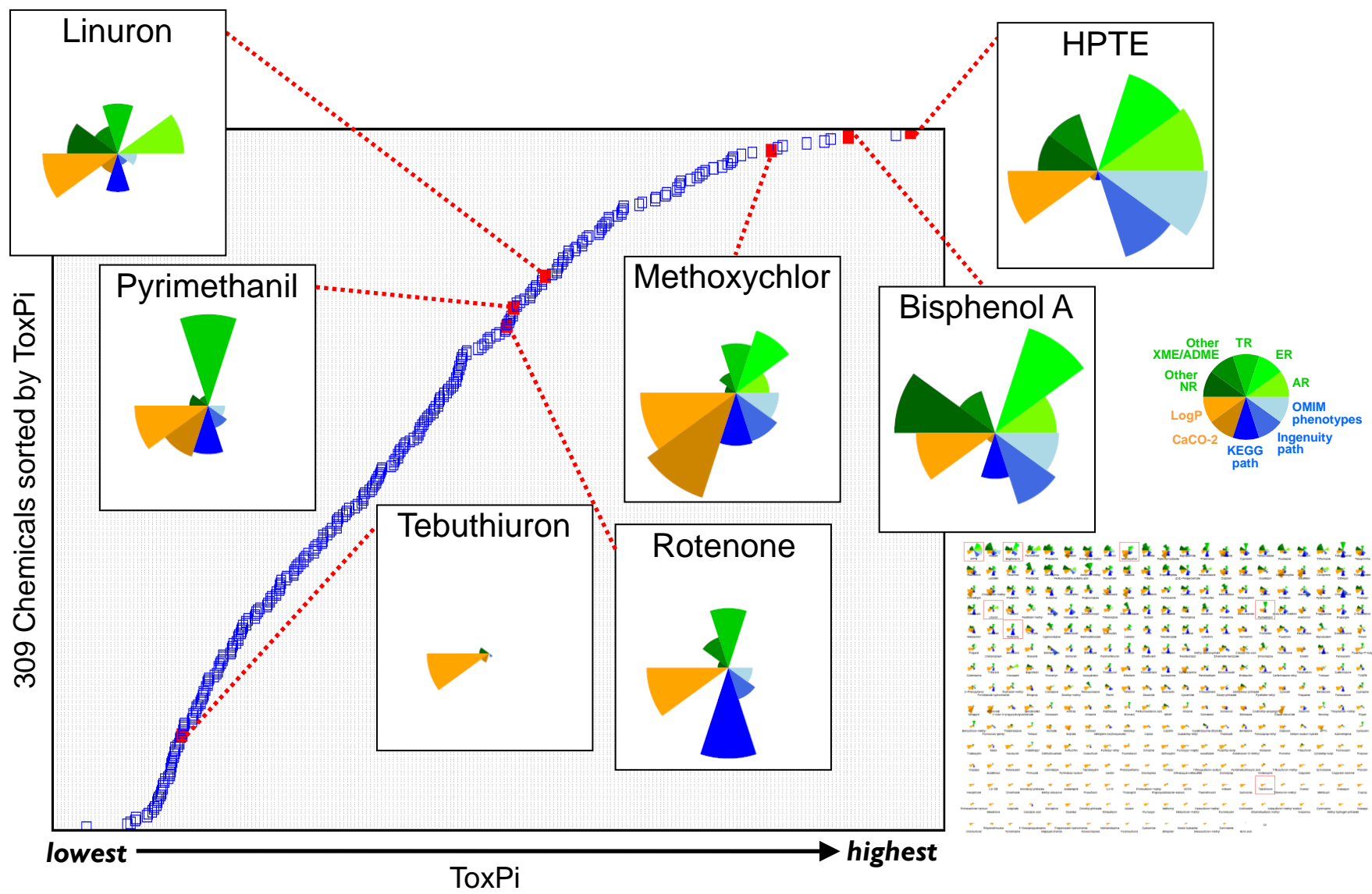
(Sorted by ToxPi; red boxes indicate "reference" chemicals)



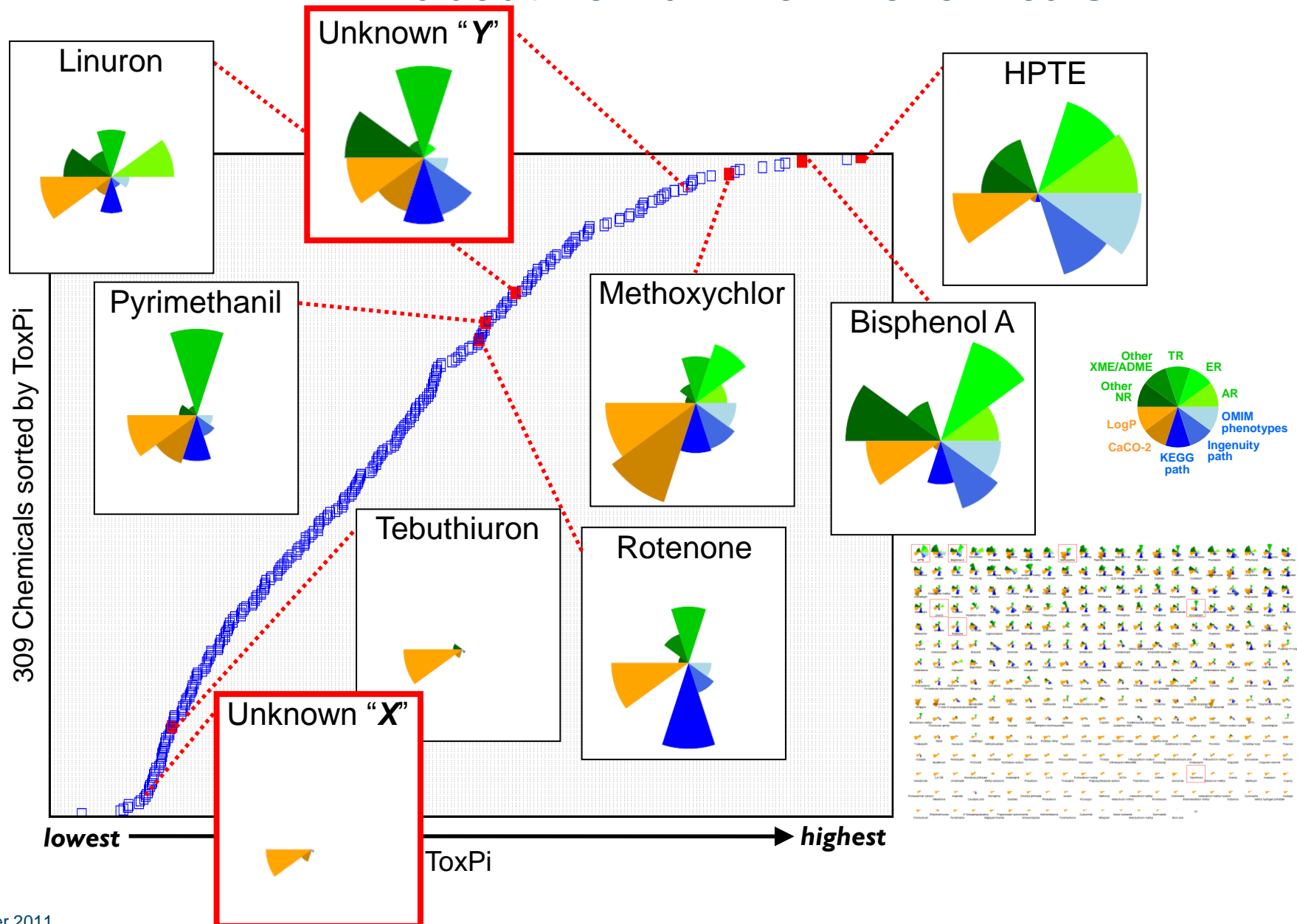
Exploring reference (“spike-in”) chemicals along the sorted ToxPi distribution



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



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



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

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.

Screenshot of the ToxPi Wizard web application. The browser address bar shows <http://134.67.216.45:9192/actor/faces/ToxMiner/ToxPiWizard.jsp>. The page title is "ToxPi Wizard | ToxCastDB | US EPA - Windows Internet Explorer".

The main content area is titled "Step 3: Review slices information". It features a table with 6 columns: ID, Name, Type, Color, Weight, and Components. To the right of the table is a pie chart representing the distribution of slices. Below the pie chart is a legend for the slice types and colors.

ID	Name	Type	Color	Weight	Components
1	Slice 1	Assay	Light Green	2	ATG_Ahr_CIS ATG_AP_1_CIS ATG_AP_2_CIS
2	Slice 2	Assay	Dark Green	2	BSK_3C_Eselectin_down BSK_3C_Eselectin_up BSK_3C_IL6ADR_down
3	Slice 3	Assay	Medium Green	2	NVS_ADME_hCYP19A1 NVS_ADME_hCYP1A1 NVS_ADME_hCYP1A2
4	Slice 4	ChemProp	Orange	1	accpHB_QP Cl_logS_QP CNS_QP
5	Slice 5	Pathway	Blue	2	PS_KEGG_0_PPAR_signaling PS_KEGG_0_Inositol_phosph PS_KEGG_0_Regulation_of_a
6	Slice 6	Pathway	Dark Blue	1	PS_Ingenuty_0_Axonal_Guidi PS_Ingenuty_0_Glucocorticoi PS_Ingenuty_0_Xenobiotic_M

Legend for slices:

- Slice 1, Type: Assay (Light Green)
- Slice 2, Type: Assay (Dark Green)
- Slice 3, Type: Assay (Medium Green)
- Slice 4, Type: ChemProp (Orange)
- Slice 5, Type: Pathway (Blue)
- Slice 6, Type: Pathway (Dark Blue)

Screenshot of the ToxPi Results web application. The browser address bar shows <http://134.67.216.45:9192/actor/faces/ToxMiner/ToxPiResults.jsp>. The page title is "ToxPi Results | ToxCastDB | US EPA - Windows Internet Explorer".

The main content area is titled "Results". It includes a note: "NOTE: results will be destroyed after your session will expire. Session expiration time: 35 minutes!". Below the note are several download options: "Download results as ZIP archive", "Download all substances as one image", "Download data file", "Download data file for selected compounds", "Select all", and "Clear selection".

A scatter plot shows "Chemicals (Sorted by ToxPi score)" on the y-axis (ranging from 0 to 351) and "ToxPi score" on the x-axis (ranging from 0.0 to 4.0). The data points form a clear upward trend, indicating that higher ToxPi scores correspond to a larger number of chemicals.

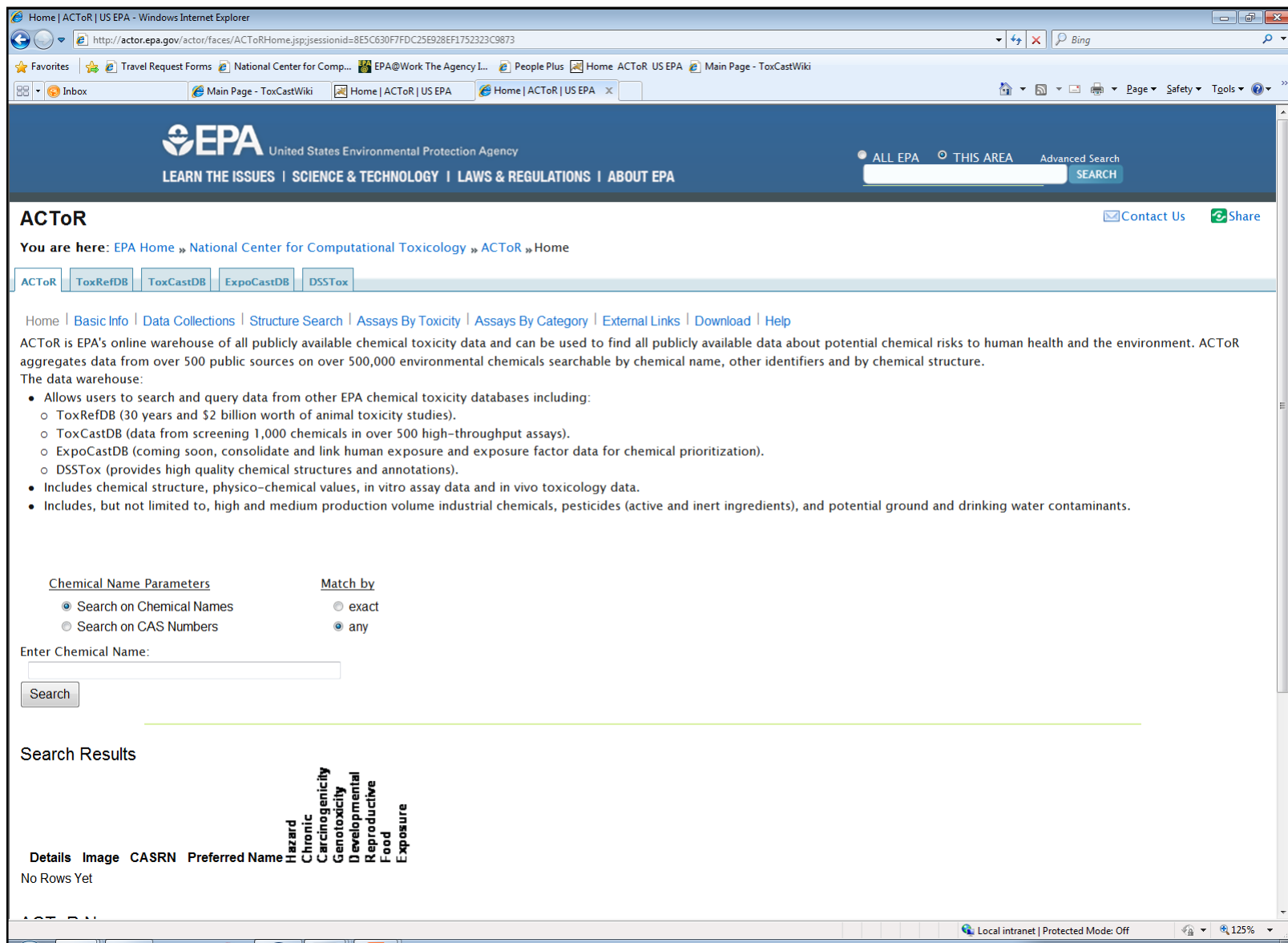
Below the plot are sorting options: "Sort by name (Descending)", "Sort by name (Ascending)", "Sort by ToxPi score (Descending)", and "Sort by ToxPi score (Ascending)".

A legend for the pie charts is provided: "- Assay.Slice 1", "- Assay.Slice 2", "- Assay.Slice 3", "- ChemProp.Slice 4", "- Pathway.Slice 5", "- Pathway.Slice 6".

The bottom section displays a grid of 10 pie charts, each representing a chemical. The chemicals listed are: IMAZAUL (DSSTOX_40498), TRIAMENOL (DSSTOX_40617), CYPRODINIL (DSSTOX_40410), BENDICARB (DSSTOX_40349), PROCHLORAZ (DSSTOX_40566), SPMOXAMINE (DSSTOX_40301), OAZOMET (DSSTOX_40415), ALACHLOR (DSSTOX_40339), DICHLORAN (DSSTOX_40422), PYRIDABEN (DSSTOX_40583), METIRAM-ZINC (DSSTOX_40527), TRIFLUMZOLE (DSSTOX_40625), FENTROTHION (DSSTOX_40466), MANER (DSSTOX_40508), MALATHION (DSSTOX_40595), PRODIMAM (DSSTOX_40300), DIMETHOMORPH (DSSTOX_40432), FENAMIDONE (DSSTOX_40455), TETRACONAZOLE (DSSTOX_40604), and AZINPHOS-METHYL (DSSTOX_40347).

Building on the ACToR infrastructure:

<http://actor.epa.gov/actor/faces/ACToRHome.jsp>



Home | ACToR | US EPA - Windows Internet Explorer

http://actor.epa.gov/actor/faces/ACToRHome.jsp;jsessionid=8E5C6307F7DC25E928EF1752323C9873

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ACToR | ToxRefDB | ToxCastDB | ExpoCastDB | DSSTox

Home | Basic Info | Data Collections | Structure Search | Assays By Toxicity | Assays By Category | External Links | Download | Help

ACToR is EPA's online warehouse of all publicly available chemical toxicity data and can be used to find all publicly available data about potential chemical risks to human health and the environment. ACToR aggregates data from over 500 public sources on over 500,000 environmental chemicals searchable by chemical name, other identifiers and by chemical structure.

The data warehouse:

- Allows users to search and query data from other EPA chemical toxicity databases including:
 - ToxRefDB (30 years and \$2 billion worth of animal toxicity studies).
 - ToxCastDB (data from screening 1,000 chemicals in over 500 high-throughput assays).
 - ExpoCastDB (coming soon, consolidate and link human exposure and exposure factor data for chemical prioritization).
 - DSSTox (provides high quality chemical structures and annotations).
- Includes chemical structure, physico-chemical values, in vitro assay data and in vivo toxicology data.
- Includes, but not limited to, high and medium production volume industrial chemicals, pesticides (active and inert ingredients), and potential ground and drinking water contaminants.

Chemical Name Parameters

Match by

Search on Chemical Names

Search on CAS Numbers

exact

any

Enter Chemical Name:

Search

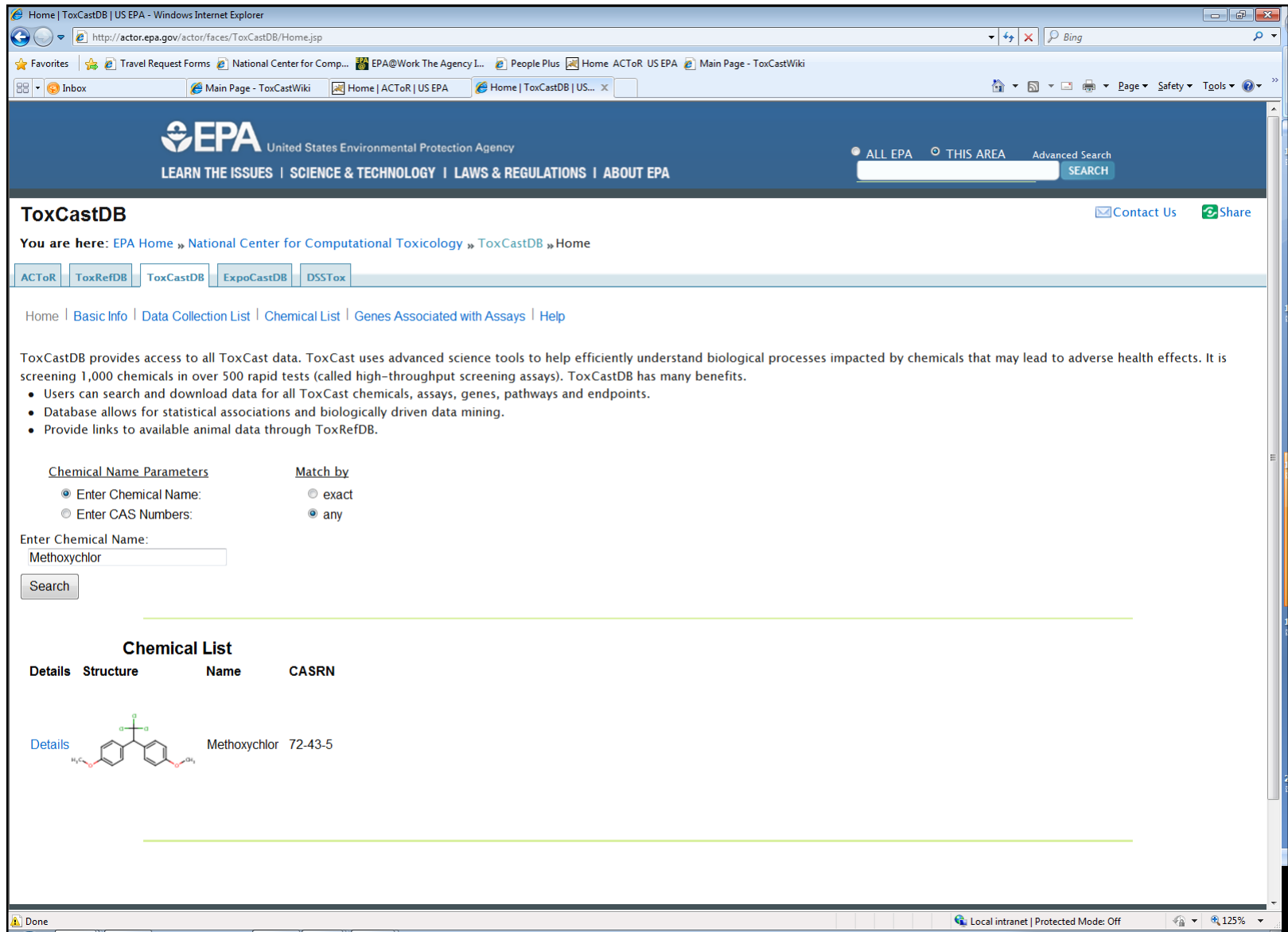
Search Results

Hazard
 Chronic
 Carcinogenicity
 Genotoxicity
 Developmental
 Reproductive
 Food
 Exposure

Details Image CASRN Preferred Name

No Rows Yet

Local intranet | Protected Mode: Off



The screenshot shows the ToxCastDB web application interface. At the top, there is the EPA logo and navigation links: "LEARN THE ISSUES | SCIENCE & TECHNOLOGY | LAWS & REGULATIONS | ABOUT EPA". A search bar is located on the right side of the header.

The main content area is titled "ToxCastDB" and includes a breadcrumb trail: "You are here: EPA Home » National Center for Computational Toxicology » ToxCastDB » Home". Below this, there are tabs for "ACToR", "ToxRefDB", "ToxCastDB", "ExpoCastDB", and "DSSTox".

Navigation links include "Home", "Basic Info", "Data Collection List", "Chemical List", "Genes Associated with Assays", and "Help".

A paragraph describes the database: "ToxCastDB provides access to all ToxCast data. ToxCast uses advanced science tools to help efficiently understand biological processes impacted by chemicals that may lead to adverse health effects. It is screening 1,000 chemicals in over 500 rapid tests (called high-throughput screening assays). ToxCastDB has many benefits." This is followed by a bulleted list of benefits:

- Users can search and download data for all ToxCast chemicals, assays, genes, pathways and endpoints.
- Database allows for statistical associations and biologically driven data mining.
- Provide links to available animal data through ToxRefDB.

Below the text, there are search options:

Chemical Name Parameters

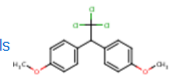
Enter Chemical Name:
 Enter CAS Numbers:

Match by

exact
 any

The "Enter Chemical Name:" field contains "Methoxychlor" and a "Search" button is visible.

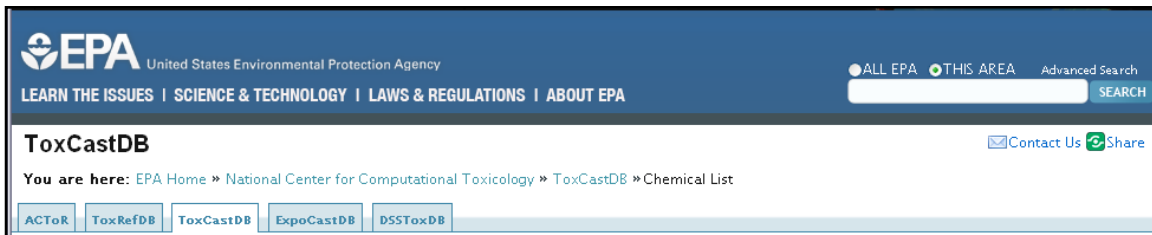
The "Chemical List" section shows a table with columns: "Details", "Structure", "Name", and "CASRN". The first entry is:

Details	Structure	Name	CASRN
Details		Methoxychlor	72-43-5

The chemical structure is a biphenyl ring system with a central carbon atom bonded to two chlorine atoms and two methoxy groups (-OCH₃).

Building on the ACToR infrastructure: ToxCast chemicals and assays

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



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You are here: EPA Home » National Center for Computational Toxicology » ToxCastDB » Chemical List

[ACToR](#) [ToxRefDB](#) [ToxCastDB](#) [ExpoCastDB](#) [DSSToxDB](#)

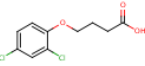
[Home](#) | [Basic Info](#) | [Data Collection List](#) | [Chemical List](#) | [Genes Associated with Assays](#) | [Help](#)

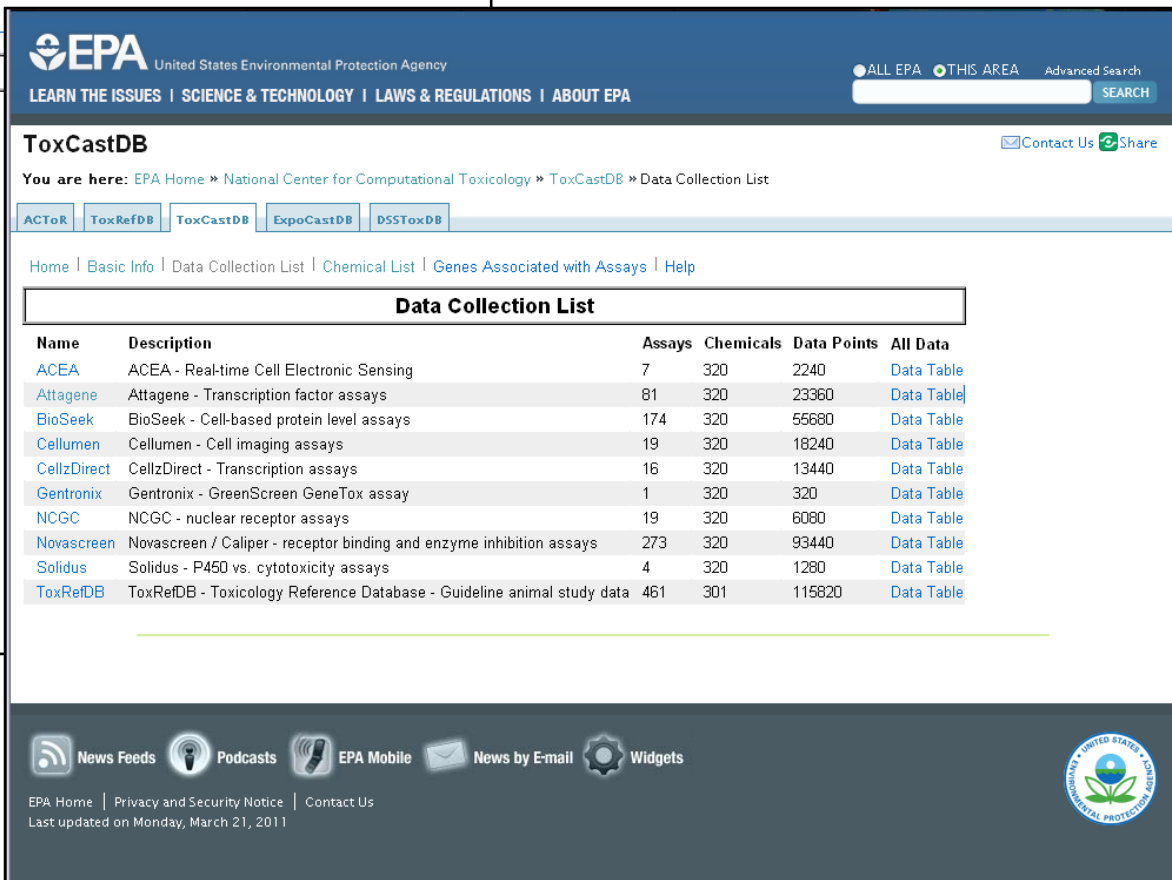
Chemical List

[Details](#) [Structure](#) **Name** CASRN

[Details](#)  **HPTE** 2971-36-0

[Details](#)  **2,4-D** 94-75-7

[Details](#)  **2,4-DB** 94-82-6



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You are here: EPA Home » National Center for Computational Toxicology » ToxCastDB » Data Collection List

[ACToR](#) [ToxRefDB](#) [ToxCastDB](#) [ExpoCastDB](#) [DSSToxDB](#)


[Home](#) | [Basic Info](#) | [Data Collection List](#) | [Chemical List](#) | [Genes Associated with Assays](#) | [Help](#)

Data Collection List

Name	Description	Assays	Chemicals	Data Points	All Data
ACEA	ACEA - Real-time Cell Electronic Sensing	7	320	2240	Data Table
Attagene	Attagene - Transcription factor assays	81	320	23360	Data Table
BioSeek	BioSeek - Cell-based protein level assays	174	320	55680	Data Table
Cellumen	Cellumen - Cell imaging assays	19	320	18240	Data Table
CellzDirect	CellzDirect - Transcription assays	16	320	13440	Data Table
Gentronix	Gentronix - GreenScreen GeneTox assay	1	320	320	Data Table
NCGC	NCGC - nuclear receptor assays	19	320	6080	Data Table
Novascreen	Novascreen / Caliper - receptor binding and enzyme inhibition assays	273	320	93440	Data Table
Solidus	Solidus - P450 vs. cytotoxicity assays	4	320	1280	Data Table
ToxRefDB	ToxRefDB - Toxicology Reference Database - Guideline animal study data	461	301	115820	Data Table

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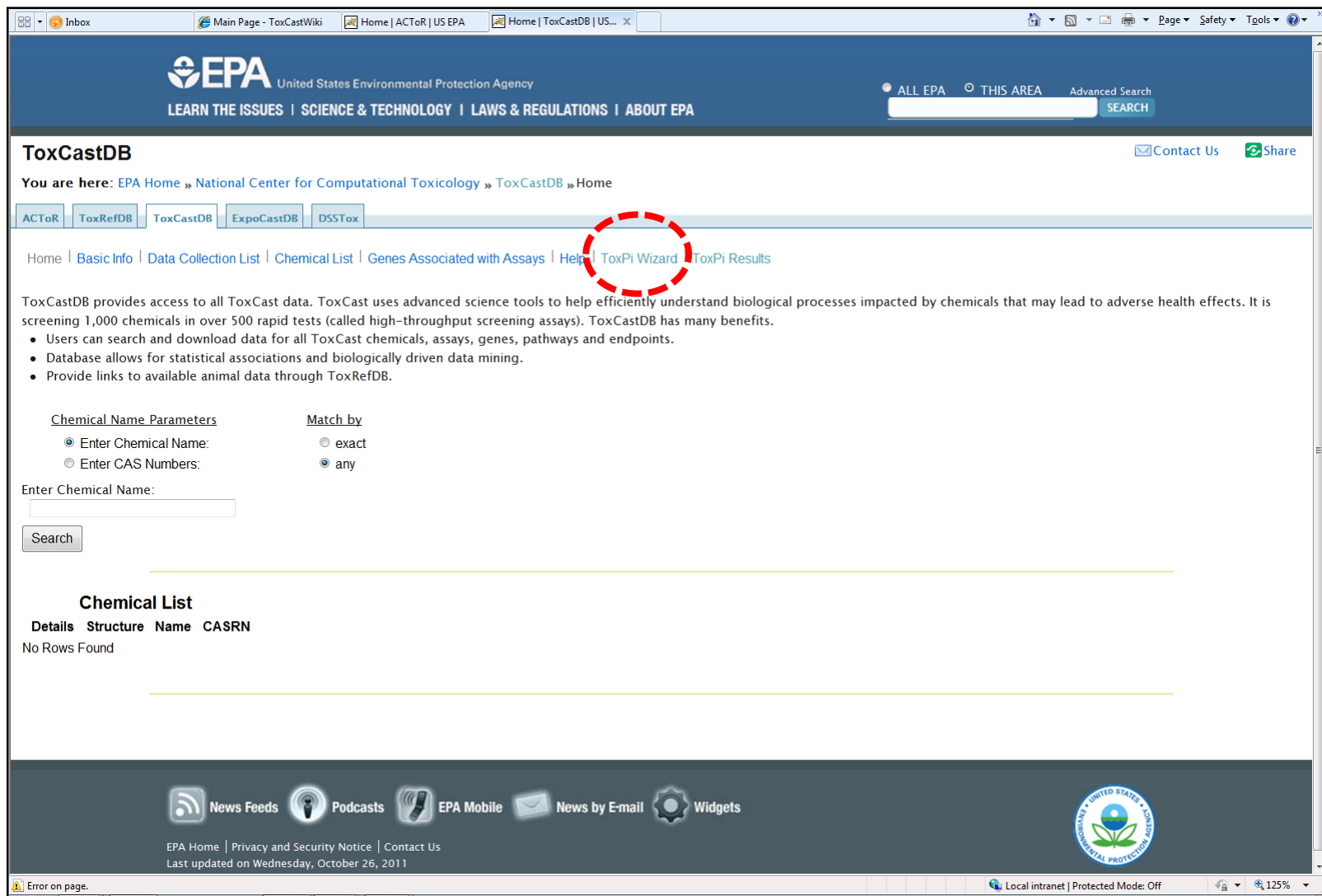
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Last updated on Monday, March 21, 2011



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

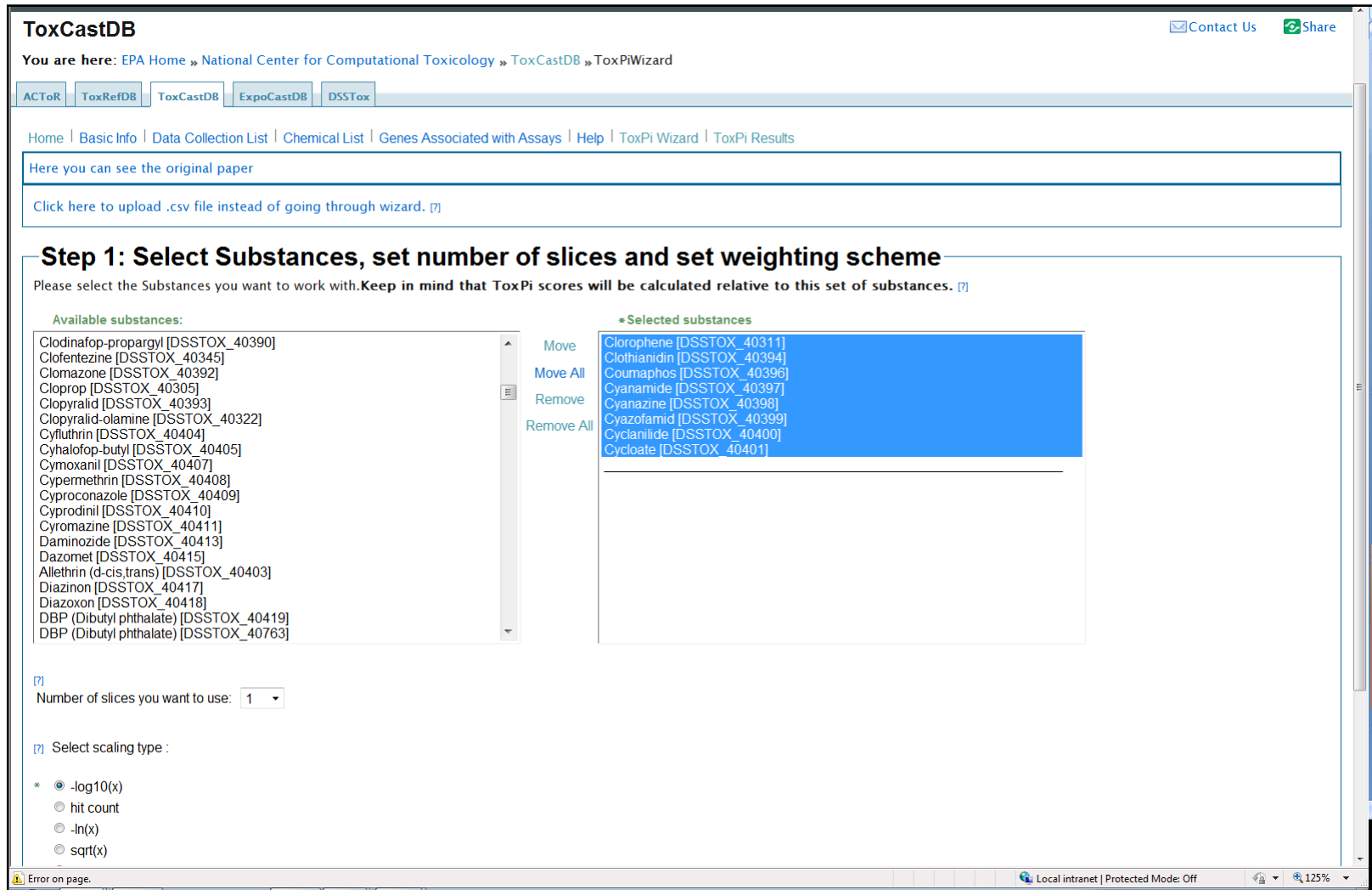
The step-by-step ToxPi wizard is implemented under the ToxCastDB tab

NOTE: The development version is undergoing final pre-release updating/testing on the EPA Intranet



The screenshot shows the EPA ToxCastDB website interface. At the top, there is the EPA logo and navigation links: "LEARN THE ISSUES | SCIENCE & TECHNOLOGY | LAWS & REGULATIONS | ABOUT EPA". A search bar is located on the right. Below the header, the "ToxCastDB" title is displayed, along with "Contact Us" and "Share" links. A breadcrumb trail reads: "You are here: EPA Home » National Center for Computational Toxicology » ToxCastDB » Home". A horizontal menu contains tabs for "ACToR", "ToxRefDB", "ToxCastDB", "ExpoCastDB", and "DSSTox". The "ToxCastDB" tab is active, and within it, the "ToxPi Wizard" link is circled in red. Other links in the breadcrumb include "Home", "Basic Info", "Data Collection List", "Chemical List", "Genes Associated with Assays", "Help", and "ToxPi Results". The main content area describes ToxCastDB's purpose: "ToxCastDB provides access to all ToxCast data. ToxCast uses advanced science tools to help efficiently understand biological processes impacted by chemicals that may lead to adverse health effects. It is screening 1,000 chemicals in over 500 rapid tests (called high-throughput screening assays). ToxCastDB has many benefits." This is followed by a bulleted list of benefits: "Users can search and download data for all ToxCast chemicals, assays, genes, pathways and endpoints.", "Database allows for statistical associations and biologically driven data mining.", and "Provide links to available animal data through ToxRefDB." Below this is a search section titled "Chemical Name Parameters" and "Match by". Under "Chemical Name Parameters", there are radio buttons for "Enter Chemical Name:" (selected) and "Enter CAS Numbers:". Under "Match by", there are radio buttons for "exact" and "any" (selected). A text input field for "Enter Chemical Name:" and a "Search" button are provided. Below the search section is a "Chemical List" section with sub-links for "Details", "Structure", "Name", and "CASRN". It states "No Rows Found". The footer contains links for "News Feeds", "Podcasts", "EPA Mobile", "News by E-mail", and "Widgets", along with the EPA logo and a copyright notice: "EPA Home | Privacy and Security Notice | Contact Us | Last updated on Wednesday, October 26, 2011". The browser's status bar at the bottom shows "Local intranet | Protected Mode: Off" and a zoom level of "125%".

Options: chemicals, number of slices, data scaling



ToxCastDB Contact Us Share

You are here: EPA Home » National Center for Computational Toxicology » ToxCastDB » ToxPiWizard

ACToR | ToxRefDB | **ToxCastDB** | ExpoCastDB | DSSTox

Home | Basic Info | Data Collection List | Chemical List | Genes Associated with Assays | Help | ToxPi Wizard | ToxPi Results

Here you can see the original paper

[Click here to upload .csv file instead of going through wizard. \[?\]](#)

Step 1: Select Substances, set number of slices and set weighting scheme

Please select the Substances you want to work with. Keep in mind that ToxPi scores will be calculated relative to this set of substances. [?]

Available substances:

- Clodinafop-propargyl [DSSTOX_40390]
- Clofentazine [DSSTOX_40345]
- Clomazone [DSSTOX_40392]
- Cloprop [DSSTOX_40305]
- Clopyralid [DSSTOX_40393]
- Clopyralid-olamine [DSSTOX_40322]
- Cyfluthrin [DSSTOX_40404]
- Cyhalofop-butyl [DSSTOX_40405]
- Cymoxanil [DSSTOX_40407]
- Cypermethrin [DSSTOX_40408]
- Cyproconazole [DSSTOX_40409]
- Cyprodinil [DSSTOX_40410]
- Cyromazine [DSSTOX_40411]
- Daminozide [DSSTOX_40413]
- Dazomet [DSSTOX_40415]
- Allethrin (d-cis,trans) [DSSTOX_40403]
- Diazinon [DSSTOX_40417]
- Diazoxon [DSSTOX_40418]
- DBP (Dibutyl phthalate) [DSSTOX_40419]
- DBP (Dibutyl phthalate) [DSSTOX_40763]

Selected substances:

- Clorophene [DSSTOX_40311]
- Clothianidin [DSSTOX_40394]
- Coumaphos [DSSTOX_40396]
- Cyanamide [DSSTOX_40397]
- Cyanazine [DSSTOX_40398]
- Cyazofamid [DSSTOX_40399]
- Cyclanilide [DSSTOX_40400]
- Cycloate [DSSTOX_40401]

[?] Number of slices you want to use:

[?] Select scaling type :

- * $-\log_{10}(x)$
- hit count
- $-\ln(x)$
- \sqrt{x}

Error on page. Local intranet | Protected Mode: Off 125%

ToxPi wizard: Step 2

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

You are here: EPA Home » National Center for Computational Toxicology » ToxCastDB » ToxPiWizard



ACToR | ToxRefDB | ToxCastDB | ExpoCastDB | DSSTox

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Here you can see the original paper

Click here to upload .csv file instead of going through wizard. [?]

Step 2: Set slices information

ID [?]	Name [?]	Type [?]	Color [?]	Weight [?]	Components [?]
1	ATG - PPAR	<input checked="" type="radio"/> Assay <input type="radio"/> Pathway <input type="radio"/> ChemProp <input type="radio"/> Exposure <input type="radio"/> ToxRef <input type="radio"/> Custom Custom type		1	Select source: [?] Attagene ATG_PPArA_TRANS ATG_PPArD_TRANS ATG_PPArG_TRANS ATG_Ahr_CIS ATG_AP_1_CIS
2	NVS - PPAR	<input checked="" type="radio"/> Assay <input type="radio"/> Pathway <input type="radio"/> ChemProp <input type="radio"/> Exposure <input type="radio"/> ToxRef <input type="radio"/> Custom Custom type		1	Select source: [?] ACEA NVS_NR_hPPArA NVS_NR_hPPArG

Color picker dialog: R: 12, G: 67, B: 4, H: 112.380, S: 94.029, B: 26.274, # 0c4304

Browser status bar: Error on page. Local intranet | Protected Mode: Off | 125%

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

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Here you can see the original paper

You can see your current ToxPi results here

[Click here to upload .csv file instead of going through wizard.](#) [?]

Step 3: Review slices information

ID	Name	Type	Color	Weight	Components [?]
1	ATG - PPAR	Assay		1	ATG_PPAPa_TRANS ATG_PPAPd_TRANS ATG_PPAPg_TRANS
2	NVS - PPAR	Assay		3	NVS_NR_hPPAPa NVS_NR_hPPAPg
3	CLZD - HMGC2	Assay		1	CLZD_HMGC2_6 CLZD_HMGC2_24 CLZD_HMGC2_48
4	LogP	ChemProp		1	logP_EPS
5	KEGG - PPAR	Pathway		2	PS_KEGG_0_PPAP_signaling_pi PS_KEGG_0_PPAP_signaling_pi PS_KEGG_0_PPAP_signaling_pi



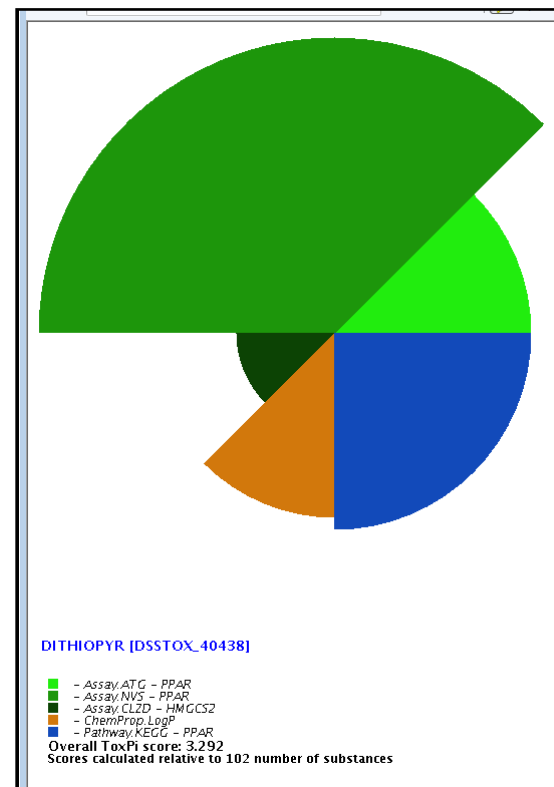
- - ATG - PPAR; Type: Assay
- - NVS - PPAR; Type: Assay
- - CLZD - HMGC2; Type: Assay
- - LogP; Type: ChemProp
- - KEGG - PPAR; Type: Pathway

[?]

[Previous](#) | [Process your data](#) [?]

ToxPi wizard: Results

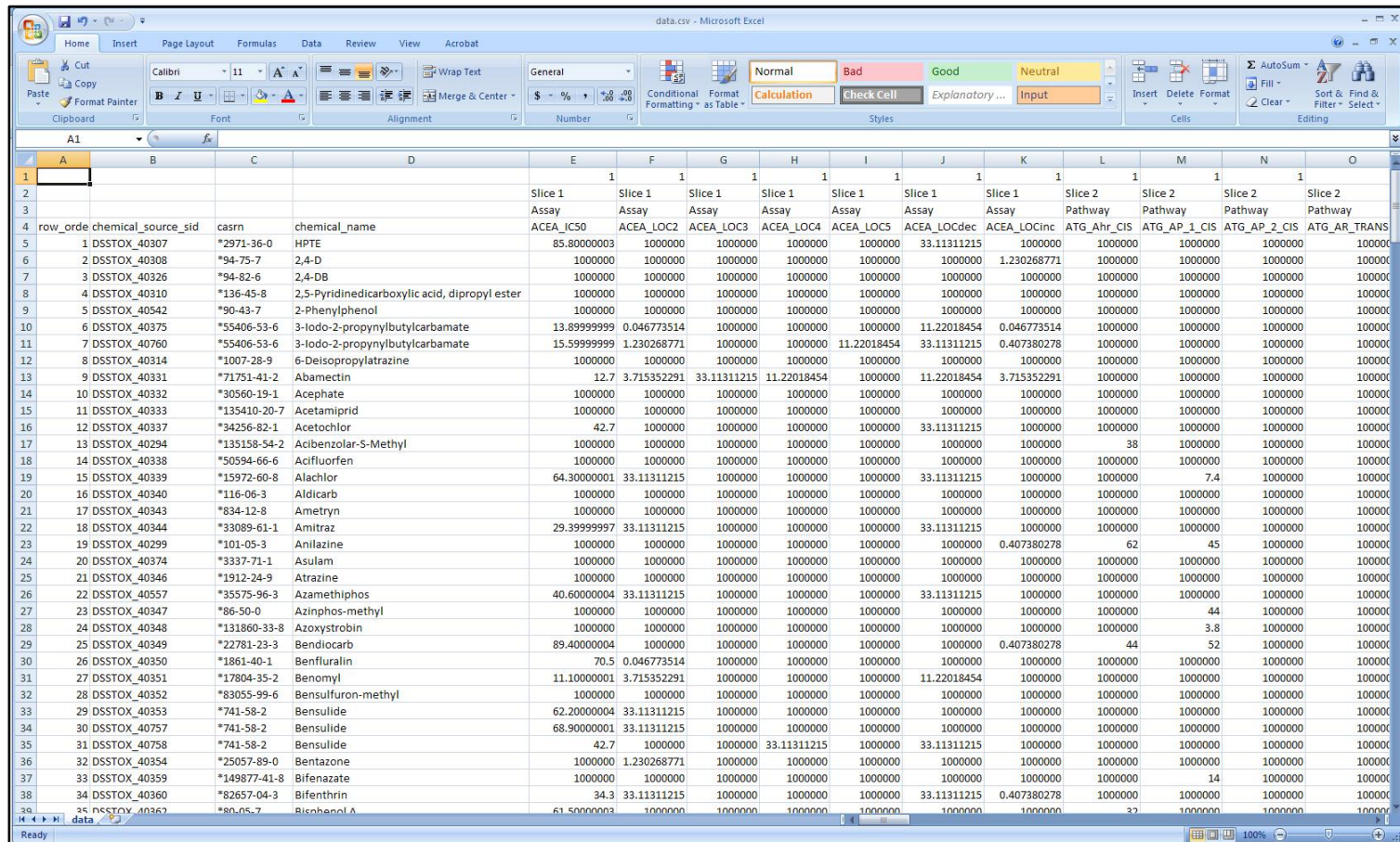
Options: dynamic sorting, modify results, highlight chemicals, download images/data/zip file(s), mouse-over to highlight particular chemicals, click to enlarge particular chemicals, return/modify previous steps



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

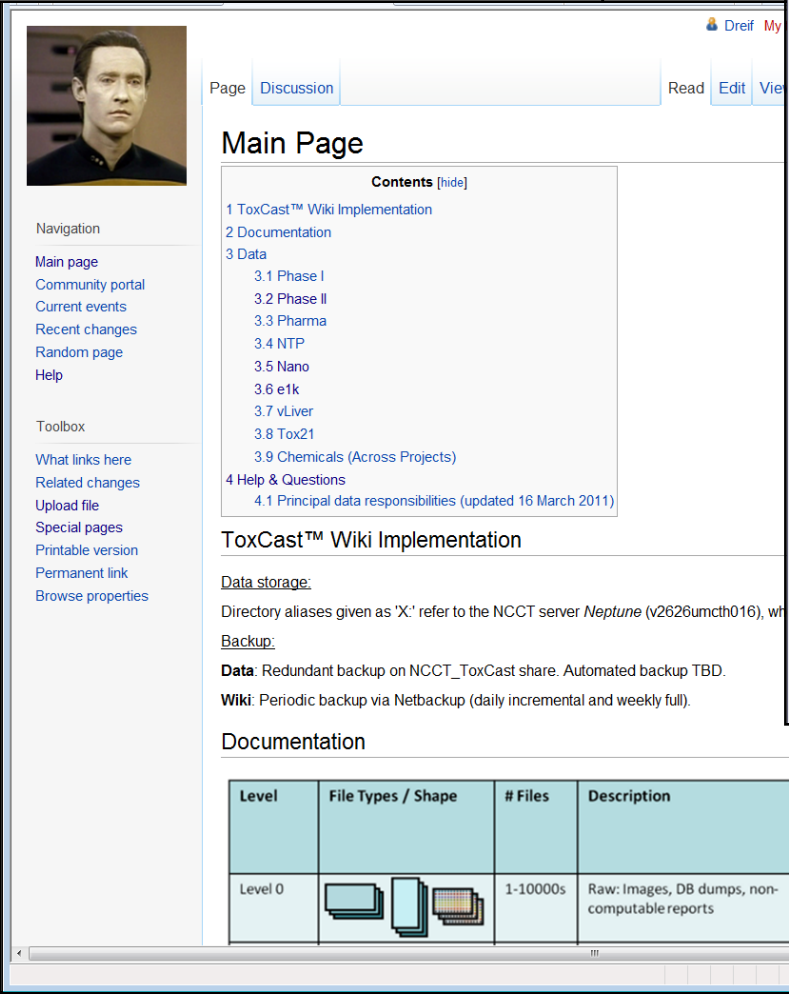


row_orde	chemical_source_sid	casrn	chemical_name	ACEA_IC50	ACEA_LOC2	ACEA_LOC3	ACEA_LOC4	ACEA_LOC5	ACEA_LOCdec	ACEA_LOCinc	ATG_Ahr_CIS	ATG_AP_1_CIS	ATG_AP_2_CIS	ATG_AR_TRANS
1	DSSTOX_40307	*2971-36-0	HPTE	85.80000003	1000000	1000000	1000000	1000000	33.11311215	1000000	1000000	1000000	1000000	1000000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

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)

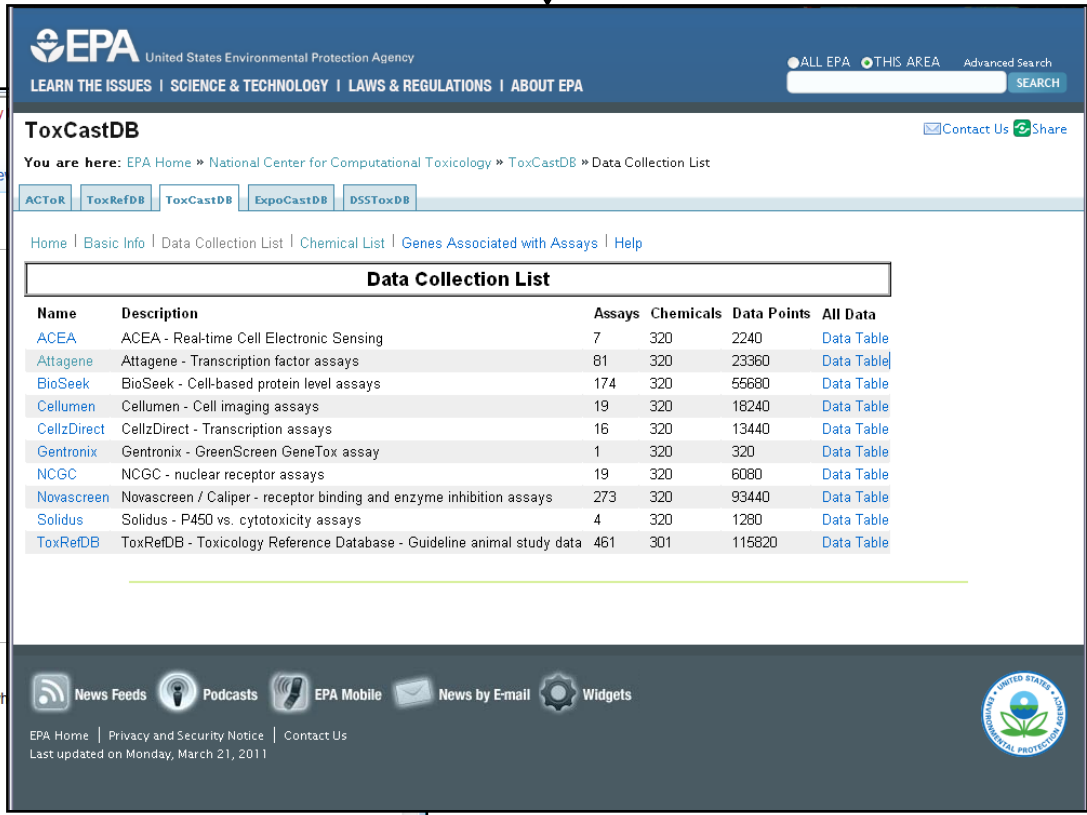


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- 1 ToxCast™ Wiki Implementation
- 2 Documentation
- 3 Data
 - 3.1 Phase I
 - 3.2 Phase II
 - 3.3 Pharma
 - 3.4 NTP
 - 3.5 Nano
 - 3.6 e1k
 - 3.7 vLiver
 - 3.8 Tox21
 - 3.9 Chemicals (Across Projects)
- 4 Help & Questions
 - 4.1 Principal data responsibilities (updated 16 March 2011)

Documentation

Level	File Types / Shape	# Files	Description	Support Files / Information Required for Next Level Output	Next Level Output
Level 0		1-10000s	Raw: Images, DB dumps, non-computable reports	Technology-specific SOPs	Level 1 files, Image archive



ToxCastDB

You are here: EPA Home » National Center for Computational Toxicology » ToxCastDB » Data Collection List

ACToR | ToxRefDB | ToxCastDB | ExpoCastDB | DSSToxDB

Home | Basic Info | Data Collection List | Chemical List | Genes Associated with Assays | Help

Data Collection List					
Name	Description	Assays	Chemicals	Data Points	All Data
ACEA	ACEA - Real-time Cell Electronic Sensing	7	320	2240	Data Table
Attagene	Attagene - Transcription factor assays	81	320	23360	Data Table
BioSeek	BioSeek - Cell-based protein level assays	174	320	55680	Data Table
Cellumen	Cellumen - Cell imaging assays	19	320	18240	Data Table
CellzDirect	CellzDirect - Transcription assays	16	320	13440	Data Table
Gentronix	Gentronix - GreenScreen GeneTox assay	1	320	320	Data Table
NCGC	NCGC - nuclear receptor assays	19	320	6080	Data Table
Novascreen	Novascreen / Caliper - receptor binding and enzyme inhibition assays	273	320	93440	Data Table
Solidus	Solidus - P450 vs. cytotoxicity assays	4	320	1280	Data Table
ToxRefDB	ToxRefDB - Toxicology Reference Database - Guideline animal study data	461	301	115820	Data Table



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?



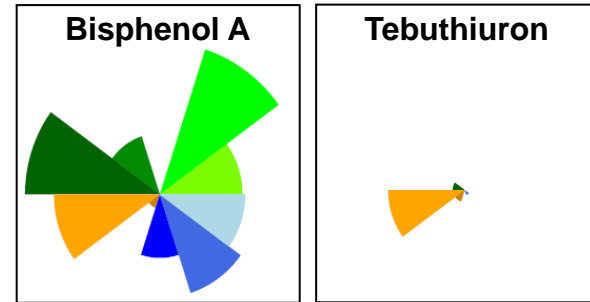
FIN

Prioritization is needed for diverse tasks

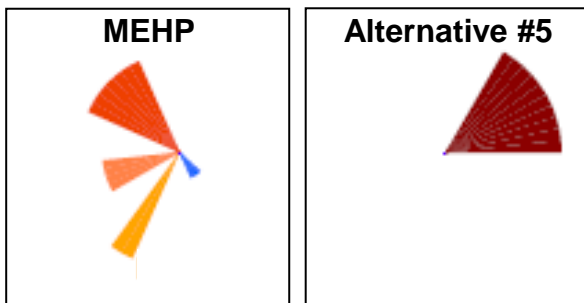
Responding to environmental emergencies:
Which dispersants are safest for remediation of the Deep Water Horizon oil spill?



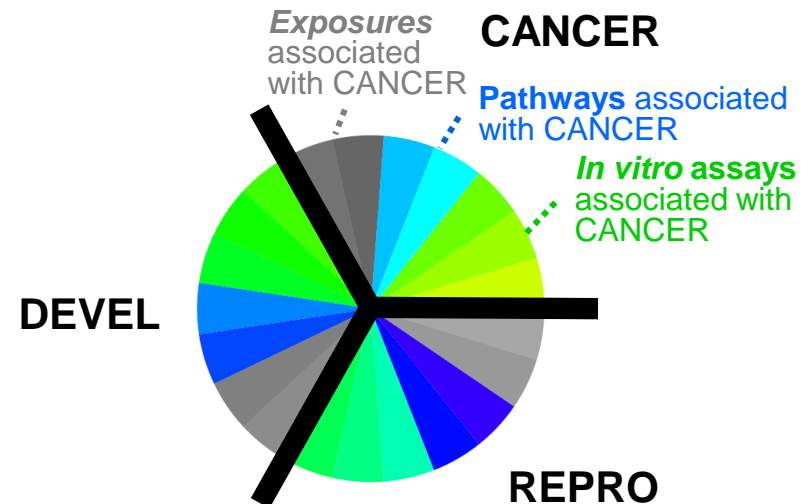
Protecting against endocrine disrupting chemicals: Supporting the Endocrine Disruptor Screening Program (EDSP)



Supporting sustainable development and Green Chemistry: Evaluating manufacturing alternatives



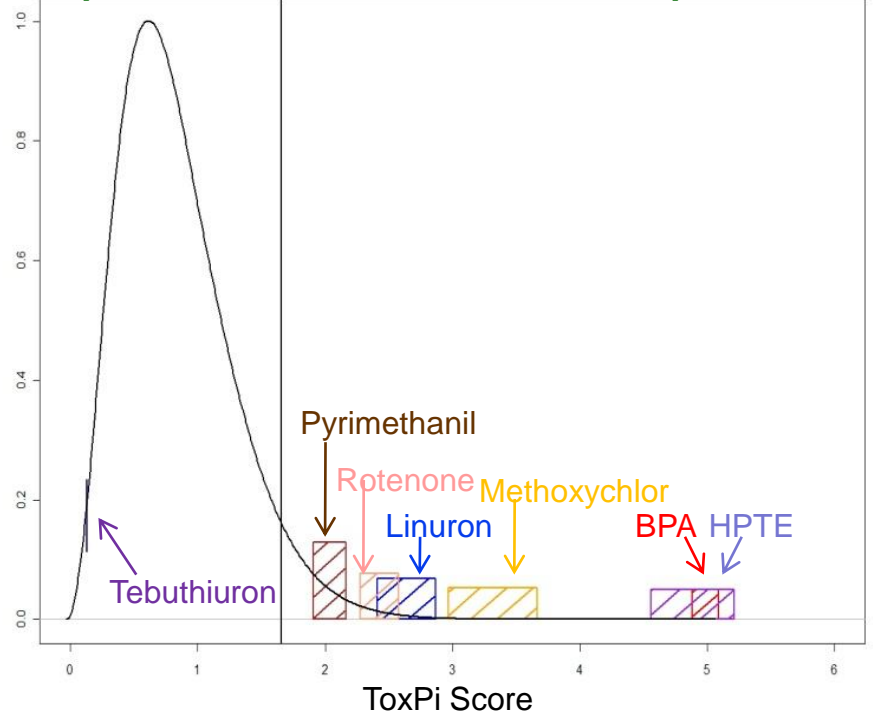
Promoting efficient, targeted testing decisions: ToxPi addressing multiple sectors of concern



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.

95% Confidence Intervals of Reference Chemicals Compared to Null Distribution, Resample Size 309



EPA United States Environmental Protection Agency

Assessing the Robustness of Chemical

Ander Wilson^{1,2}, Sumit Gangwal¹, Matt

¹US EPA, ORD, National Center for Computat

Abstract

A central goal of the U.S. EPA's ToxCast™ program is to provide empirical scientific evidence to aid in prioritizing the toxic testing of thousands of chemicals. The agency has developed a prioritization approach, the Toxicological Prioritization Index (ToxPi™), that calculates a comprehensive toxicity potential and a relative priority rank by incorporating information from ToxCast in vitro bioactivity data (high-throughput screening results from over 500 diverse assays), inferred toxicity pathways, in vitro to in vivo dosimetry estimates, chemical structural descriptors, and exposure considerations. Here, we assess the potential to use ToxPi prioritization scores to identify the subset of chemicals that is truly high priority. We estimate the distribution of scores that could reasonably be expected from a group of chemicals that are not active on the assays and pathways used in ToxCast and compare the distribution of ToxCast Phase I chemical against the null distribution. Results are consistent with expectations; reference chemicals that have previously shown endocrine activity in other in vivo experiments were concluded to have scores higher than would be expected from chemicals that were not active on these assays, while the opposite was found for the reference chemical that failed to show endocrine activity in in vivo experiments. Our analysis also explores how the chemical makeup of the experiment affects scores and likewise our ability to efficiently prioritize chemicals. This work was reviewed by EPA and approved for presentation but does not necessarily reflect Agency policy.

Project Outline

OBJECTIVE: Develop a metric to summarize the robustness of chemical prioritizations.

1. Develop a null distribution.
 - 1.1 Estimate distribution of chemicals that are not active on these assays and pathways.
 - The probability of an assay being nonzero is $Y \sim \text{Bernoulli}$ active on these assays and pathways has a nonzero score.
 - The distribution of nonzero scores follow $X \sim Y \sim 1 \sim \chi^2$.
 - 1.2 Determine resampling size for bootstrap confidence intervals of ToxPi Scores.
 2. Test Phase I chemicals.
 - 2.1 Bootstrap confidence intervals for Phase I chemicals.
 - 2.2 Compare results of reference chemicals to results from other in vivo studies.
 3. Determine a testing rule.

ToxPi™ Score Calculation

ToxPi prioritization score is the weighted sum of eight component scores, 5 assays and 3 pathways.

Most varieties of the ToxPi prioritization score also include chemical properties LogP and pCACO (see example plots for two chemicals, below), but these have been excluded from this analysis.

Each of the eight component scores is the average of between 5 and 38 subcomponent scores (see table, below).

*The assays comprising these subcomponent scores are log transformed AC_{50} values. The minimum (least active) score for all assays and pathways is 0.

*The weights are normalizing constants that insure that the maximum normalized component score is 1 for each sub-component (1).

$$\text{ToxPi} = \sum_{j=1}^5 w_{aj} \text{assay}_j + \sum_{j=1}^3 w_{pj} \text{pathway}_j$$

Component Name	Number of Sub-Component
Assay components	
Androgen Receptor (AR)	5
Estrogen Receptor (ER)	6
Thyroid Receptor (TR)	5
Nuclear Receptor Other(NR)	5
Absorption, Distribution, Metabolism, and Excretion (ADME)	38
Pathway components	
KEGG	12
Ingenity	8
OMM	7

Radial Plots of Two Reference Chemicals

*The maximum possible ToxPi score equals 8 (the number of components), and can only occur if one chemical has the highest score for all eight components.

*The observed scores for Phase I chemicals range from 0 to 5.

*The 7 example chemicals used in Reif et al. 2010 are highlighted in blue throughout (1).

*Chemicals representing the quartiles are highlighted in red.

Results for Phase I Reference Chemicals

Proportion of ToxPi Scores Above 95th Percentile of Null Distribution by Median ToxPi Score, Resample Size 309

95% Confidence Intervals of Reference Chemicals Compared to Null Distribution, Resample Size 309

95% Confidence Intervals of Quartile Chemicals Compared to Null Distribution, Resample Size 309

Conclusions & Next Steps

Conclusions

- This experiment suggests that a method of testing against a null distribution representing the scores of chemicals that are not active on these assays and pathways is viable.
- Even with substantial variation due to the chemical makeup of the experiment, chemicals having high activity scores would have been identified as "high priority" over 97.5% of the time.

Next Steps

- Further analysis is needed to determine the appropriateness of the null distribution, most effective resample size, and testing rule.
- The robustness of the testing procedure needs to be examined to determine the effects of missing data, false positives, and other sources of variation.

References

1. Reif, D., M. T. Martin, S. Tan, K. A. Houck, R. Judson, A. M. Richard, T. B. Knudsen, D. J. Dix, and R. J. Kavlock. "Endocrine Profiling and Prioritization of Environmental Chemicals Using ToxCast Data." *Environmental Health Perspectives*. 118(12):2-8, (2010).
[2. www.epa.gov/nctc](http://www.epa.gov/nctc)

Support

AW was supported by NIH training grant GM081057: Biostatistics Training in the Omics Era.