Lessons Learned in Building the CompTox Chemicals Dashboard

Engineering a more sustainable web-based chemical database

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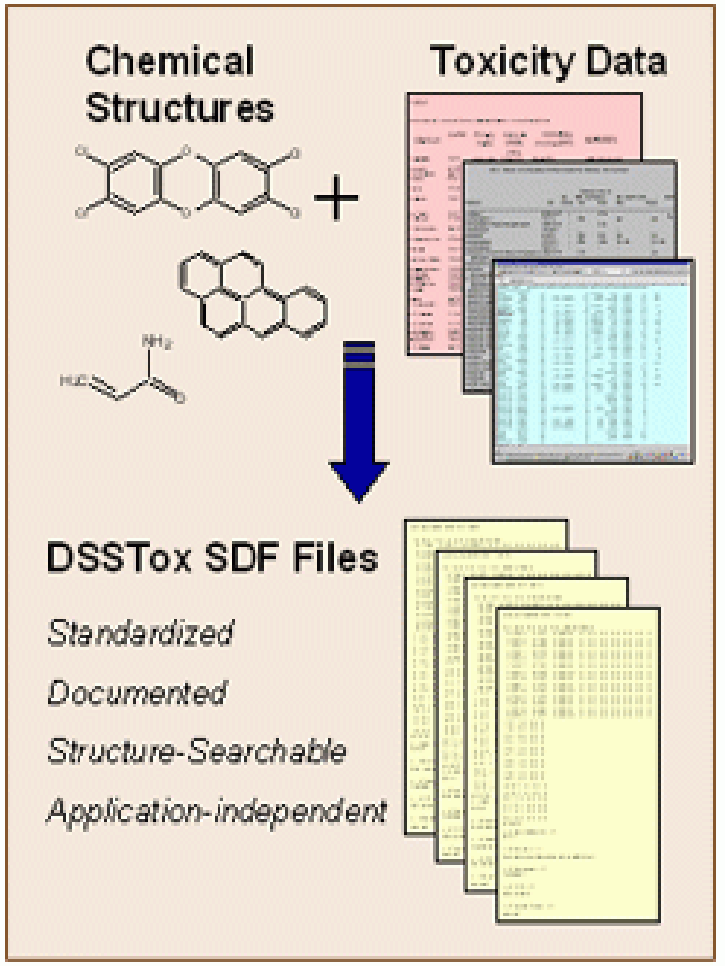
1. National Center of Computational Toxicology, U.S. EPA
(soon to be the Center for Computational Toxicology and Exposure)

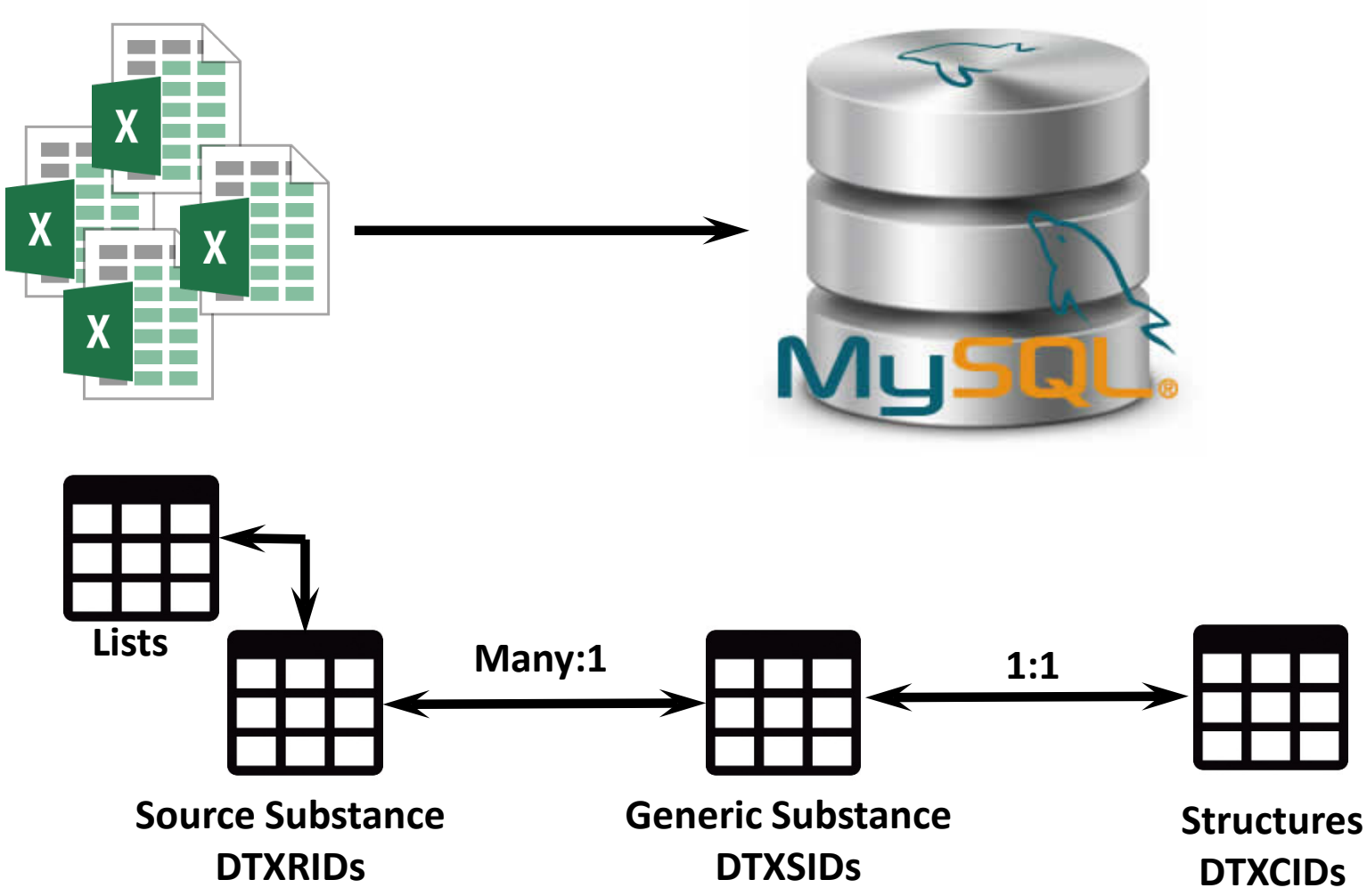
DSSTox Ancient History

Goal: Linking chemical structures to data enabling SAR

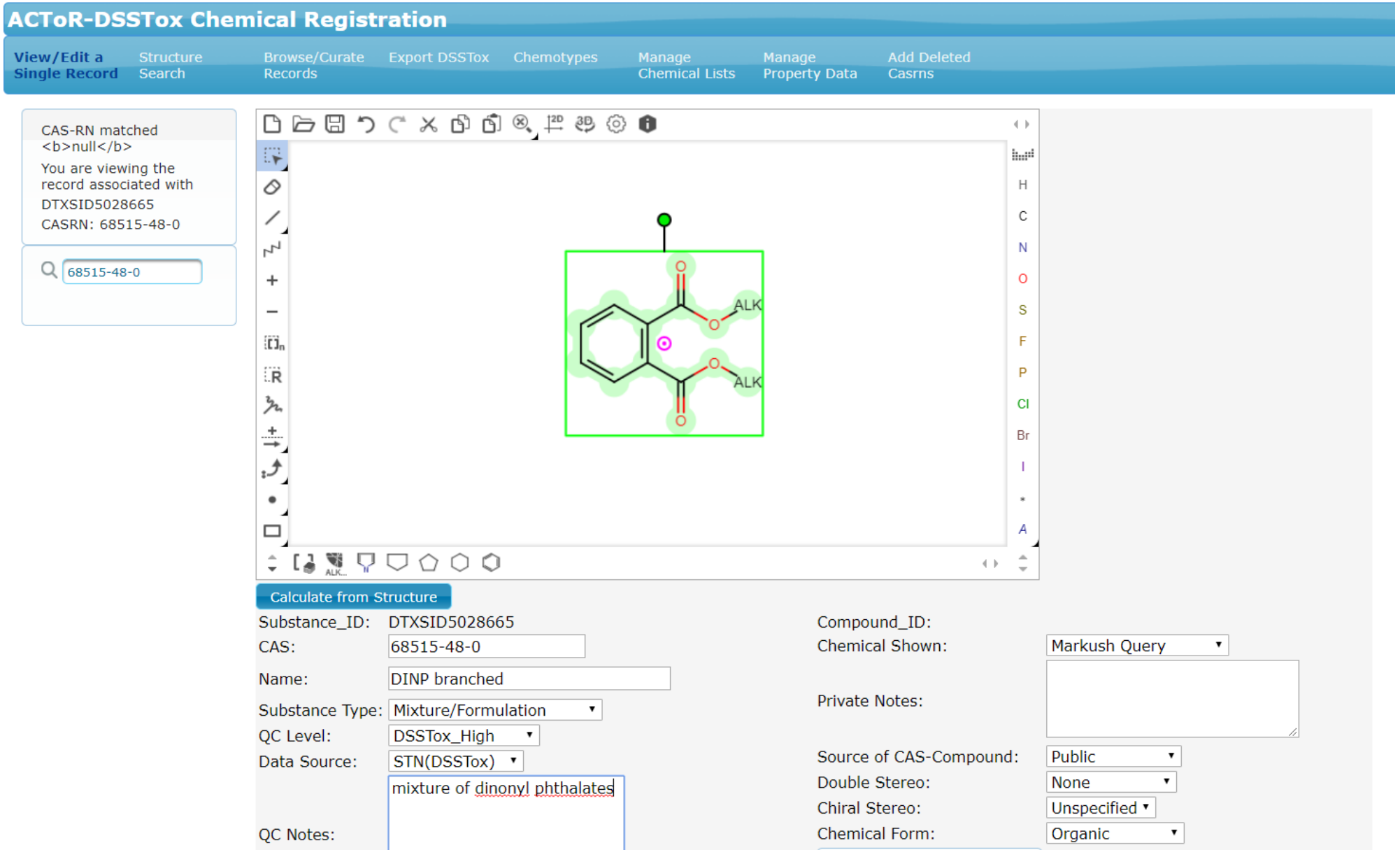
- First release of data files in 2004
- Focused on high impact sets of data
  - Carcinogenic Potency Database
  - Drinking water disinfection by-products
  - EPA's Integrated Risk Information System
  - FDA's Maximum Daily Dose dataset
  - EPA's Fat Head Minnow Toxicity dataset
  - etc...
- Managed all chemical registration for ToxCast and Tox21 chemicals
- By 2014, roughly 20K manually curated substance records



Generalized DSSTox Storage Architecture



Chemical Registration



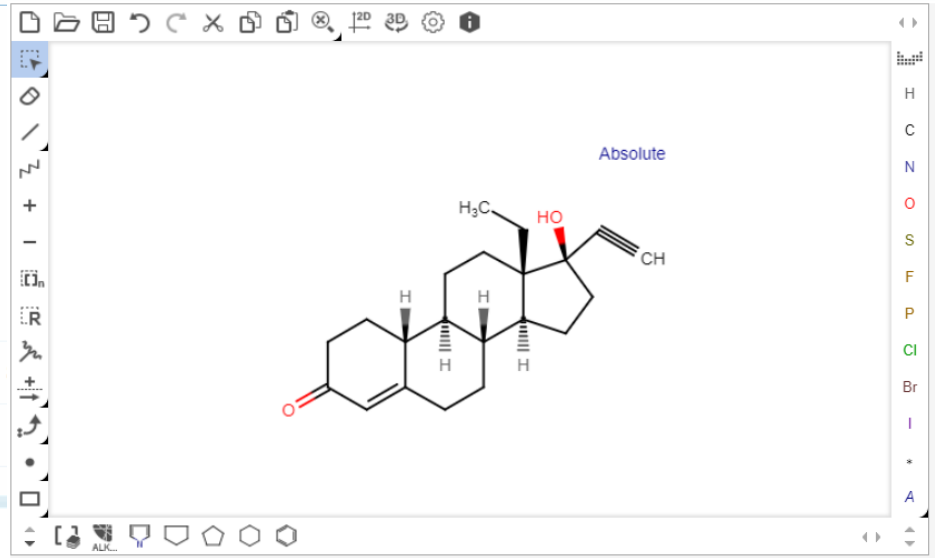
Chemical List Registration

Hits

	ssCAS-RN	ssName	Hit Desc	Hit Substance_ID	Hit Casrn	Hit Name
●		Norgestrel	Structure matched **SMILES**	DTXSID10859541	NOCAS_859541	13-Ethyl-17-ethynyl-17-hydroxy-1,2,6,7,8,9,10,11,12,13,14,15,16,1 tetradecahydro-3H-cyclopenta[a]phenanthren-3-one (non-preferred name)
●		Norgestrel	Mapped Identifier matched **NAME1**	DTXSID3036496	797-63-7	Levonorgestrel
●		Norgestrel	Mapped Identifier matched **NAME1**	DTXSID3047477	6533-00-2	dl-Norgestrel

Map hit | Cancel

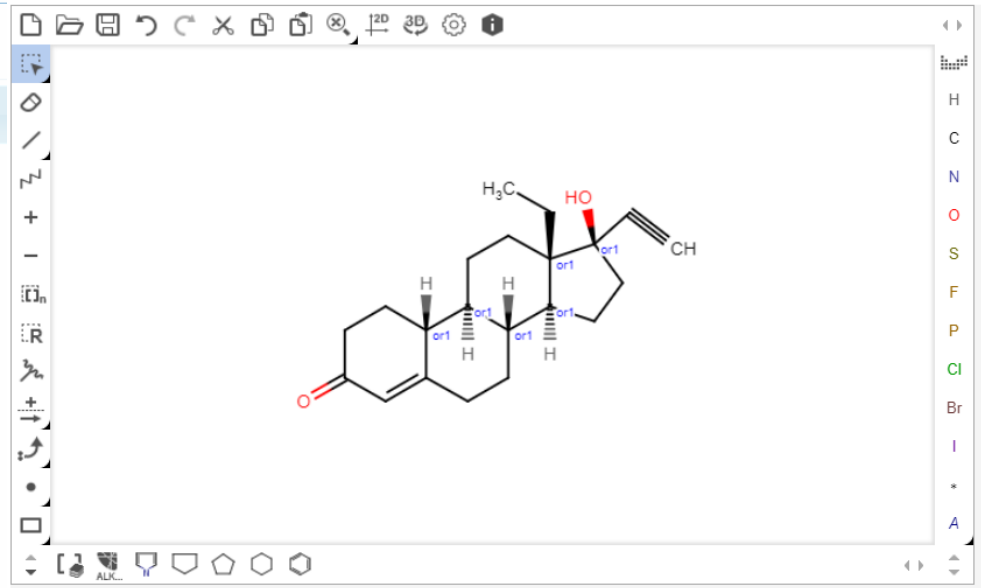
SMILES
Valid Synonym matched **NAME2**
Preferred Name matched **NAME1**
Valid Synonym matched other record: **NAME1**
Unique Synonym matched other record: **NAME2**
Unique Synonym matched other re
Mapped Identifier matched **NAME1**
Mapped Identifier matched **NAME2**
Name2Structure
Export All



Calculate from Structure

Substance_ID: DTXSID3036496
CAS: 797-63-7
Name: Levonorgestrel
Substance Type: Single Compound
QC Level: DSSTox_High
Data Source: STN(DSSTox)

Compound_ID:
Chemical Shown:
Private Notes:
Source of CAS-Compound:



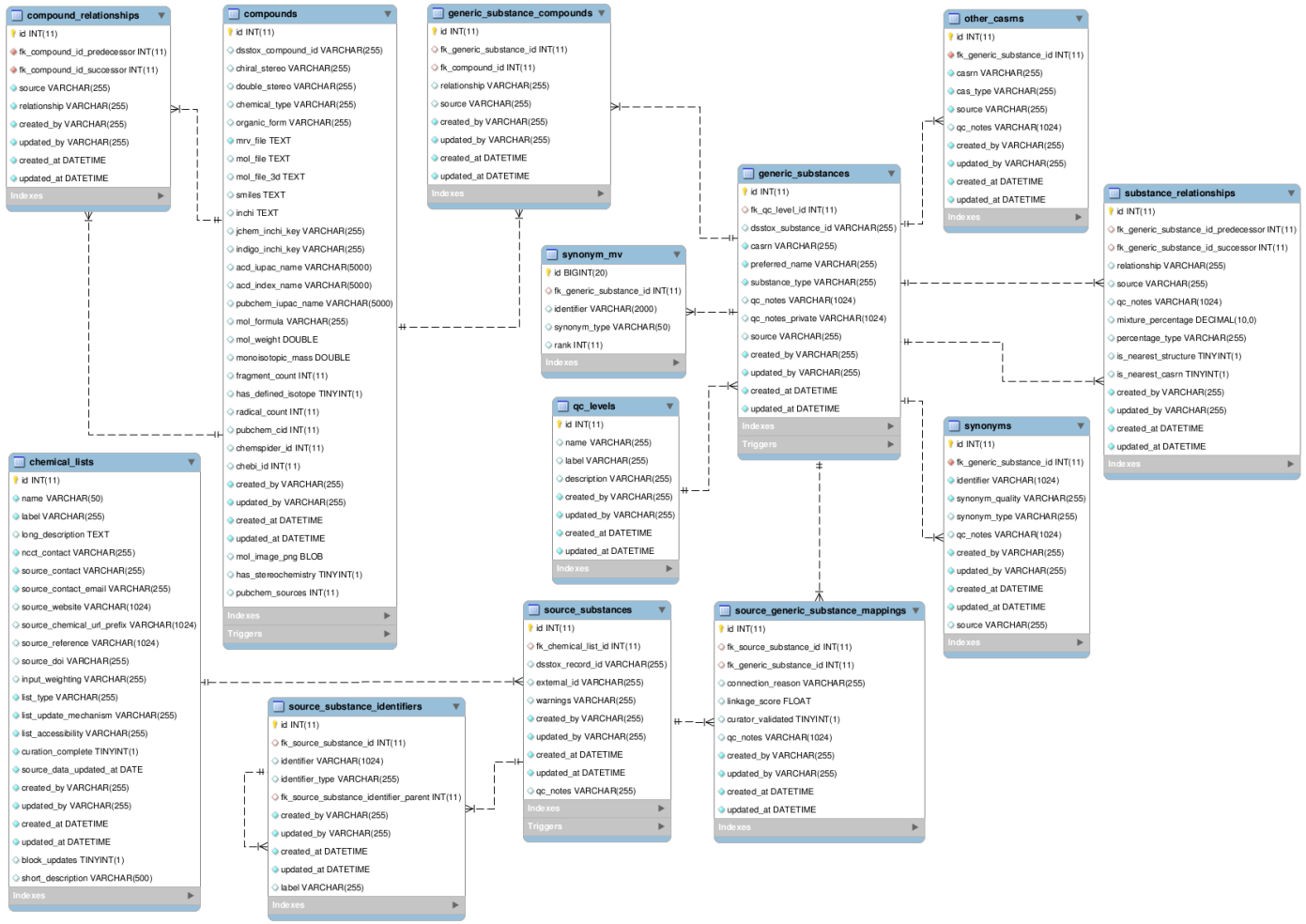
Calculate from Structure

Substance_ID: DTXSID3047477
CAS: 6533-00-2
Name: dl-Norgestrel
Substance Type: Mixture of Stereoisomers
QC Level: DSSTox_High

Compound_ID:
Chemical Shown:
Private Notes:

DSSTox Chemistry Schema

19 Tables



ChemTrack Bottles

ChemTrack | Inventory | Partnerships | Ordering | Data | Single Chemical Search | Hi Chris !

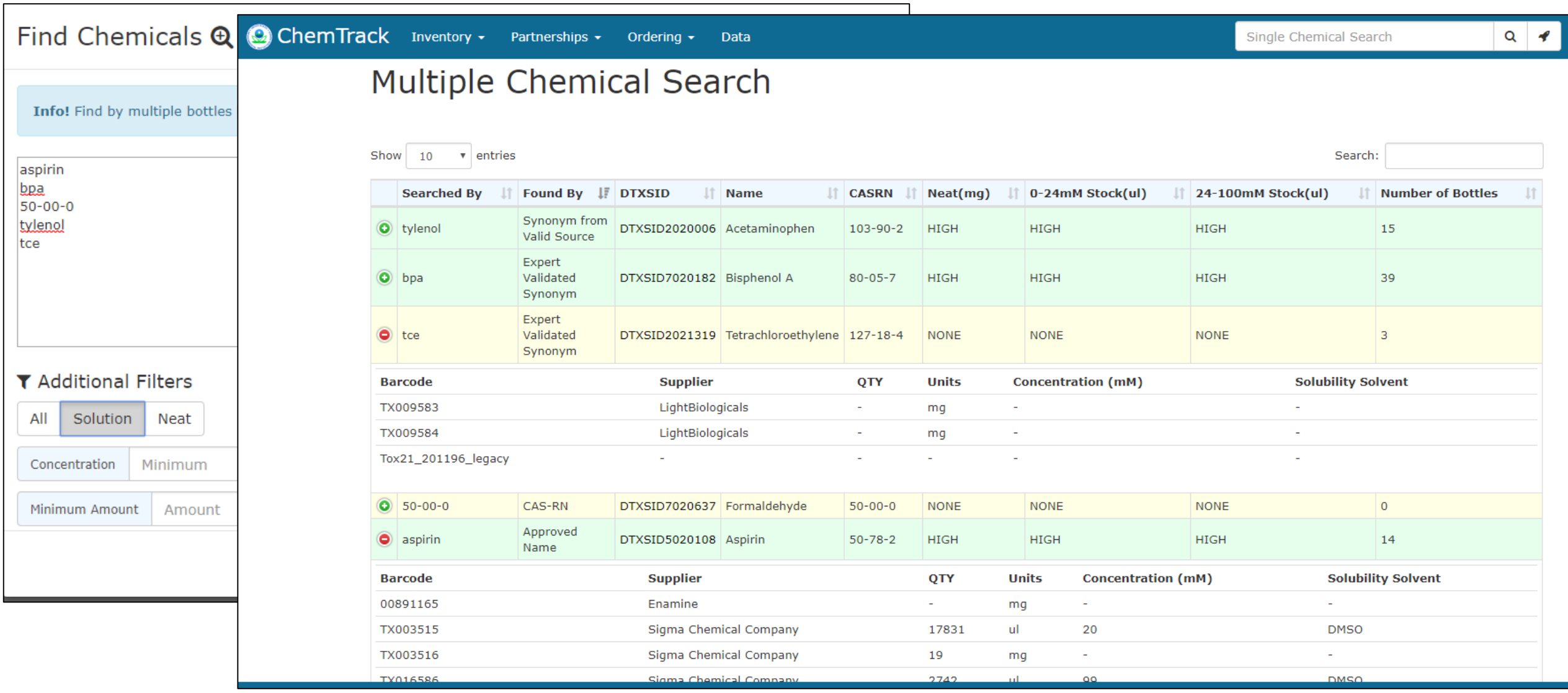
Uploaded MOSAIC Files 25 | Mapped & Available Bottles 29850 | Unmapped Bottles 449 | External Bottles 98 | Add New MOSAIC | Create External Bottle

Mapped & Available Bottles

Show 10 entries | Search:

Barcode Type	Barcode	COA Summary	Compound Name	CAS	QTY Available	Units	Vendor	SAM	CPD	Can Plate?	Comment	
INVALID_SUPTX0013222_INVALID	ALID_SUPTX0013222_INVALID	2660	Aluminium phthalocyanine chloride	14154-42-8	1000	mg	Sigma Chemical Company	SAM004888816	CPD003650672	Yes		Edit
INVALID_SUPTX0013294_INVALID	ALID_SUPTX0013294_INVALID	2735	Nickle(III) carbonate basic hydrate	12607-70-4	250000	mg	Sigma Chemical Company	SAM004888887	CPD003650704	Yes		Edit
EPA_Vial_Source_Storage	BF00079587	18768	Pentabromophenol	608719	178	mg	Sigma Chemical Company	SAM006061824	CPD001224527	Yes		Edit
EPA_Vial_Source_Storage	BF00079581	18774	Phthalic anhydride	85-44-9	193	mg	Sigma Chemical Company	SAM006061820	CPD001252223	Yes		Edit
EPA_Vial_Source_Storage	BF00079583	18772	TRIPOLI	7631-86-9	196	mg	Sigma Chemical Company	SAM006061823	CPD001252283	Yes		Edit
EPA_Vial_Source_Storage	BF00079582	18773	4,4'-Methylenebis(2-chloroaniline)	101144	188	mg	Sigma Chemical Company	SAM006061819	CPD001307314	Yes		Edit
EPA_Vial_Source_Storage	BF00079585	18770	4-sec-Butyl-2,6-di-tert-butylphenol	17540-75-9	188	mg	Sigma Chemical Company	SAM006061825	CPD004560495	Yes		Edit
EPA_Vial_Source_Storage	BF00079584	18771	Creosote	8001-58-9	178	mg	Sigma Chemical Company	SAM006061821	CPD004757028	Yes		Edit
EPA_Vial_Source_Storage	BF00079586	18769	tert-Amyl methyl ether	994-05-8	194	mg	Sigma Chemical Company	SAM006061822	CPD004757029	Yes		Edit
EPA_Vial_Source_Storage	BF00079580	18775	3,3'-	91-94-	188	mg	Sigma Chemical	SAM006061826	CPD004757030	Yes		Edit

ChemTrack Search



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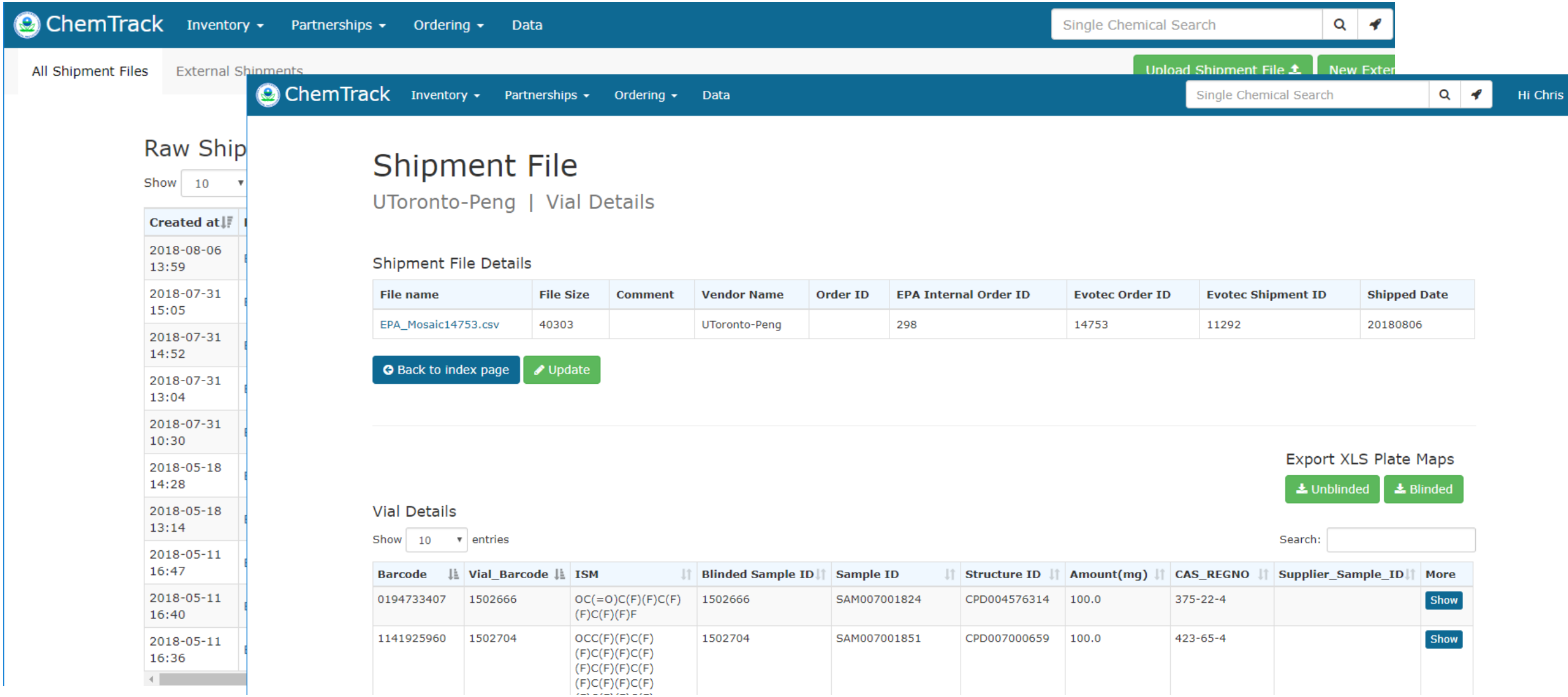
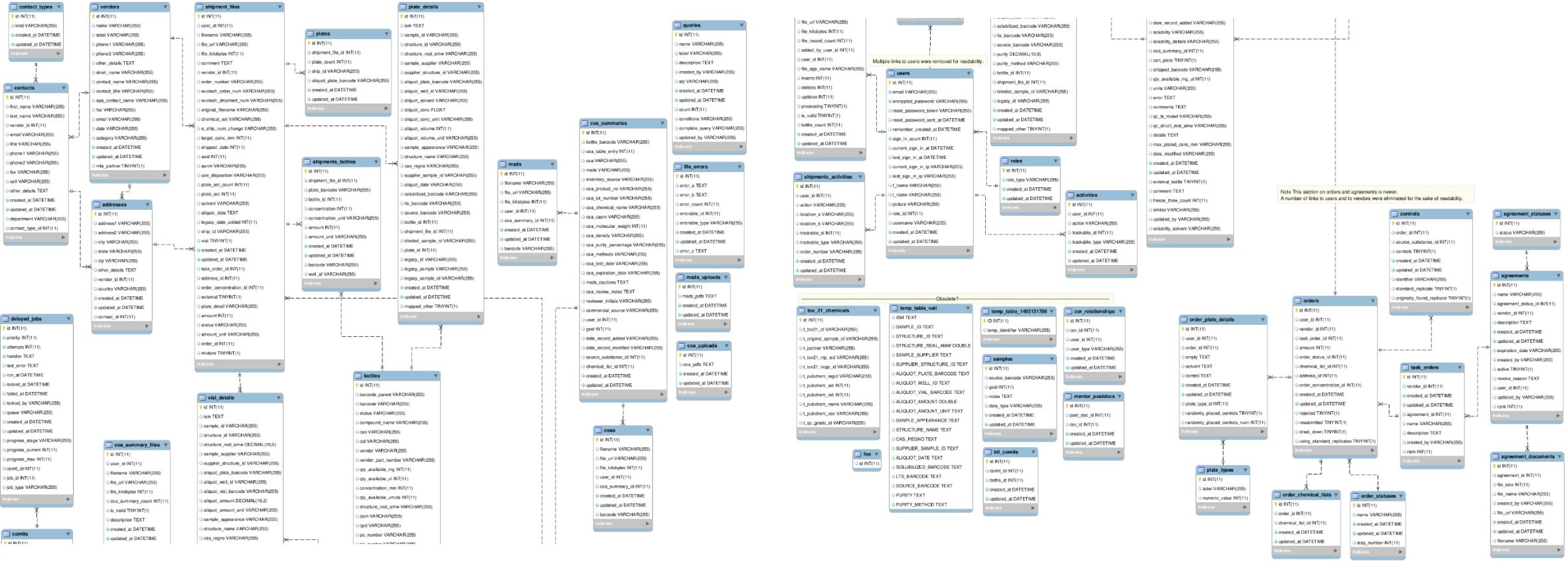
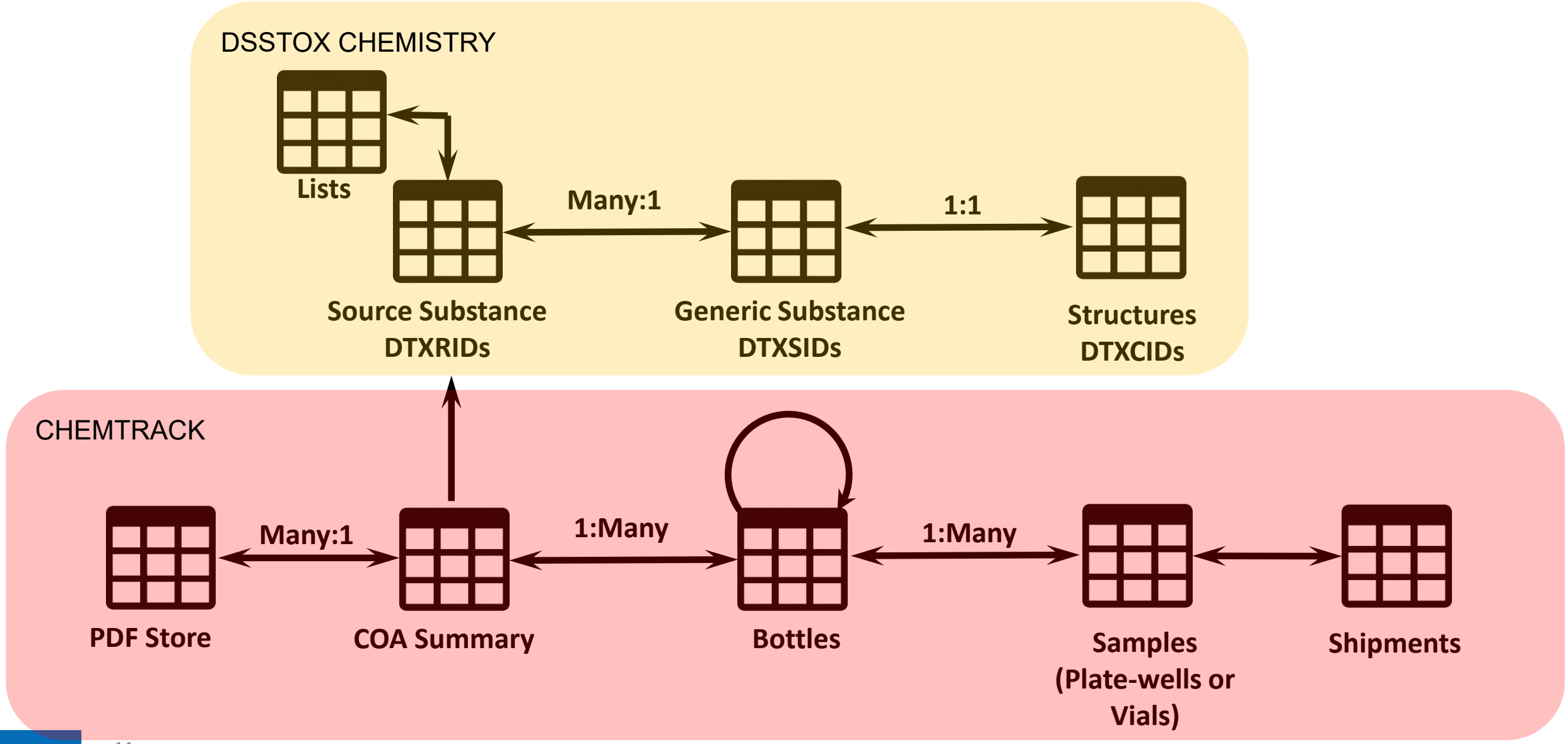


ChemTrack Schema

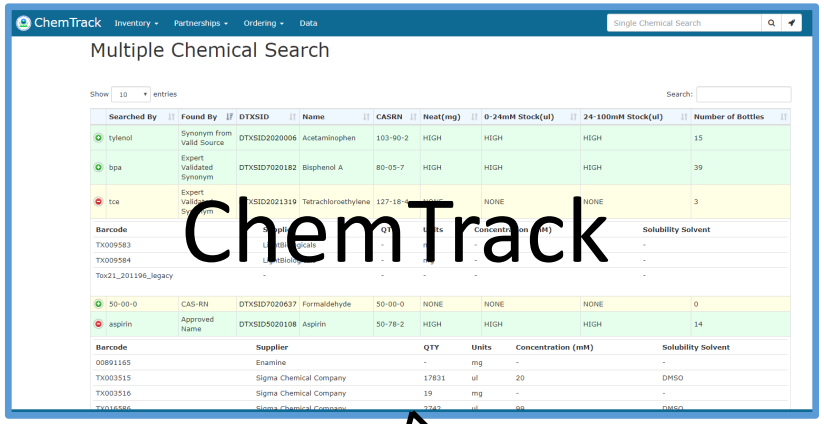
57 Tables

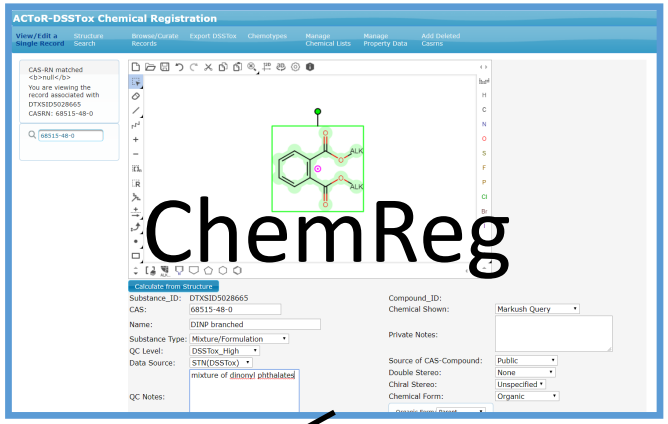


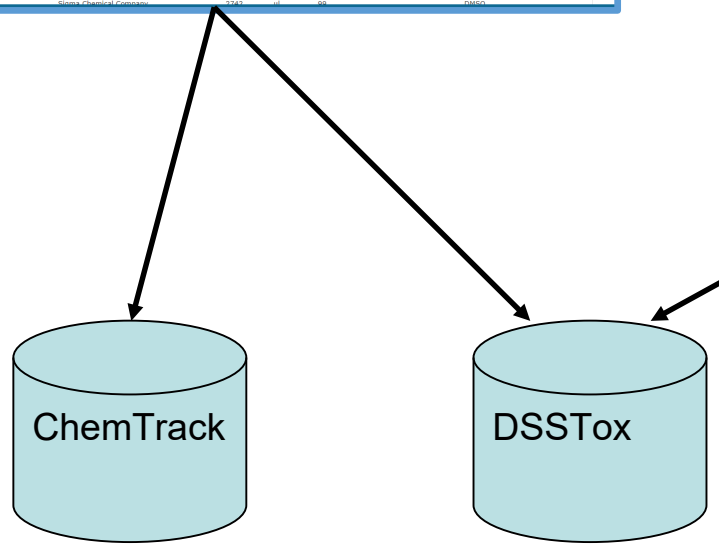
Generalized Data Model



Sharing the DSSTox Database



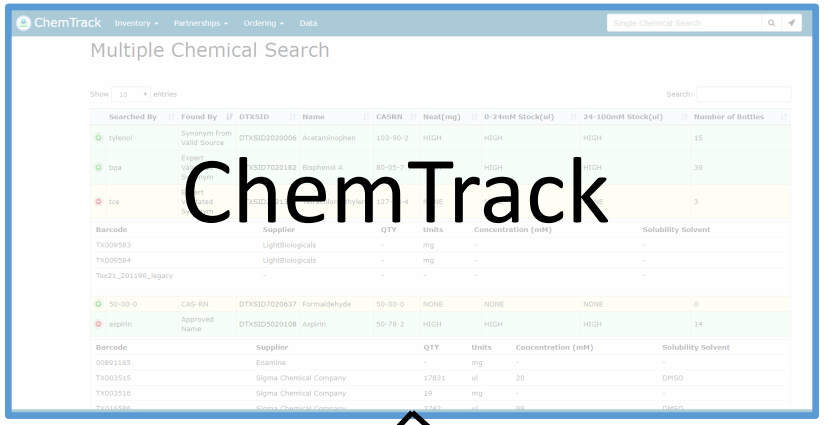




“ChemSpiderMan” comes to NCCT (2015)

- DSSTox: ~700K substance records (25K manually curated)

Sharing the DSSTox Database



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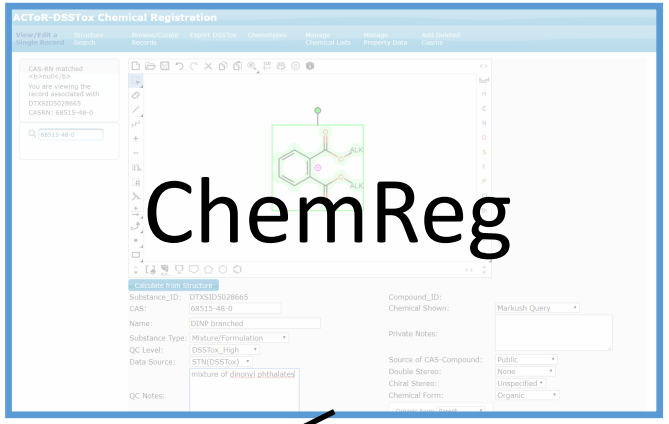
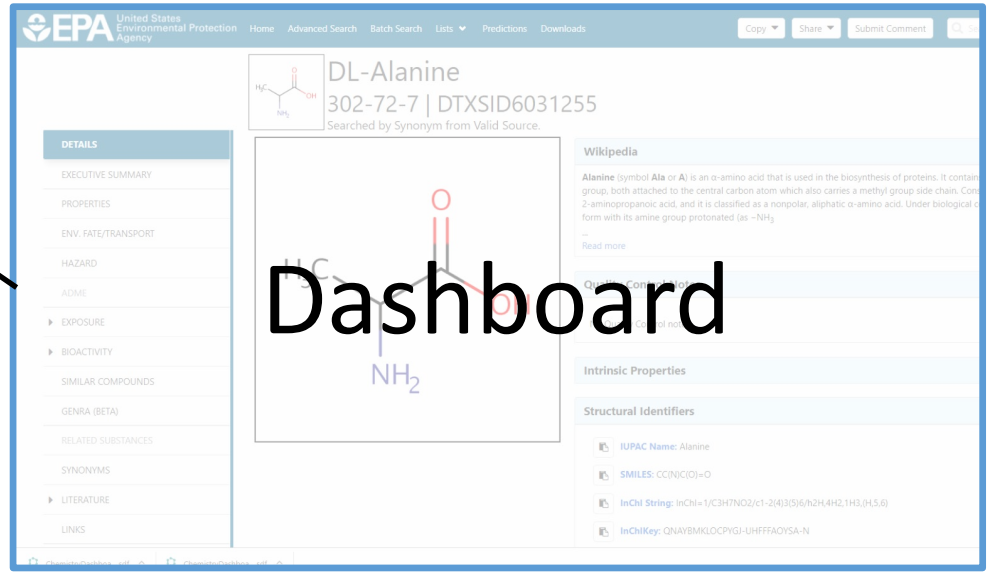


ChemReg

ChemTrack

DSSTox



Dashboard

The Dashboard Taskmaster

I Need
QSAR Predictions

I Need
ToxCast Results

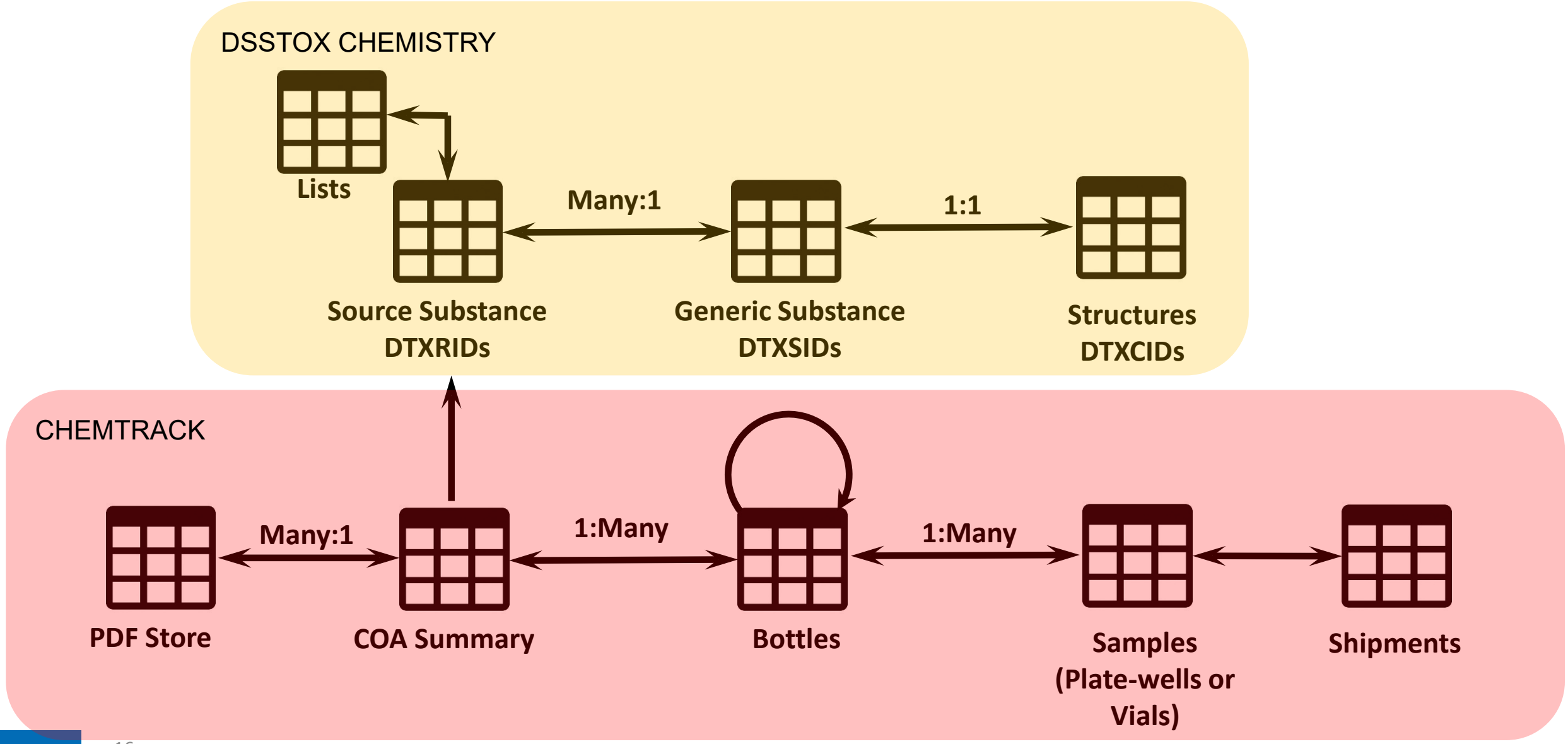
I Need
Analytical QC Data

I Need
PhysChem Data

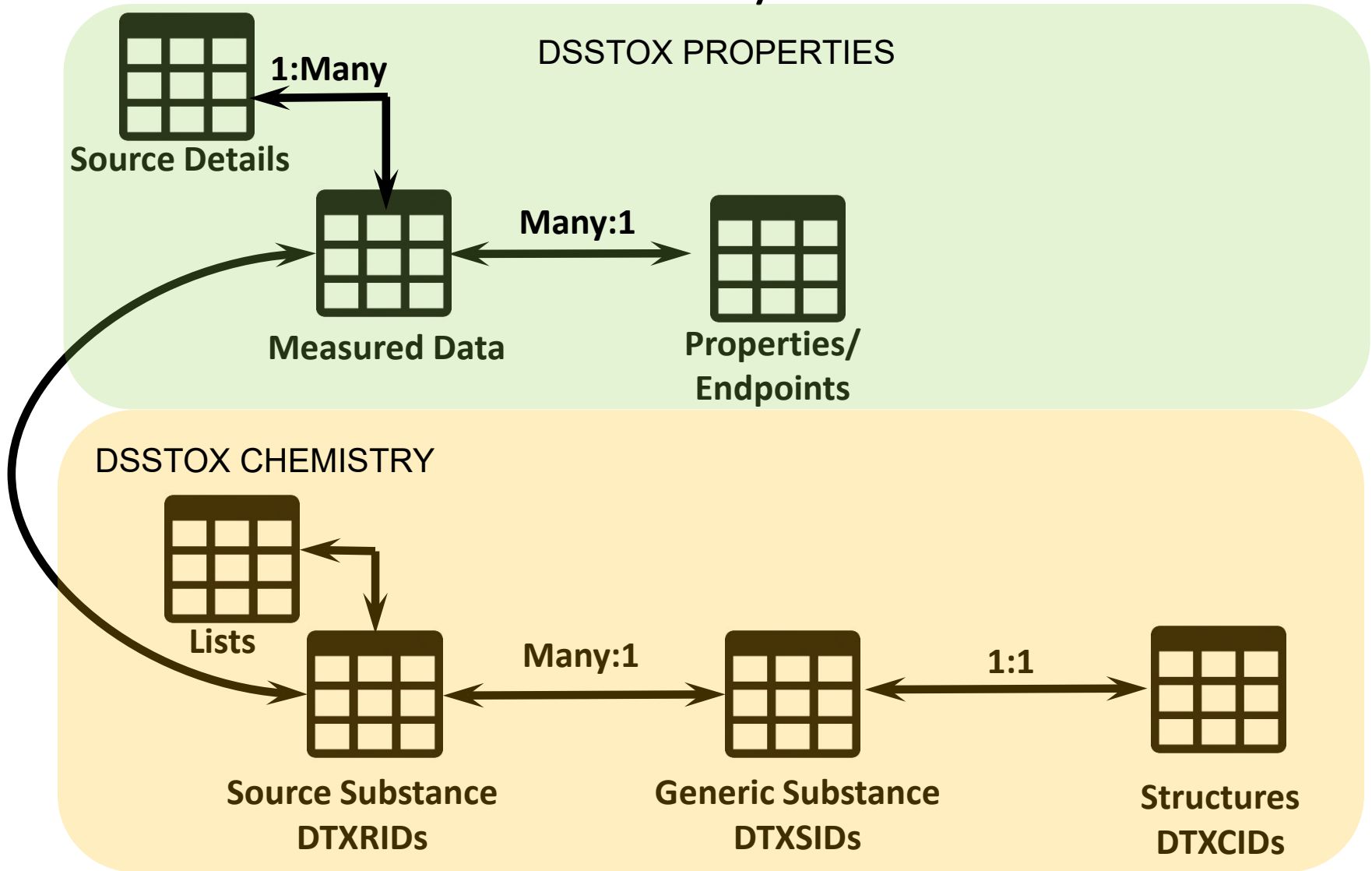
I Need
In Vivo Toxicity
Data

I Need
Consumer Product
Information

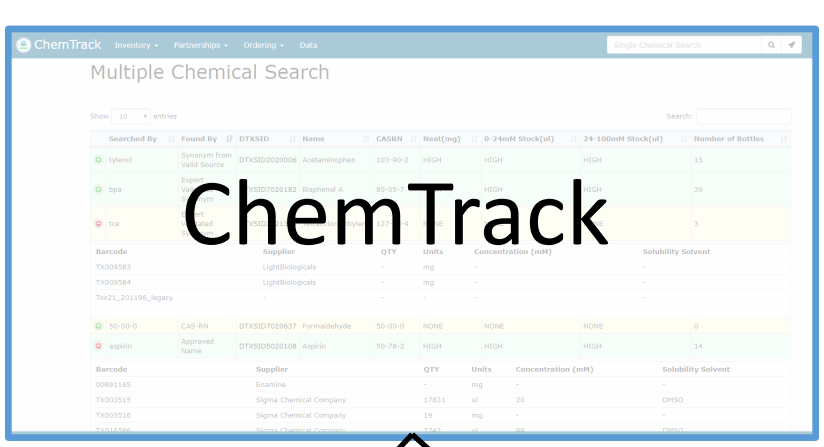
I Need PhysChem Data…

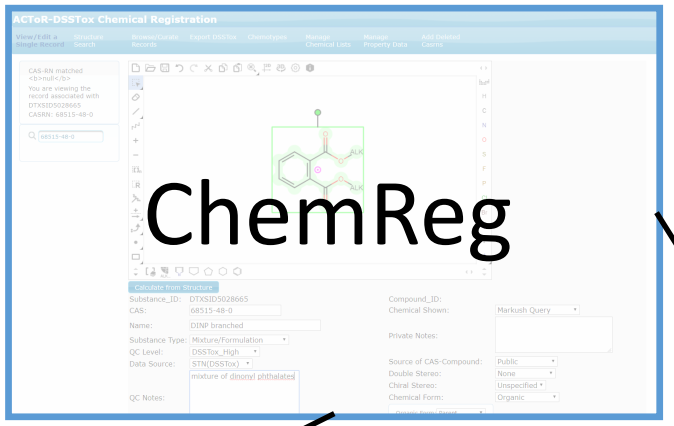


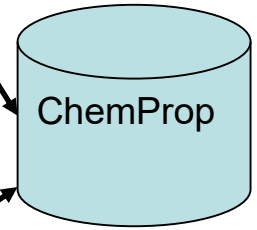
I Need PhysChem Data…

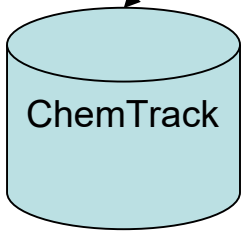


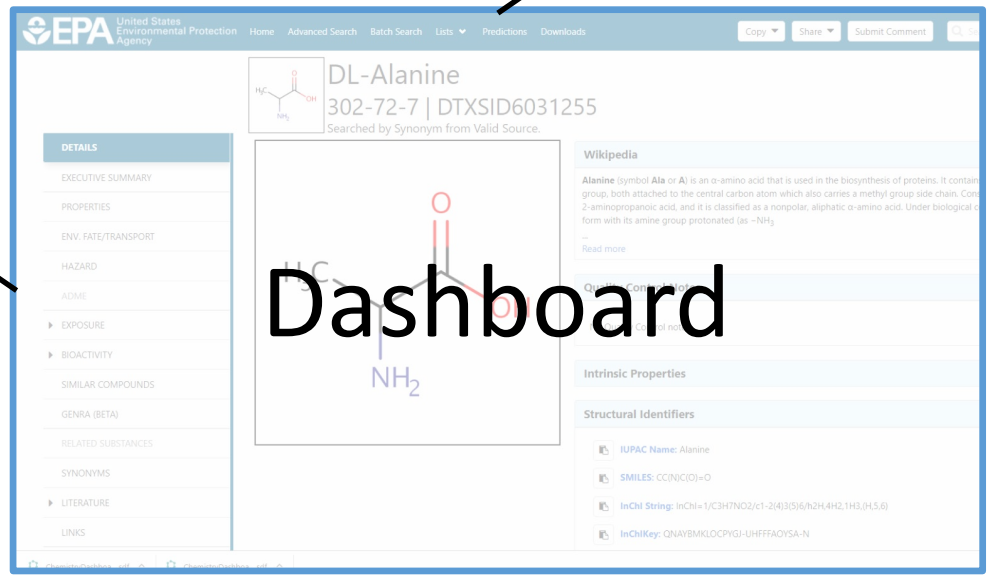
Sharing the DSSTox Database



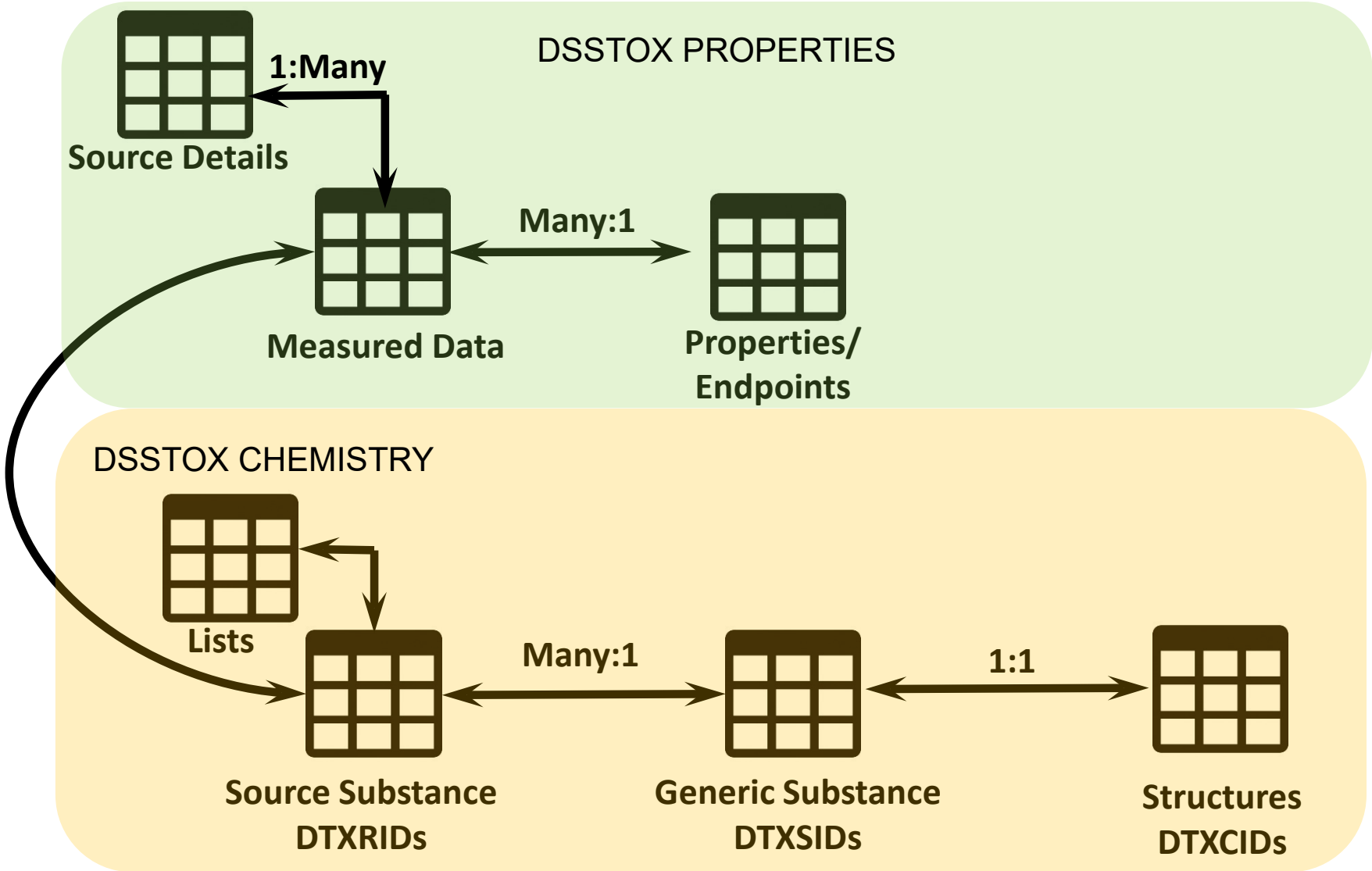




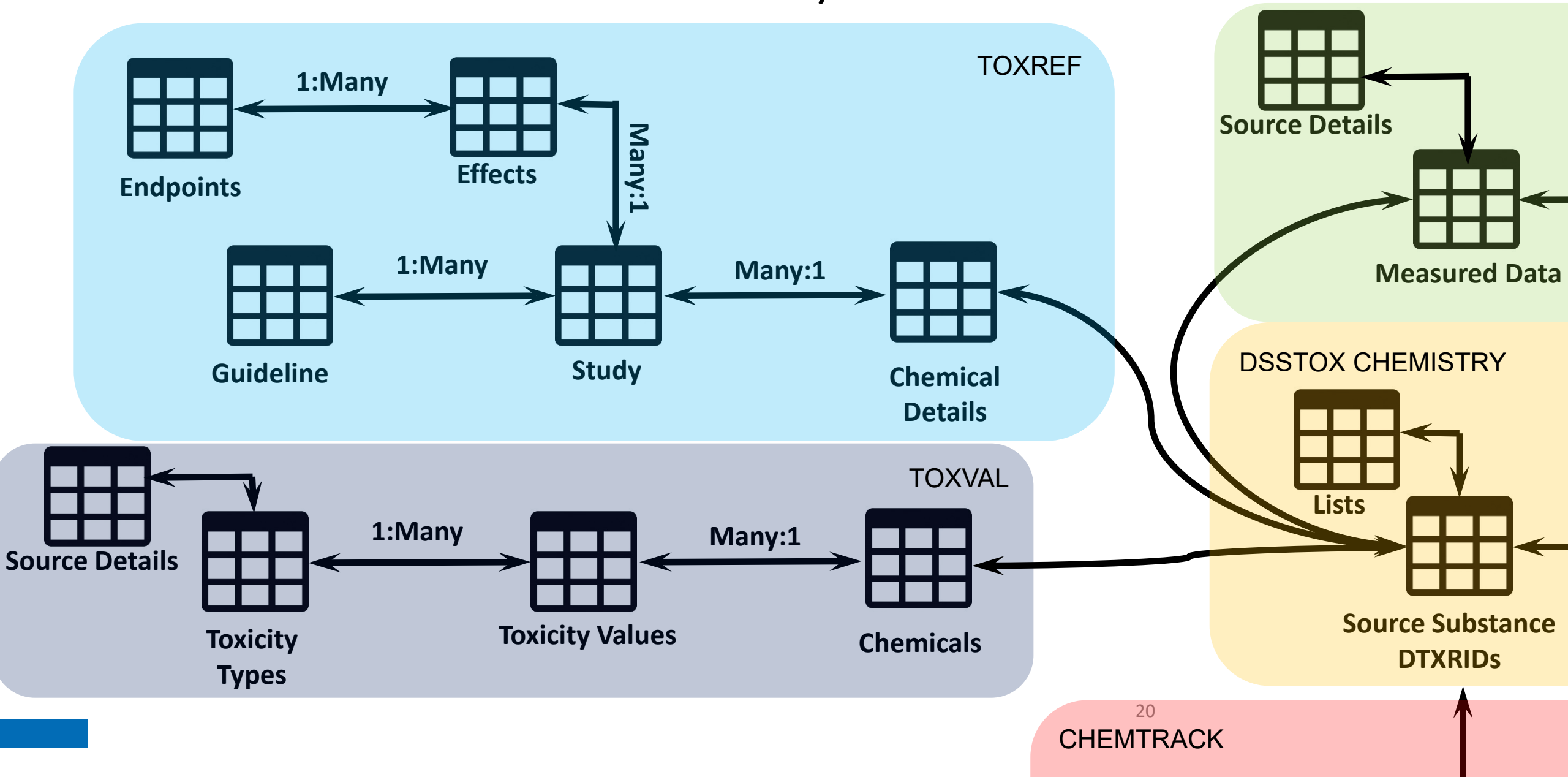




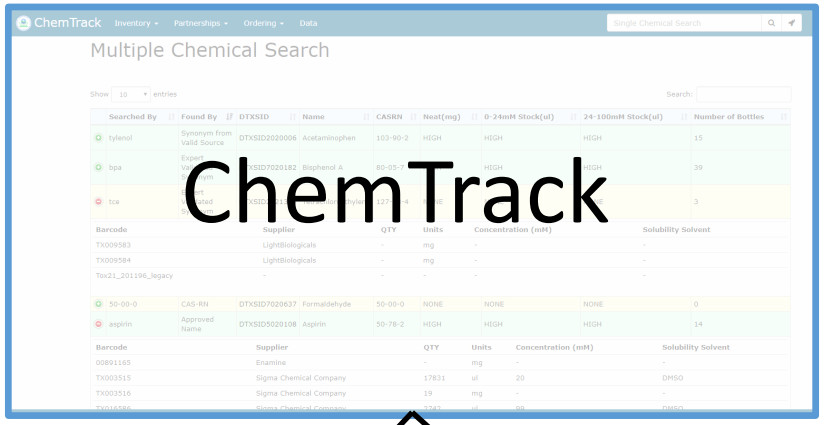
I Need *In Vivo* Toxicity Data…



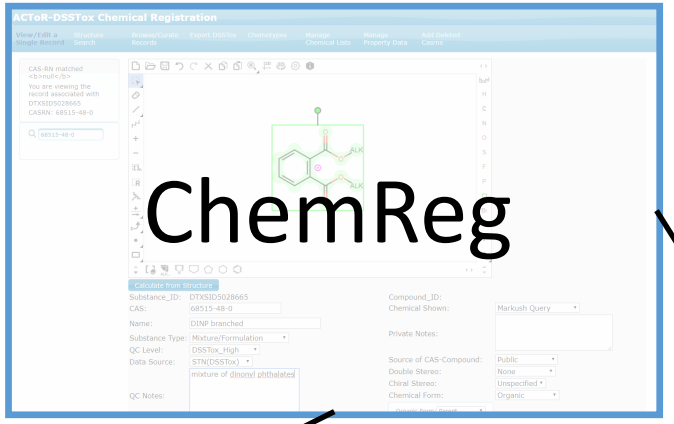
I Need *In Vivo* Toxicity Data…



Sharing the DSSTox Database



ChemTrack



ChemReg

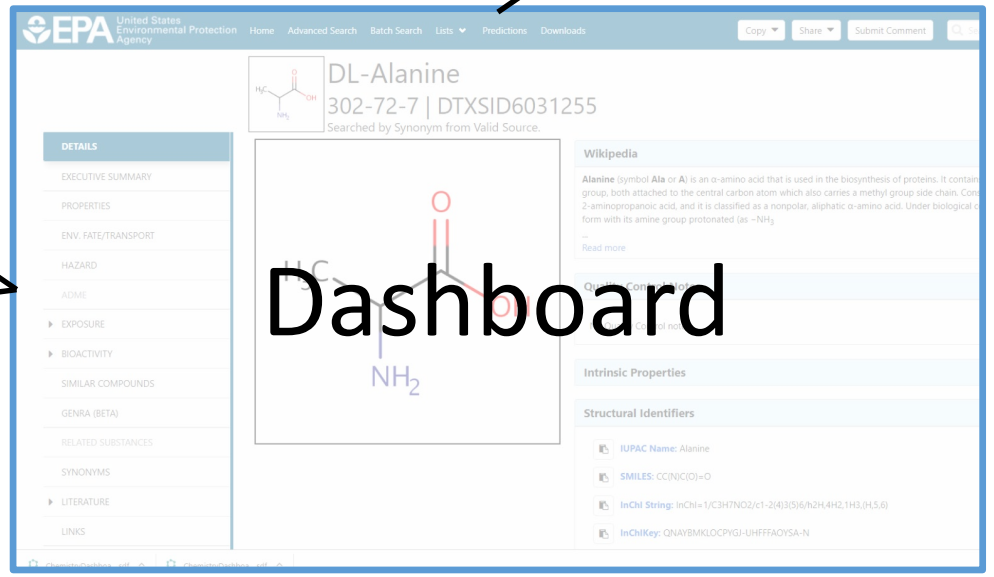
ChemProp

ChemTrack

DSSTox

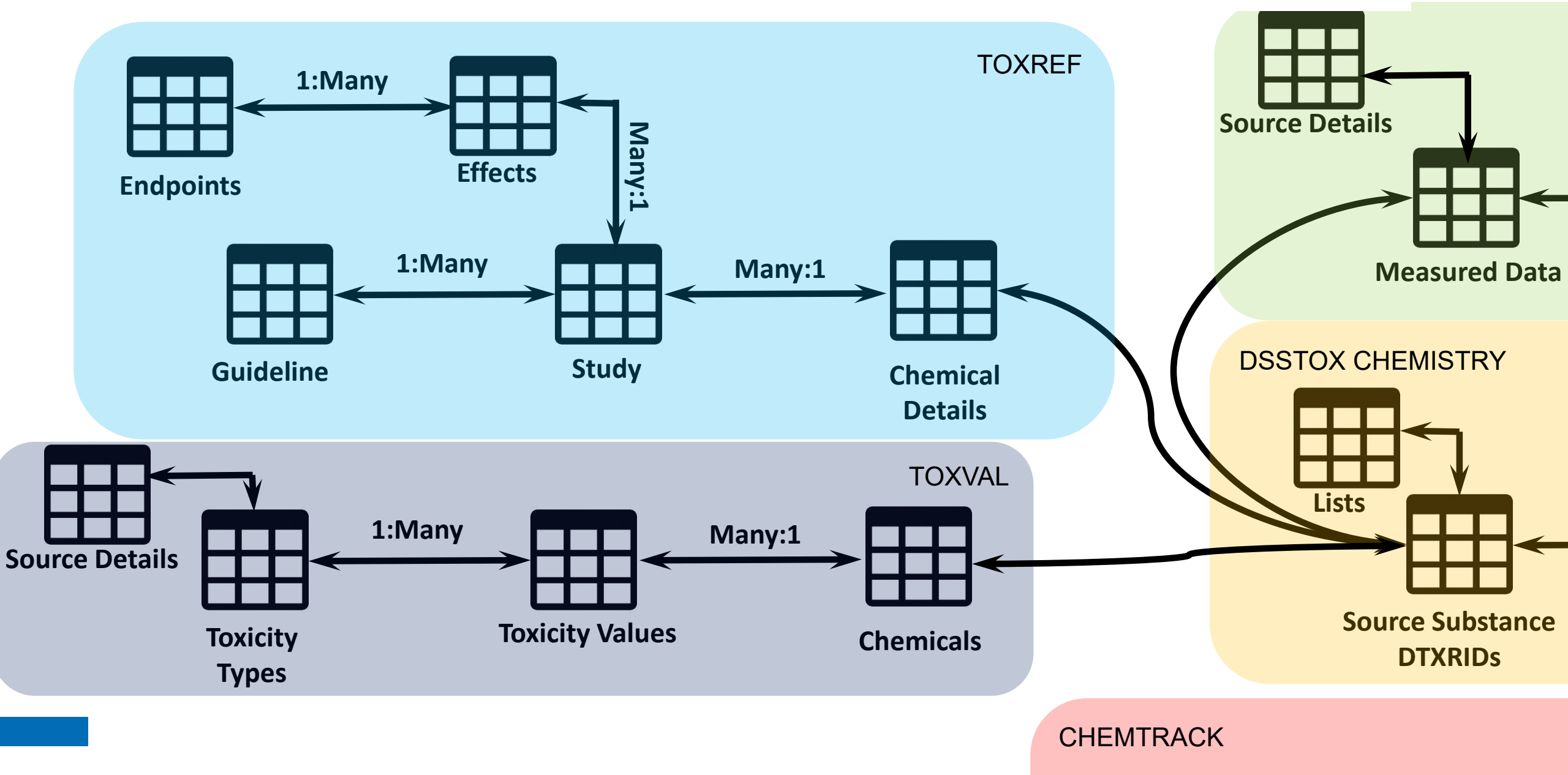
ToxVal Load Scripts

ToxVal



Dashboard

I Need CPDat…


TOXREF
1:Many
Endpoints
Effects
Many:1
1:Many
Guideline
Study
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Chemical Details
Source Details
Measured Data
DSSTOX CHEMISTRY
Lists
Source Substance DTXRIDs
TOXVAL
Source Details
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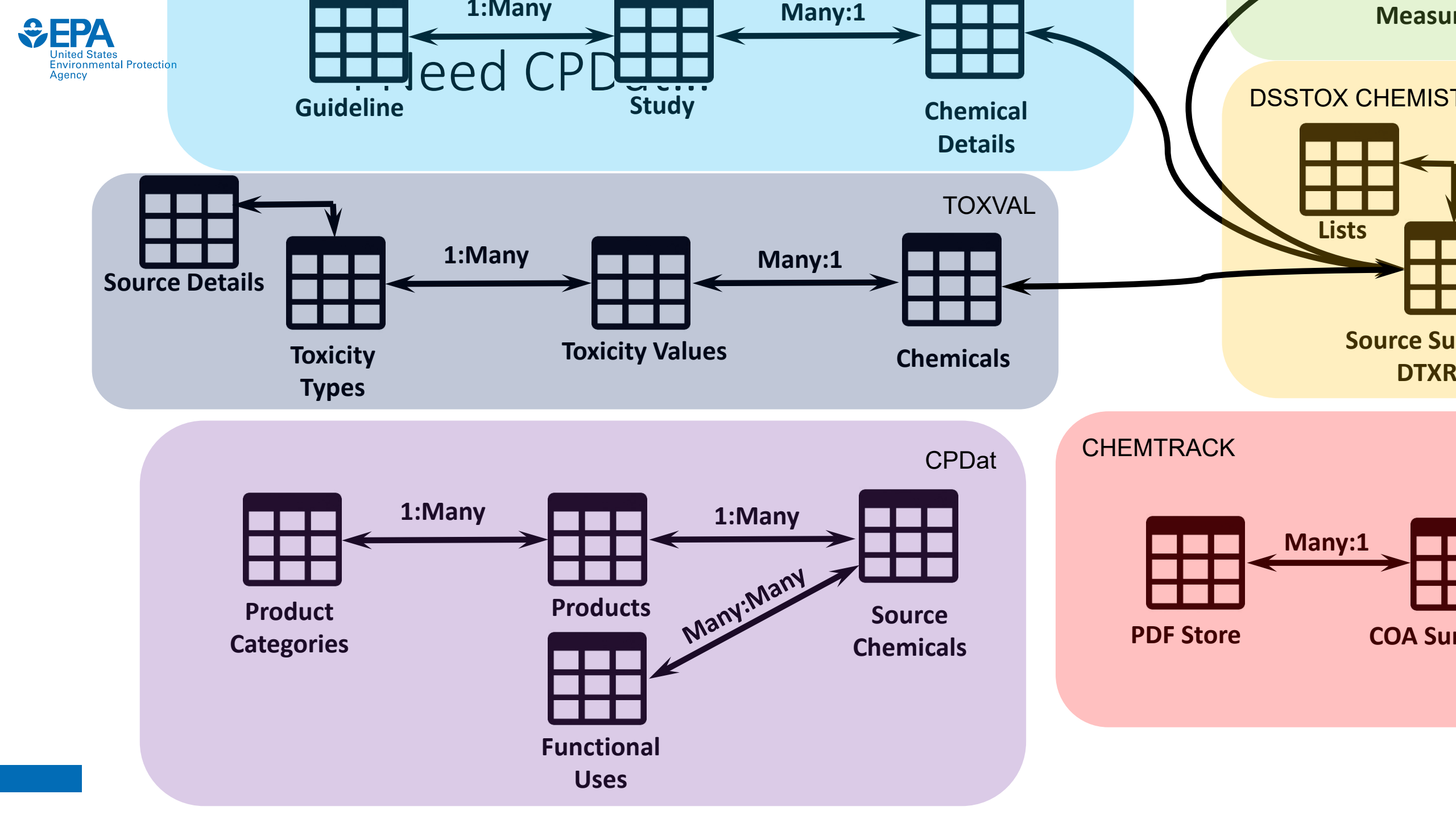
Toxicity Types
Toxicity Values
Many:1
Chemicals
CHEMTRACK


EPA
United States
Environmental Protection
Agency
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Study
Chemical
Details
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Lists
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DTXR
TOXVAL
Source Details
Toxicity
Types
1:Many
Toxicity Values
Many:1
Chemicals
CPDat
1:Many
1:Many
Product
Categories
Products
Source
Chemicals
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Functional
Uses
CHEMTRACK
Many:1
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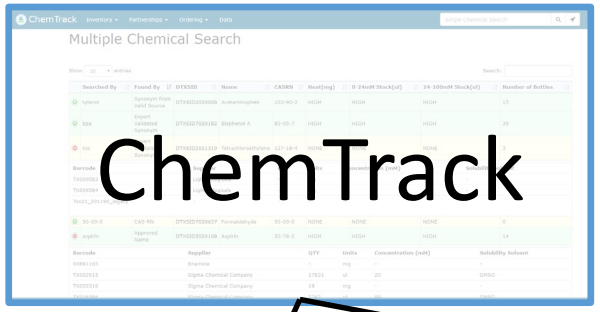
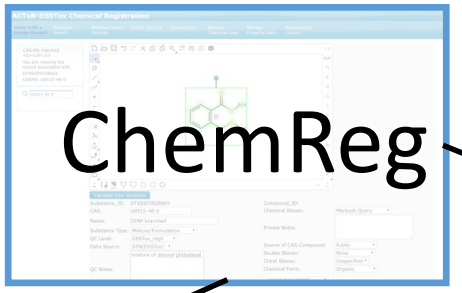
COA Su

EPA United States Environmental Protection Agency





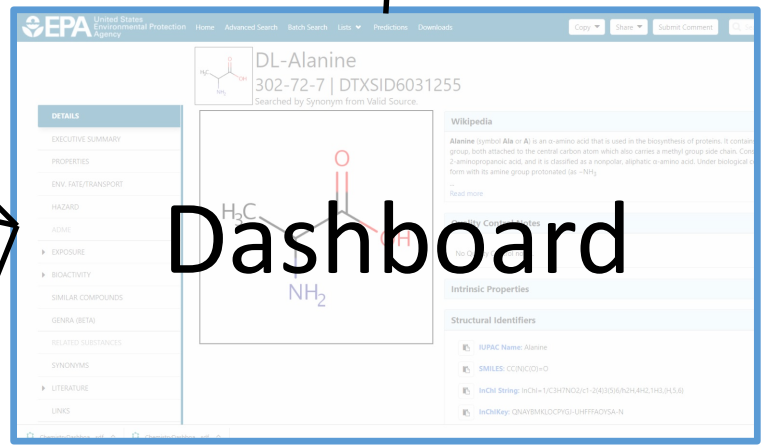
ChemProp

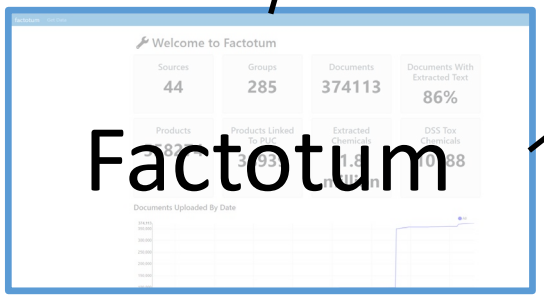
DSSTox

ChemTrack

ToxVal Load Scripts

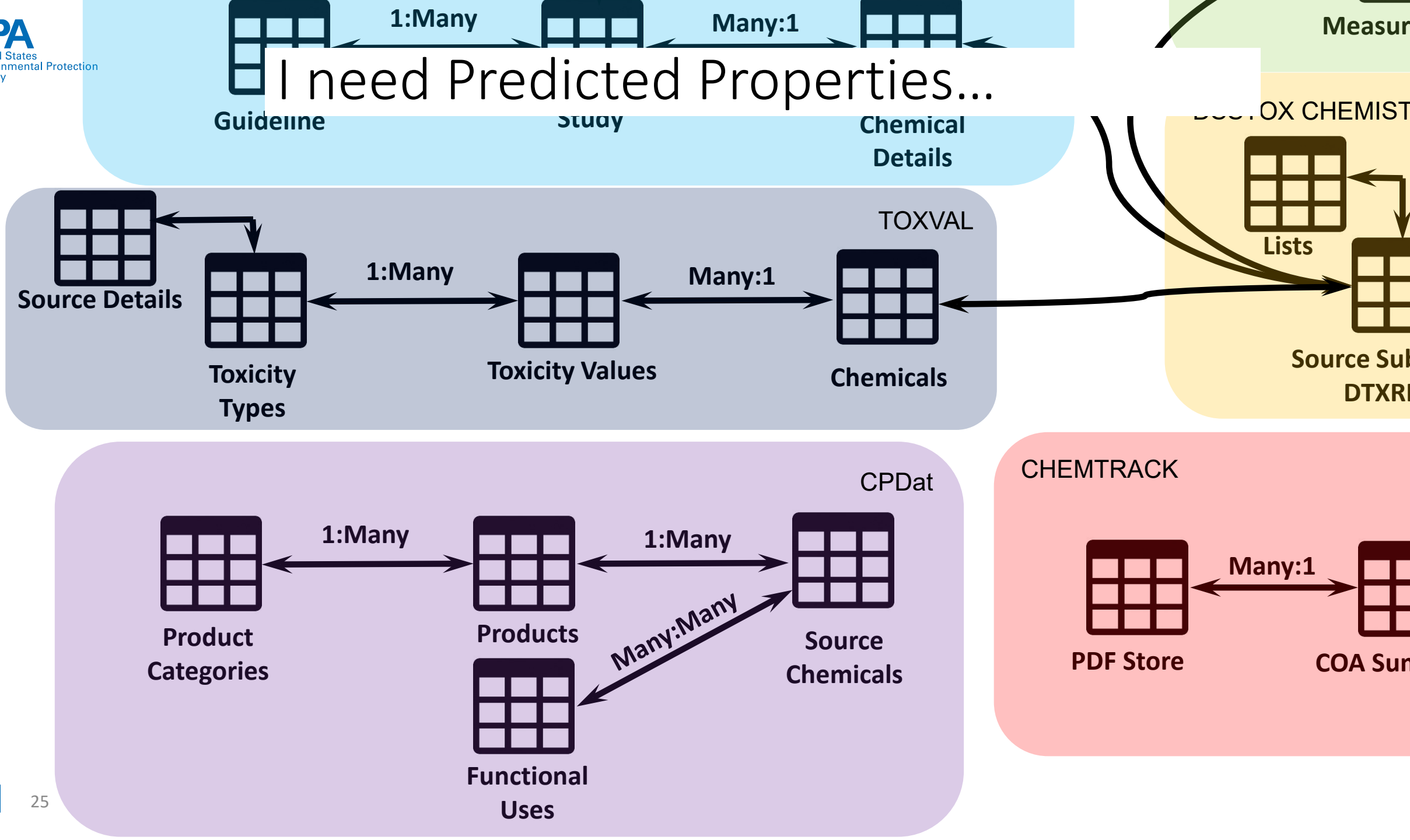
ToxVal



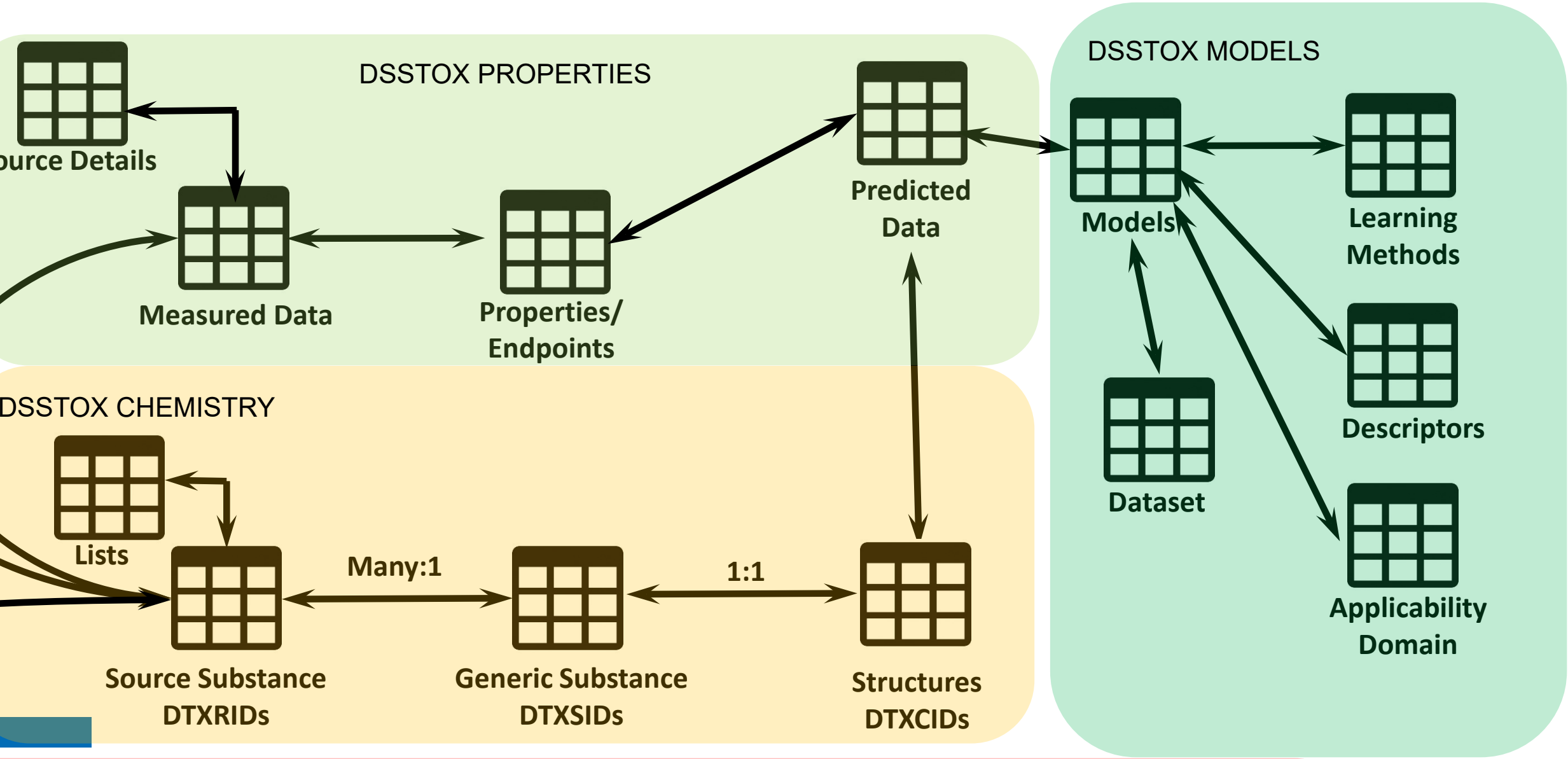


CPDat

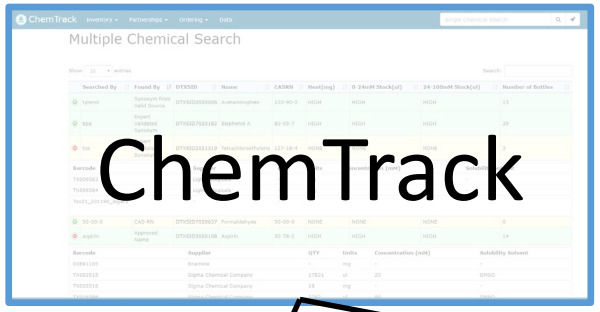
I need Predicted Properties…

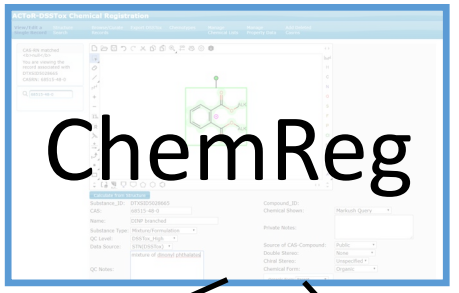


I need Predicted Properties…



EPA United States Environmental Protection Agency





Modeling Scripts

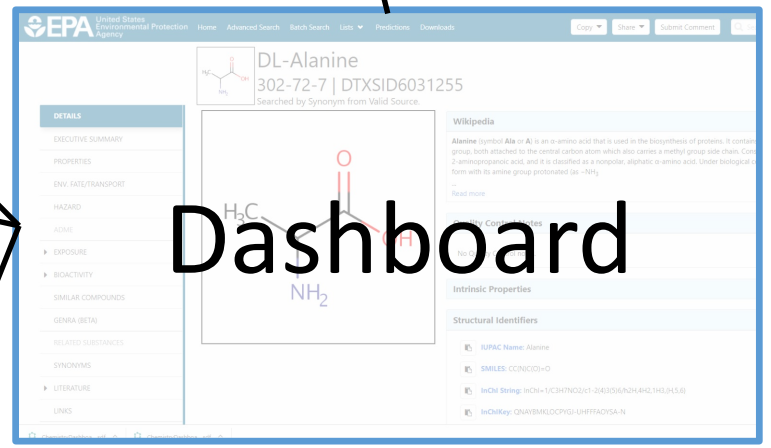
DSSTox

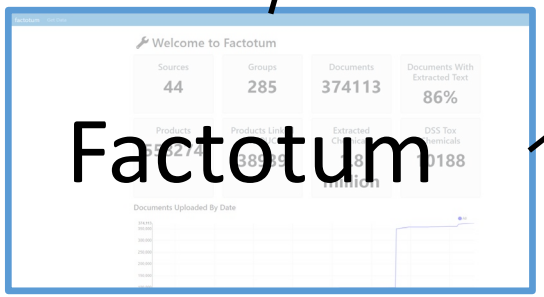
ChemTrack

ChemProp

ToxVal Load Scripts

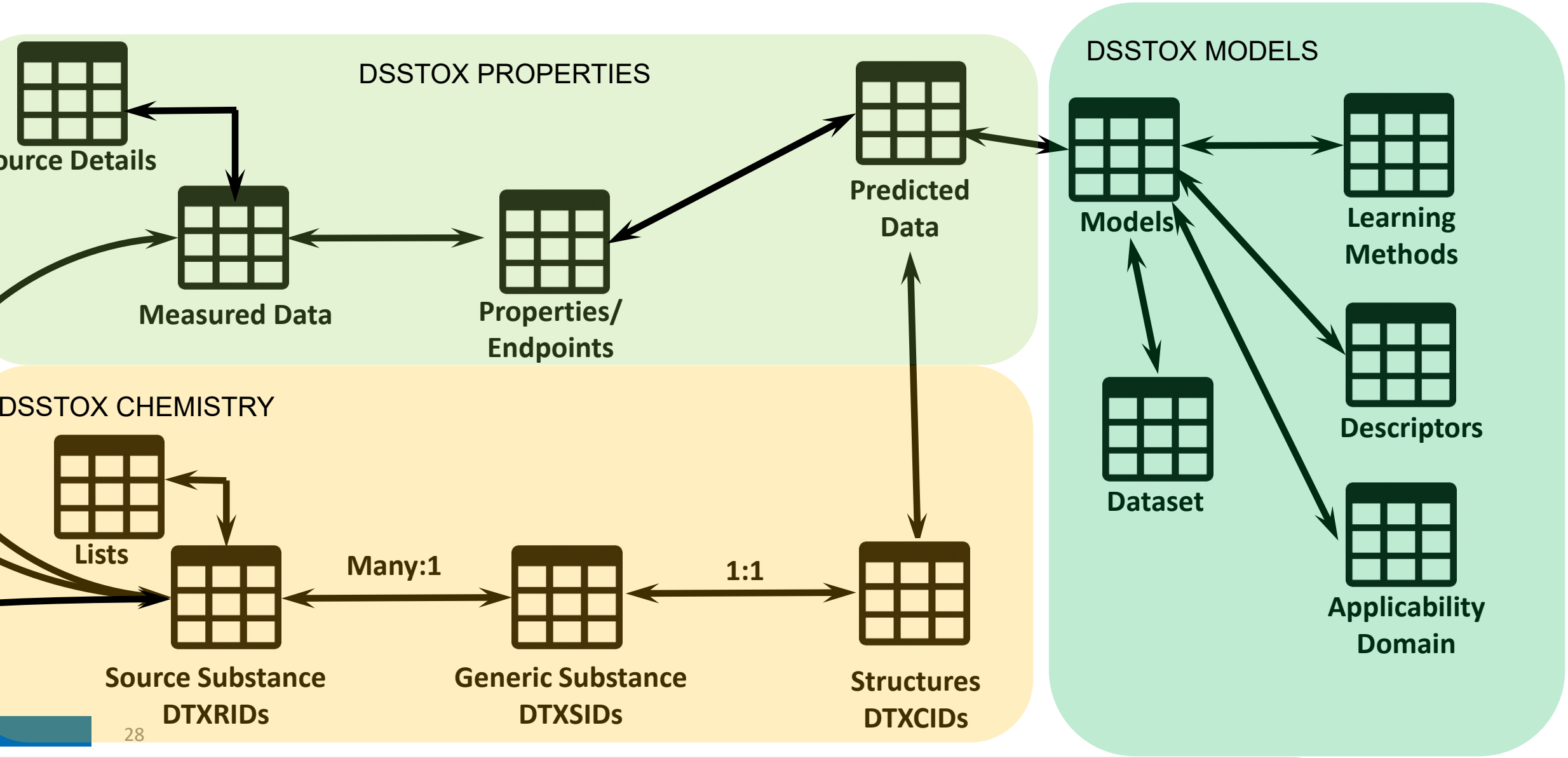
ToxVal



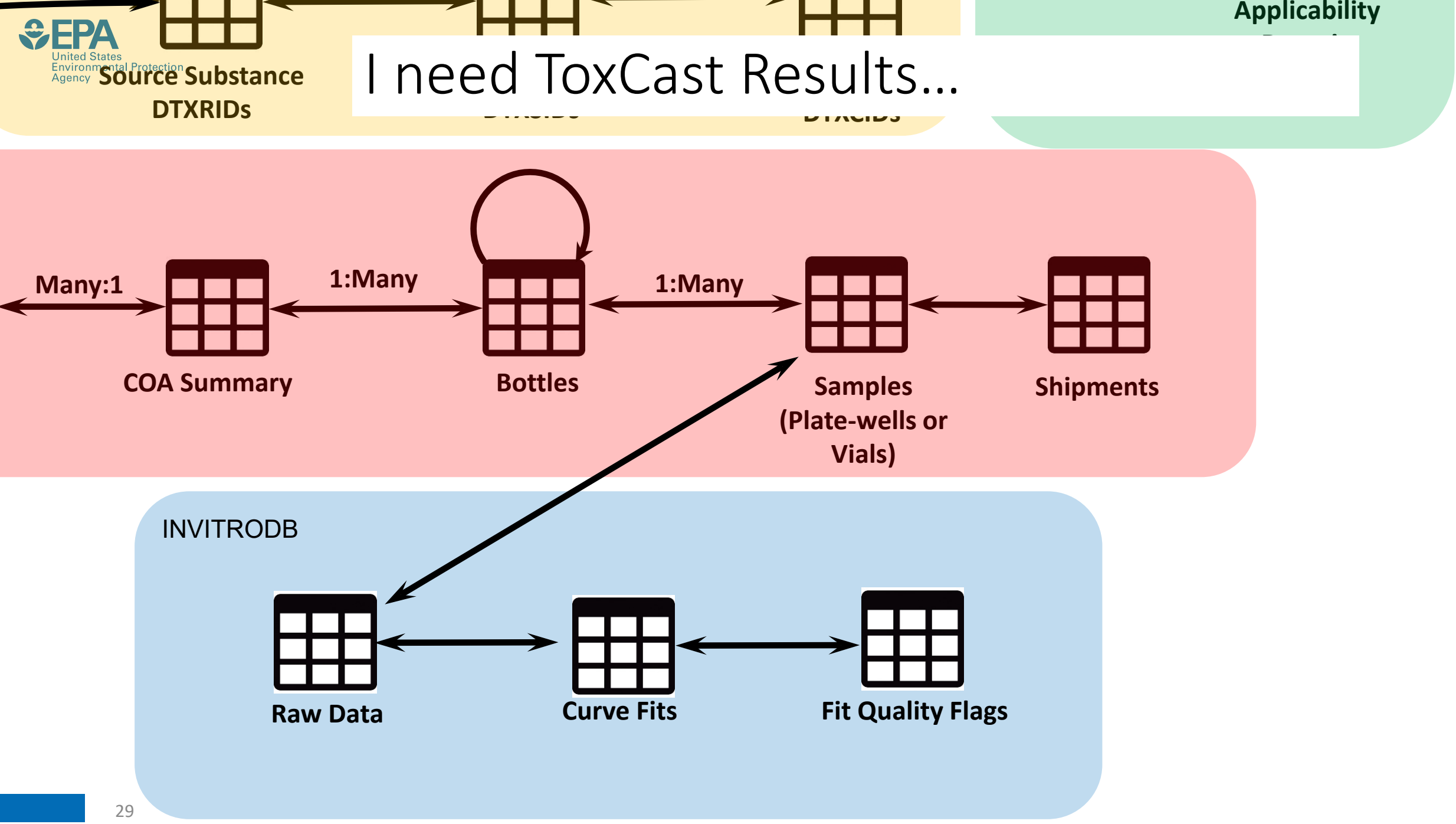


CPDat

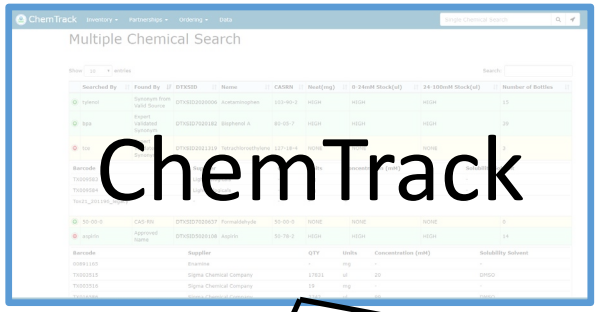
I need ToxCast Results…

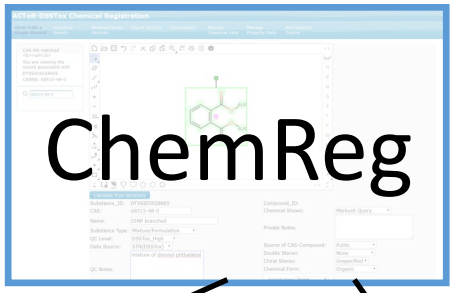


I need ToxCast Results…



EPA United States Environmental Protection Agency





Modeling Scripts

DSSTox

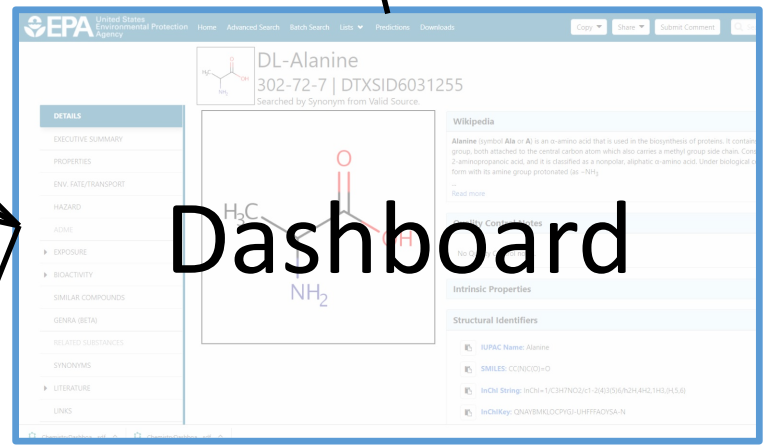
ChemTrack

ChemProp

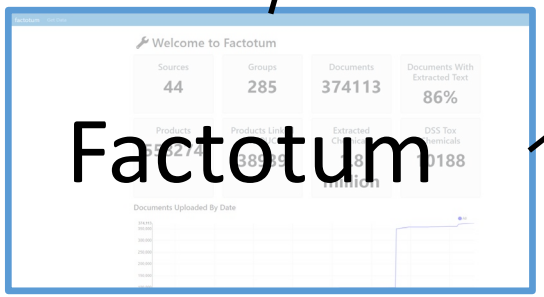
ToxVal Load Scripts

ToxVal

InVitroDB

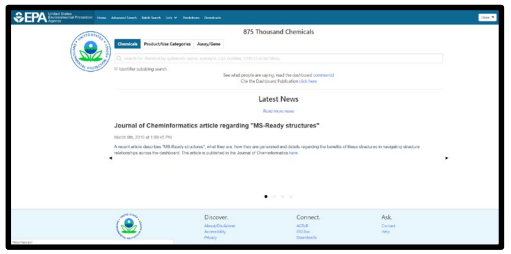


TCPL



CPDat

Proposed EPA-ORD Data Structure



Production Application Layer

Virtual or Physical Application Databases – Data Structured to efficiently support our external production applications

Presentation Layer
(Fit-for-Purpose)

ORD Data Lake

Data Analytics/ Learning

Generalized data model providing integration across the domains for scientific exploration

Integration Layer

ChemTrack App
ChemTrack

ChemReg Application
DSSTox
ChemProp

TCPL R Package
InVitroDB

Toxicity QC App
ToxRef DB

Facto
CPDat

Model + Pred App
Models

Transactional Layer

Raw data processing and data curation, quality tools

EPA United States Environmental Protection Agency

Conclusions

- The Comptox Chemicals Dashboard is great
- The desire to make our data available resulted in a web of tight coupling
- This tight coupling inhibits improvement and flexibility
- Separation of concerns in different data layers adds complexity and overhead but removes restrictions
- APIs provide greater flexibility for maintaining backward compatibility than direct database querying

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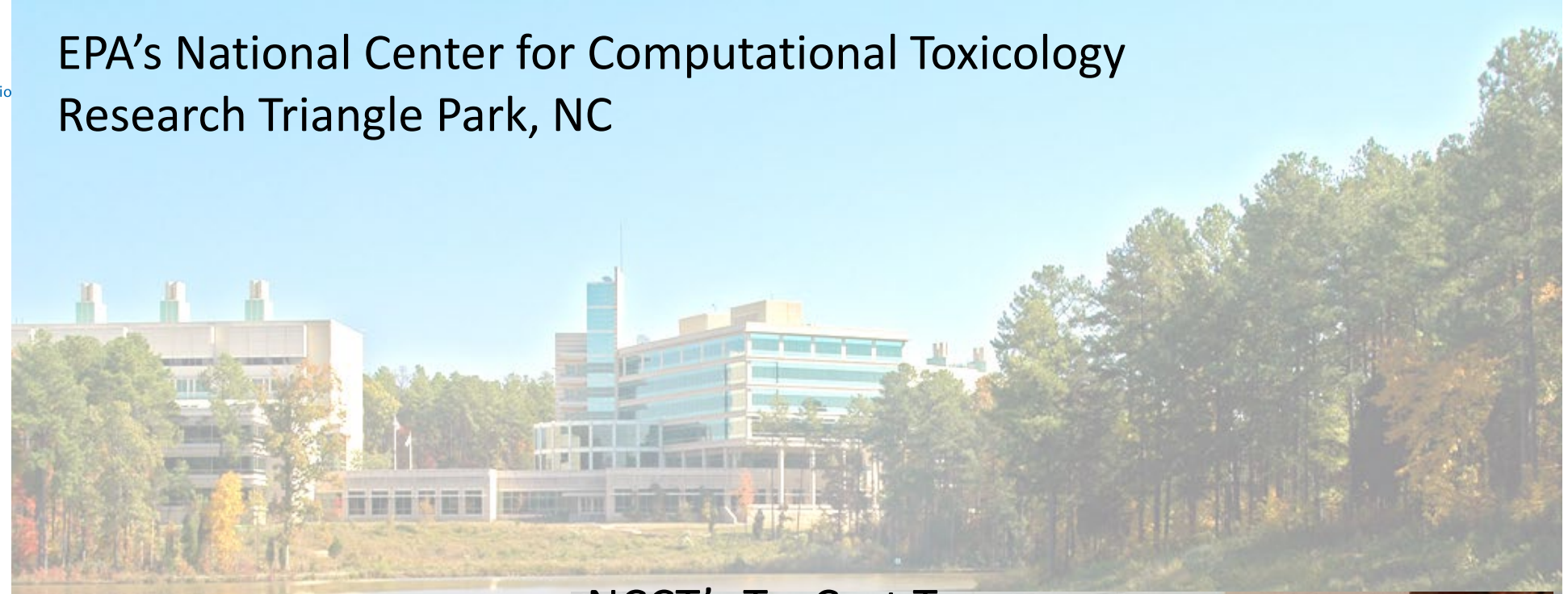

NCCT's ToxCast Team

EPA United States Environmental Protection Agency

Questions?