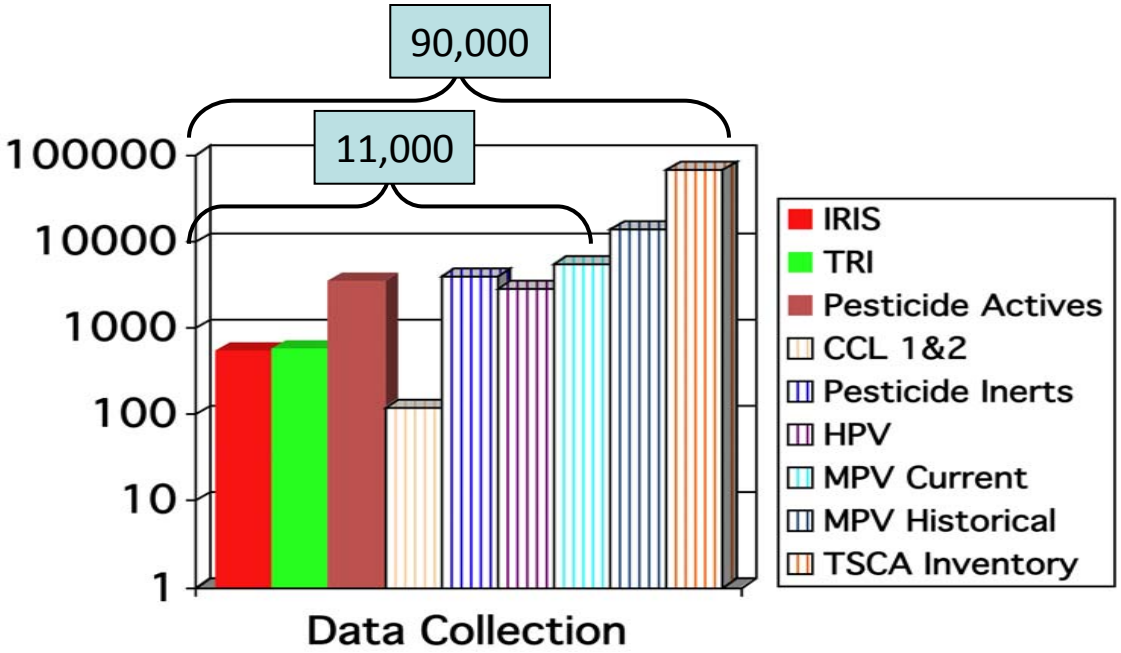
EPA
United States
Environmental Protection
Agency

ACToR
Aggregated Computational Toxicology Resource

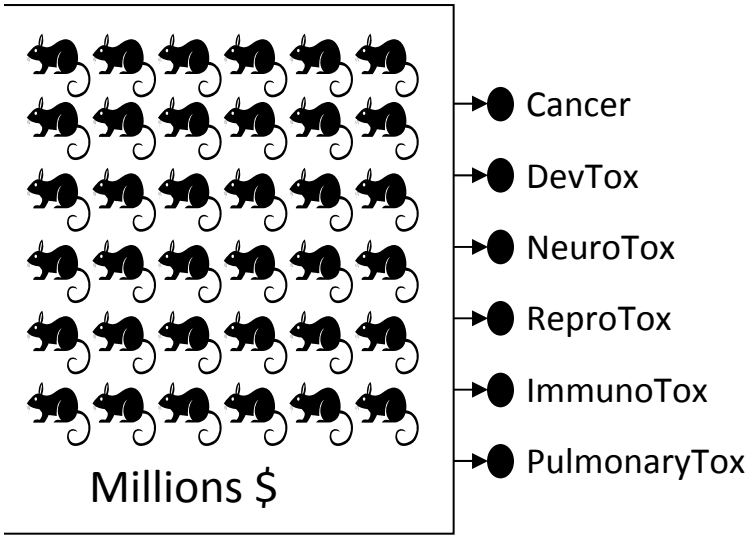
Office of Research and Development
National Center for Computational Toxicology

Change Needed Because …..

Too Many Chemicals



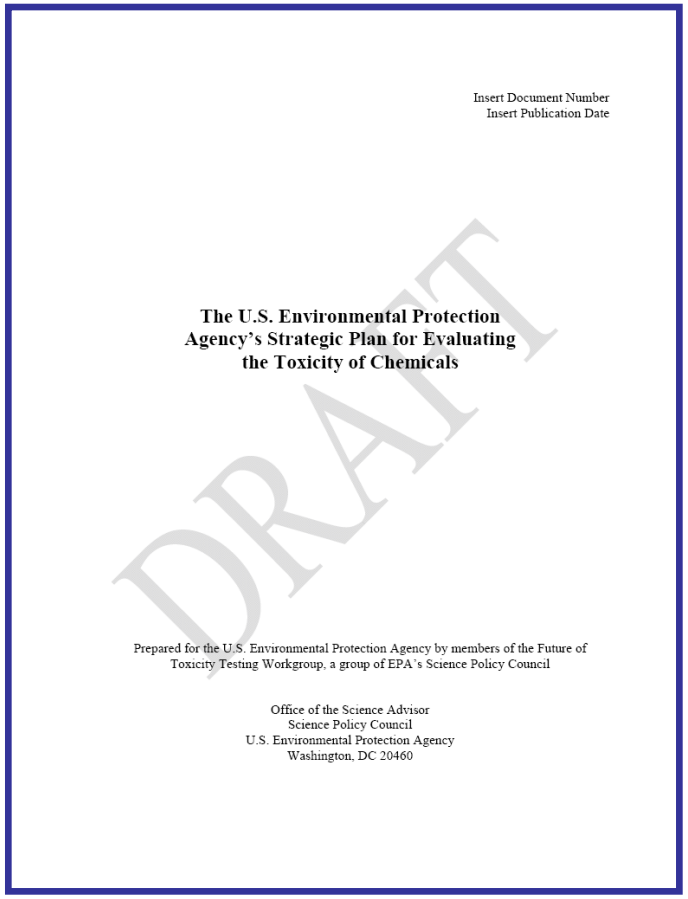
Too High a Cost



…and not enough data.

Judson, et al *EHP in press*

EPA Reacts to Challenge of the NRC on the Future of Toxicity Testing



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The U.S. Environmental Protection Agency's Strategic Plan for Evaluating the Toxicity of Chemicals

DRAFT

Prepared for the U.S. Environmental Protection Agency by members of the Future of Toxicity Testing Workgroup, a group of EPA's Science Policy Council

Office of the Science Advisor
Science Policy Council
U.S. Environmental Protection Agency
Washington, DC 20460

Strategic Goals

- Toxicity Pathway ID and Screening
- Toxicity Based Risk Assessment
- Institutional Transition

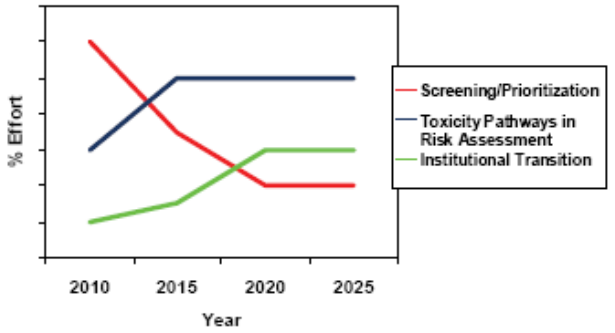

Figure 6. Relative (%) emphasis of the three main components of this strategic plan over its expected 20-year duration.

The Chemical Landscape Project

- What is the unique set of chemicals EPA is most concerned with?
- Targets for the overall ToxCast Program
- How much is know about these chemicals?
- Where are the data gaps?
- Collaboration across EPA
  - ORD, OPP, OPPT, OW, GLNPO, EDSP
- Running this study required building a database
  - Origin of the ACToR project

Summary of Chemical Landscape Analysis

- Total Count: 9,912

- Fraction of chemicals evaluated for specific classes of toxicity:
  - General Hazard (usually acute data) 59%
  - Carcinogenicity 26%
  - Genotoxicity 28%
  - Developmental Toxicity 29%
  - Reproductive Toxicity 11%

EHP Electronic Publication, December 2008

ACToR
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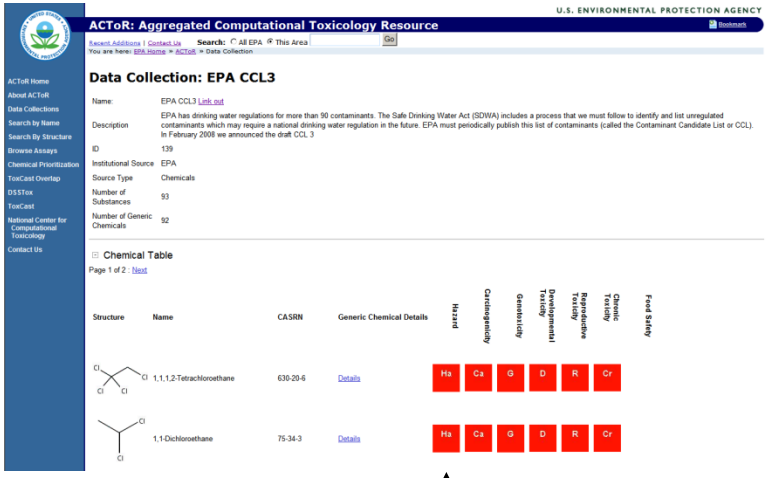


ACToR Web Browser

ACToR API

Chemical

Chemical ID, Structure

Targeted Testing

Assay

Tabular Data, Links to Web Resources

ToxRefDB

…

DevToxDB

Specialized Toxicology Databases

Genomics

MicroArray Data

BioRefDB

Biological Reference Data

ToxMiner

Data Mining

Internet Searches

http://actor.epa.gov/

ACToR Definitions

- Substance
  - A chemical from one source
  - Name(s), CASRN
  - Source-specific unique ID
  - Assay Data
- Compound
  - Chemical structure from one source
  - Source-specific unique ID
- Generic Chemical
  - CASRN
  - Link to many substance (each with same CASRN)
  - Link to at most one compound
  - Links to all assay data from susbtances with same CASRN

ACToR Definitions

- Assay
  - A collection of data on one or more substances
  - Comes from one data source
  - Can have several types of data included
  - Looks like and Excel spreadsheet
- Assay Component
  - One column of an assay table
- Assay Result
  - A data value for one substance and one assay component

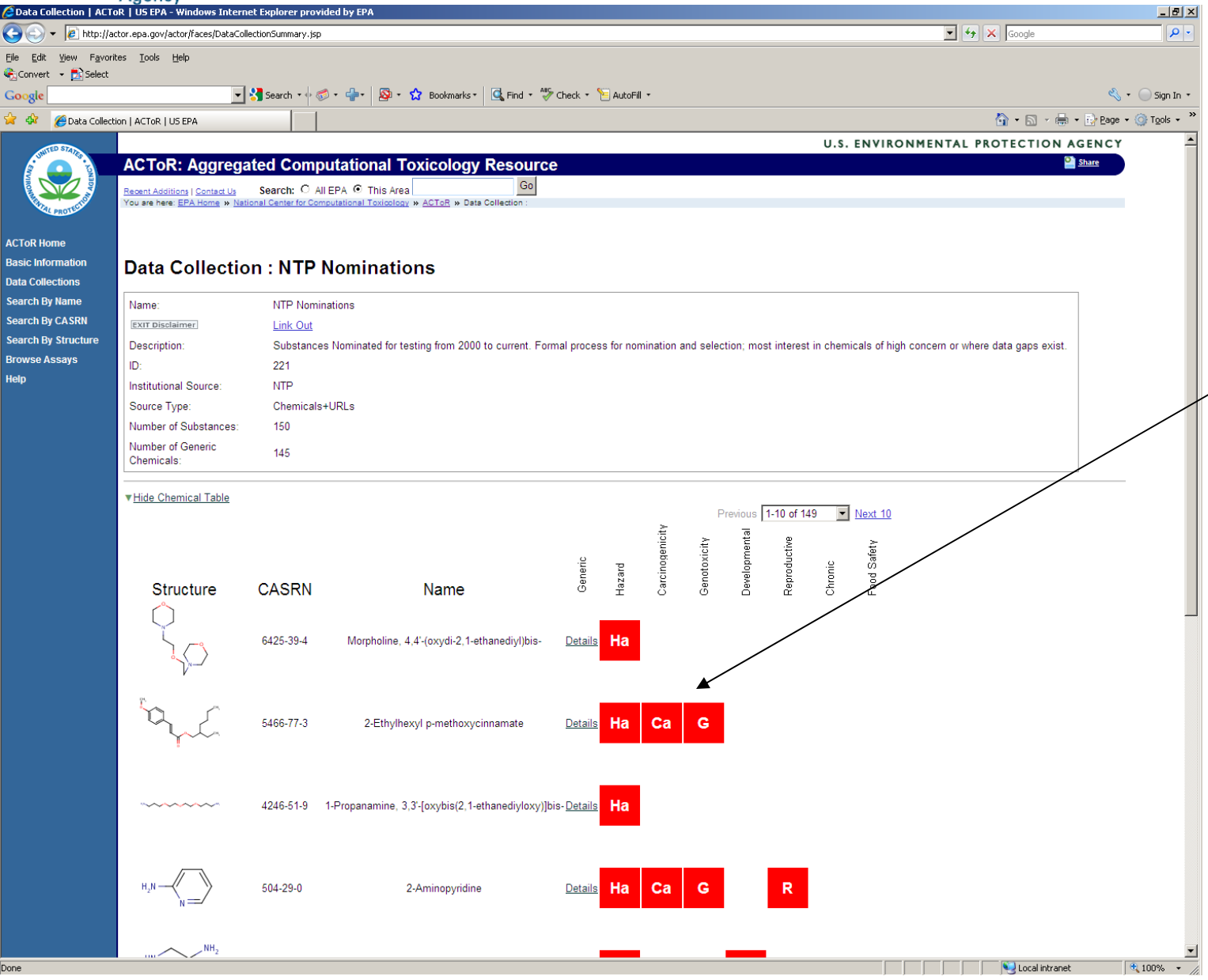
ACToR Definitions

- Assay Phenotype
  - Type of disease associated with the assay
    - Carcinogenicity, GeneTox, …
- Assay Category
  - Type of data: tabular, links to the web, human exposure
  - Allows assays to be grouped together
- Data Collection
  - A source of data
  - Substances
  - Compounds
  - Assays

Main Data Views

- Search by names, CASRN, Structure
- View lists of chemicals
- View lists of assays
- View list of assay collections
- View data associated with a generic chemical

Chemical List View



Red box indicates that data is available for that phenotype, not that chemical causes that phenotype

United States Environmental Protection Agency

Statistics

Category	Count
Data Collections	261
Substances	1,578,922
Compounds	955,016
Generic Chemicals	531,517
Generic Chemicals with Structure	418,191
Assays	1,357
Assay Components	3,910
Assay Results	3,553,507

What's Next?

- More Data Collections
  - Development version >400
  - Current Focus on exposure / biomonitoring / food residues
- ToxRefDB
  - Compiling tabular information from guideline studies
    - EPA
    - NTP
    - Literature
- Cleanup of chemical structures
- Enhance generic chemical page

ToxRefDB

- Relational phenotypic/toxicity database
- Provides in vivo anchor for ToxCast predictions
- Three study types
  - Chronic/Cancer rat and mouse (Martin, et al, EHP 2008)
  - Rat multigenerational Reproduction (Martin, et al, submitted)
  - Rat & Rabbit developmental (Knudsen, et al, internal review)
- Two types of synthesis
  - Supervised (common individual phenotypes)
  - Unsupervised (machine based clustering of phenotype patterns)

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EPA Community of Practice
Jobs and Opportunities
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ToxRefDB Program

Toxicology Reference Database

ToxRefDB was developed by the National Center for Computational Toxicology (NCCT) in partnership with EPA's Office of Pesticide Programs (OPP), to store data from in vivo animal toxicity studies. The initial focus was populating ToxRefDB with pesticide registration toxicity data that has been historically stored as hard-copy and scanned documents by OPP. A significant portion of these data have now been processed into ToxRefDB in a standardized and structured format. ToxRefDB currently includes chronic, cancer, sub-chronic, developmental, and reproductive studies on hundreds of chemicals, many of which are pesticide active ingredients. These data are now accessible and computable within ToxRefDB, and are serving as reference toxicity data for ORD research and OPP retrospective analyses. The primary research appliction of ToxRefDB is to provide toxicity endpoints for the development of ToxCast™ predictive signatures.

Data Set	Description	Download	Publication
Data Entry Tool & Controlled Vocabulary	The Data Entry Tool provided the user interface for all initial data input into ToxRefDB. The controlled vocabulary standardized the capturing of regulatory animal toxicity studies performed across various study types.	Download (15.5 MB, ZIP)	Martin et al. (2008) "Profiling Chemicals Based on Chronic Toxicity Results from the U.S. EPA ToxRef Database" Environmental Health Perspectives doi:10.1289/ehp.0800074
Chronic & Cancer Endpoints	Based on incidence, severity and potency, 26 primarily tissue-specific pathology endpoints were selected to uniformly classify 310 chemicals included in the manuscript's analysis. The 310 chemicals in this analysis largely overlap with the 320 ToxCast Phase I chemicals.	Download (2.7 MB, XLS)	Martin et al. (2008) "Profiling Chemicals Based on Chronic Toxicity Results from the U.S. EPA ToxRef Database" Environmental Health Perspectives doi:10.1289/ehp.0800074

ToxRefDB website: http://www.epa.gov/ncct/toxrefdb/

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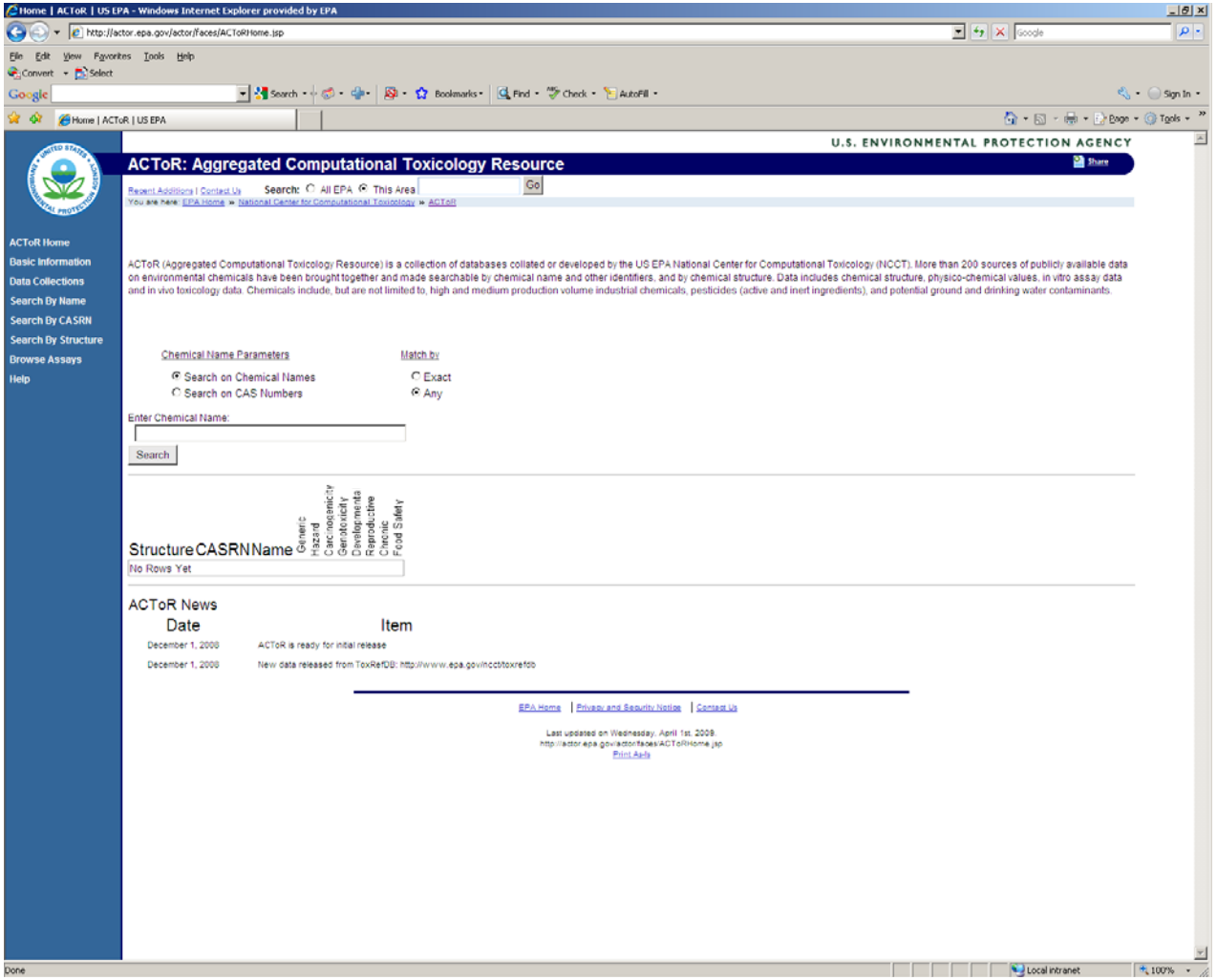
Demo



http://actor.epa.gov