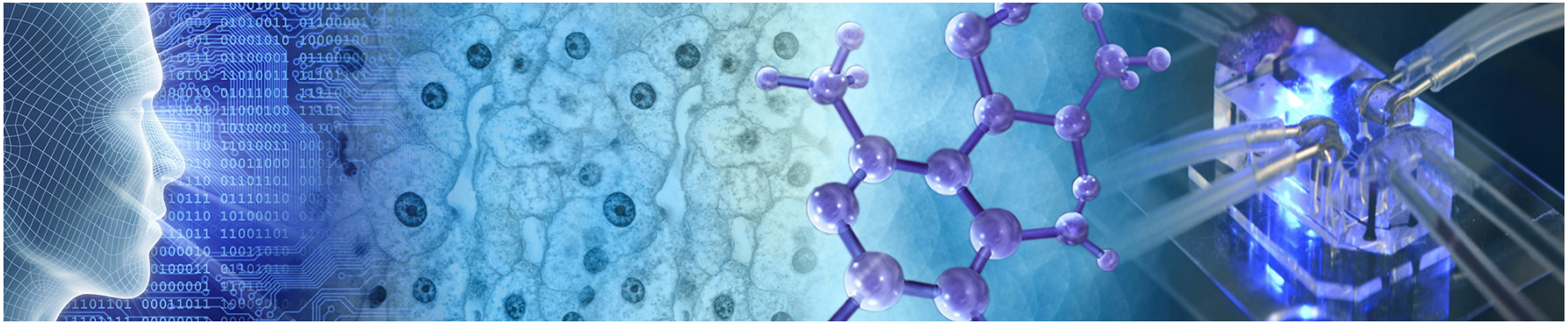
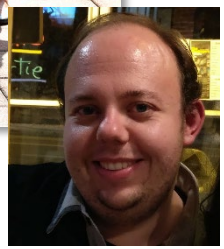
NTP
National Toxicology Program



Introduction to Computational Tools

SACATM Meeting

September 2-3, 2020



20 YEARS OF ICCVAM
Advancing Alternatives to Animal Testing

DEPARTMENT OF HEALTH & HUMAN SERVICES • USA

Computational Toxicology Tools

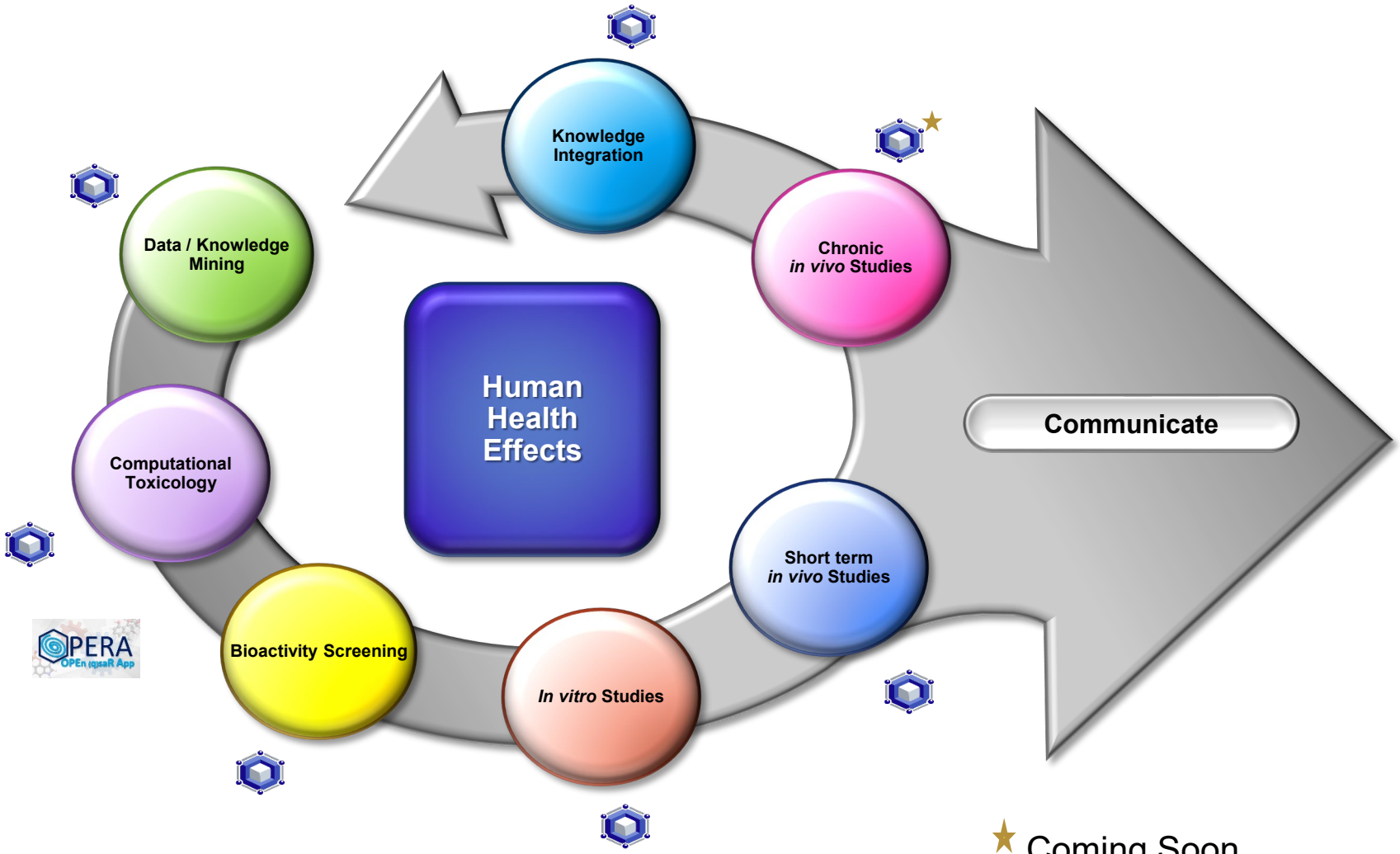
- Computational tools and resources play a critical role in chemical evaluations such as:
  - Data aggregation
  - Exploring chemical properties
  - In vitro to in vivo extrapolation
  - Mapping high-content data to biological systems
  - Generating predicted values

Integrated
Chemical
Environment

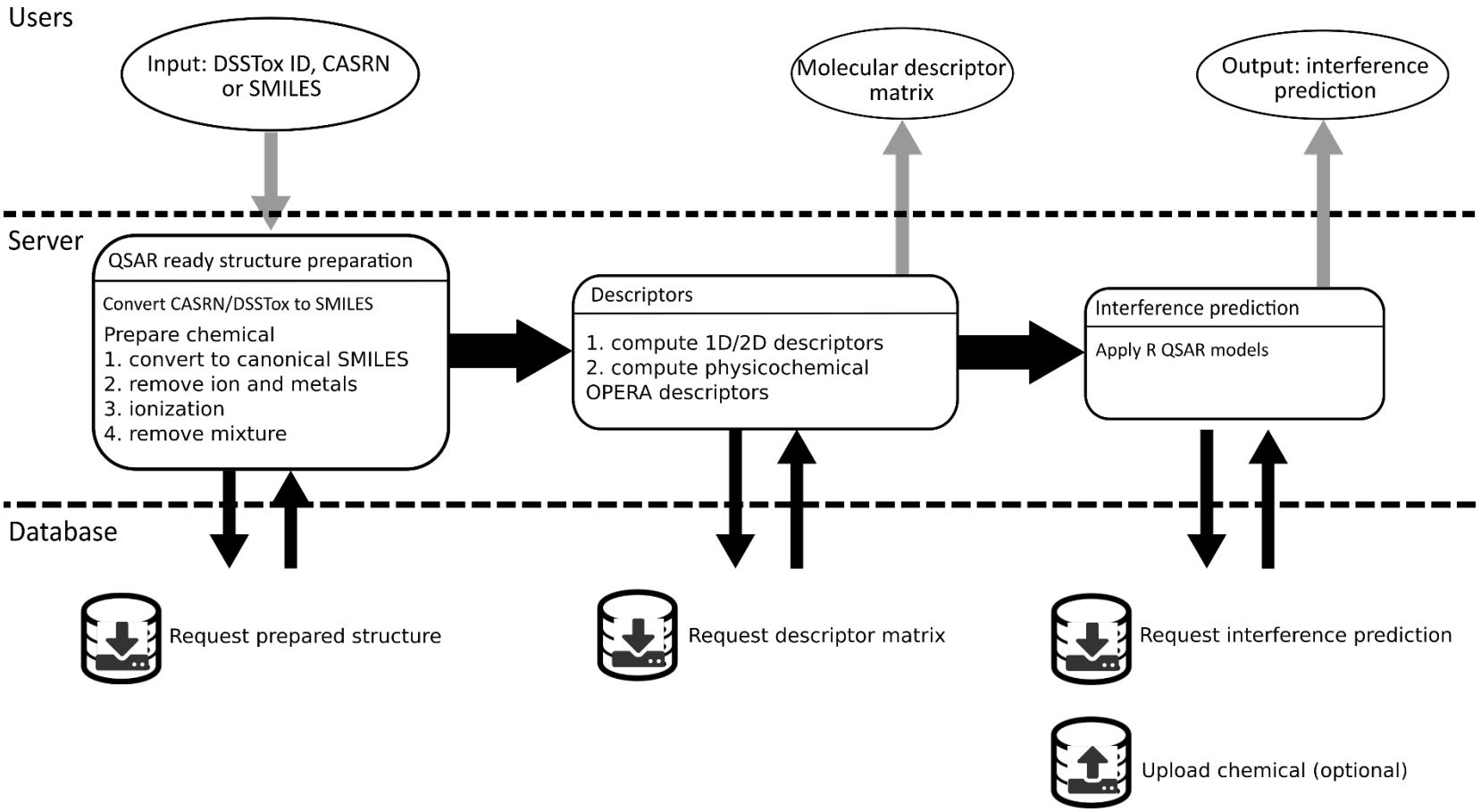
Feedback from SACATM 2019

- Increase accessibility, transparency, and utility of datasets
- Allow users to upload their own data to IVIVE workflow
- Increase documentation for tools, data, and search function
- Form ICE Advisory Group to provide timely feedback on:
  - new features/needs to serve ICCVAM, NICEATM and NTP stakeholders
  - the usability of ICE UI and tools
  - proposed changes to functionality or the user interface
- Increase chemical structural support for both input and output
- Curate and integrate human data and engage biomedical research community
- Engage with CROs to generate data on environmental chemicals

NTP Translational Toxicology Pipeline



InterPred: Assay Interference Prediction

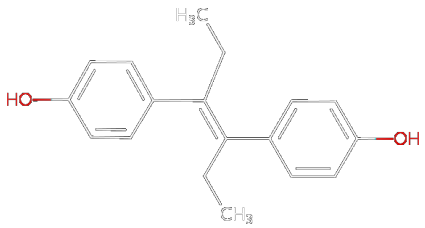


https://sandbox.ntp.niehs.nih.gov/interferences/

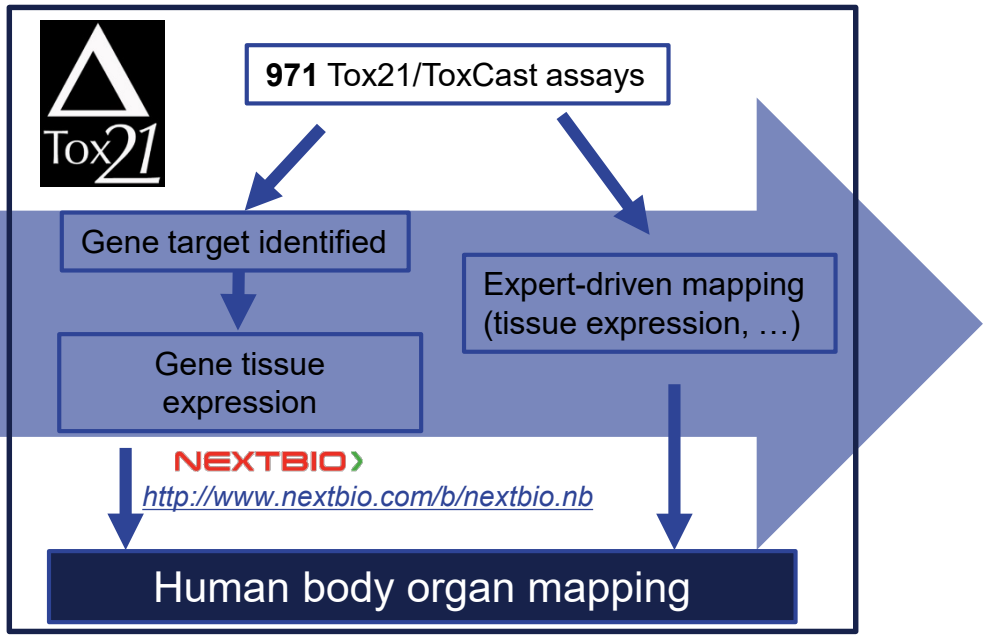
Tox21 BodyMap: Hypothesis Generation

- Knowledge-mapping exercise to visualize where a chemical may produce effects in the body

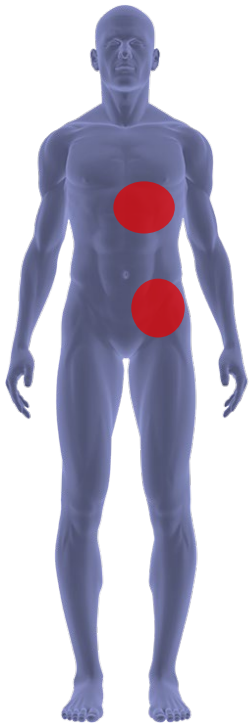
9,270 chemicals selected
(from Tox21 chemical library)



Select chemical



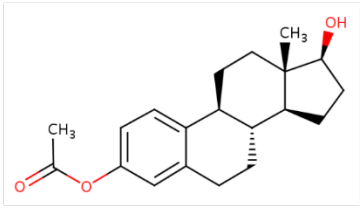
Activity (AC50) on the 971 assays



https://sandbox.ntp.niehs.nih.gov/bodymap/

Tox21 BodyMap: Hypothesis Generation

Chemical information



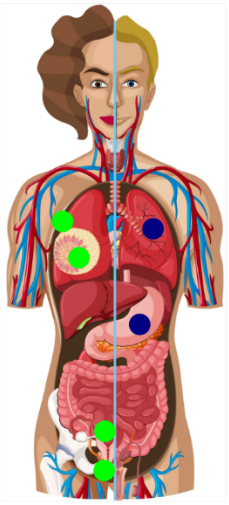
CASRN: 4245-41-4

Name: Estradiol acetate

DSSTOX ID: DTXSID7045867

SMILES: CC(=O)OC1=CC=C2[C@H]3CC[C@]4(C)[C@@H](O)CC[C@H]4[C@@H]3CCC2=C1

Body mapping



AC50 cutoff: 20 μM

Tissue expression threshold:

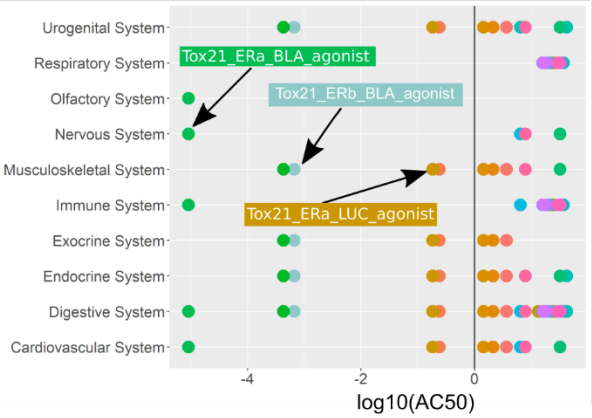
10*folds control

List of organ: Uterus; Vagina; Peritoneum; Mammary gland; Immune System; Stomach; Lung

mapped using assay gene target

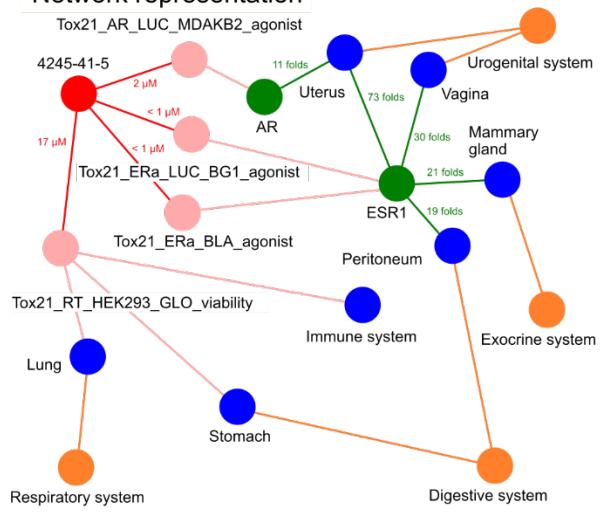
mapped using assay tissue

Assay mapping



Visualisation of the log10(AC50) by assay grouped by organ system.

Network representation



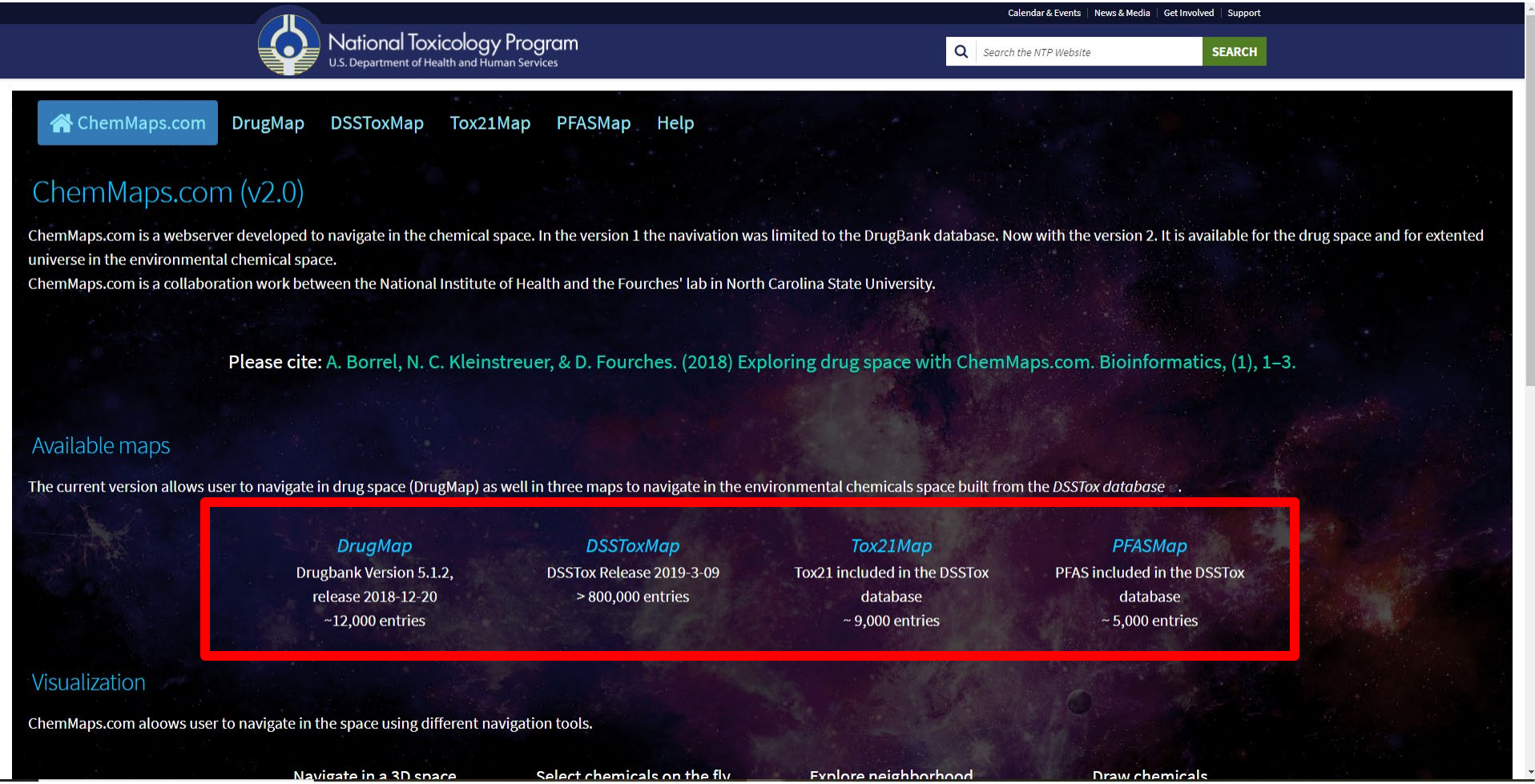
Input: Chemical name or CASRN, set assay activity and gene expression thresholds

Output: visualization including body mapping, assay mapping and a results network

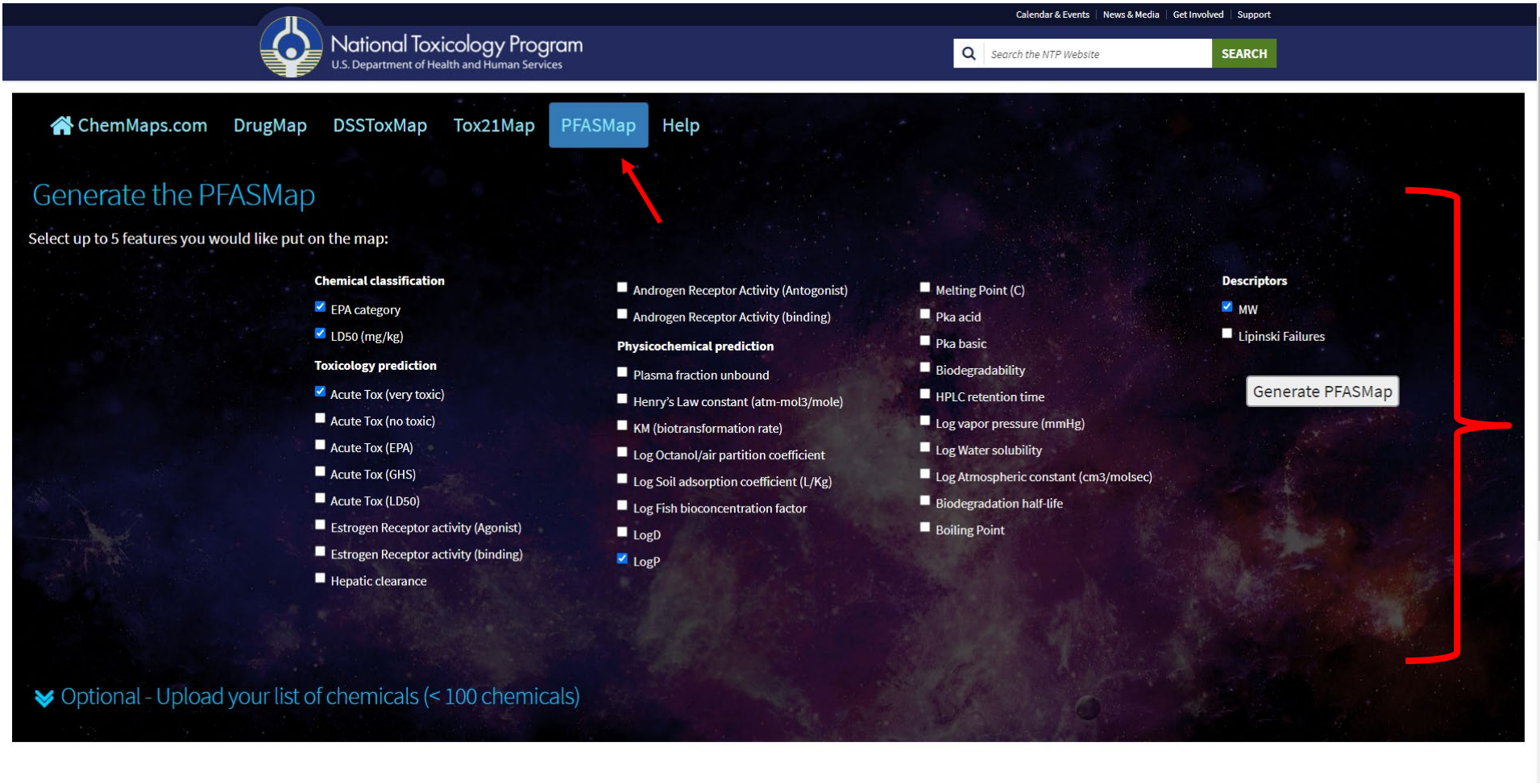
https://sandbox.ntp.niehs.nih.gov/bodymap/

ChemMaps: Visualizing the Chemical Universe

https://sandbox.ntp.niehs.nih.gov/chemmaps/

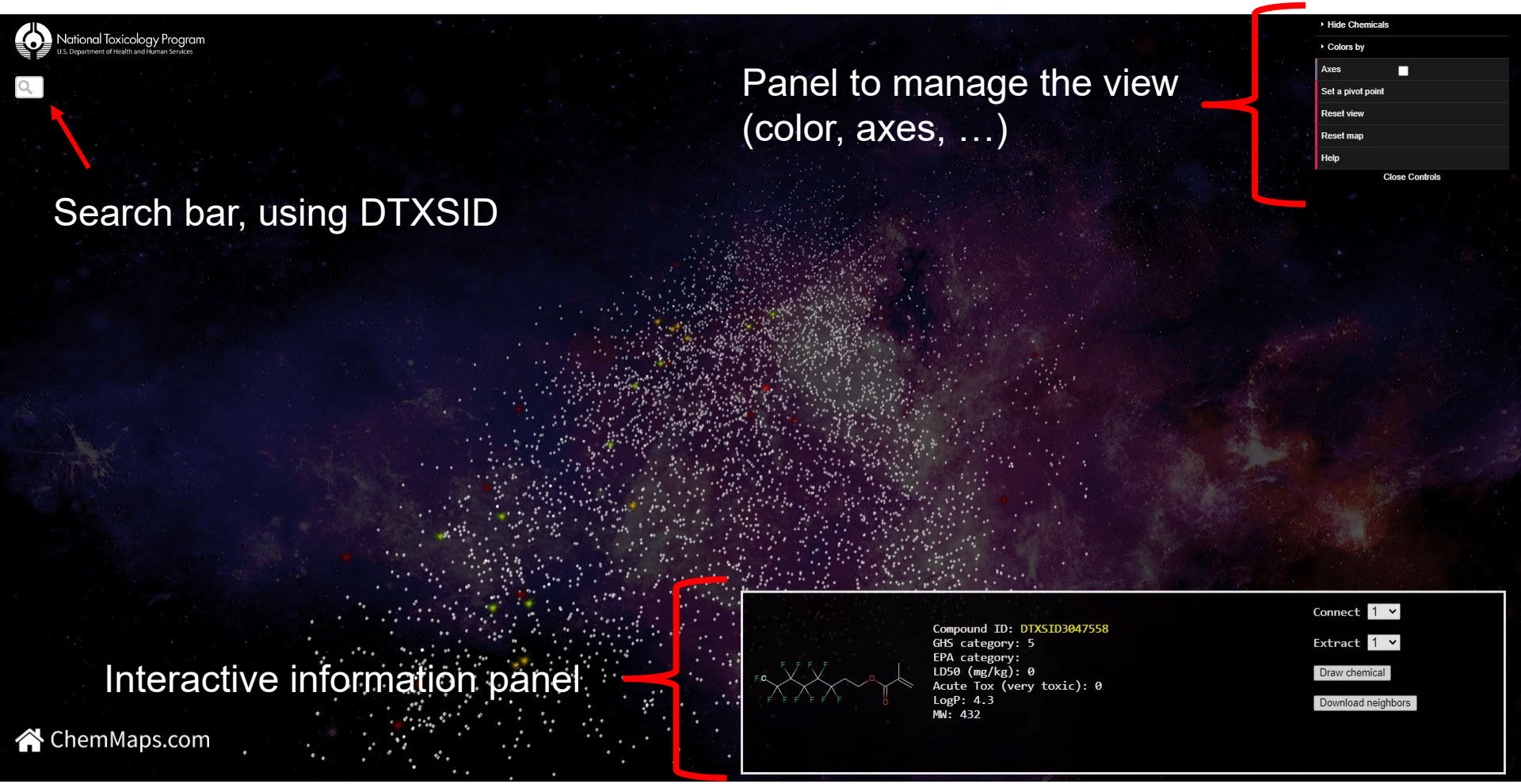


ChemMaps: Visualizing the Chemical Universe



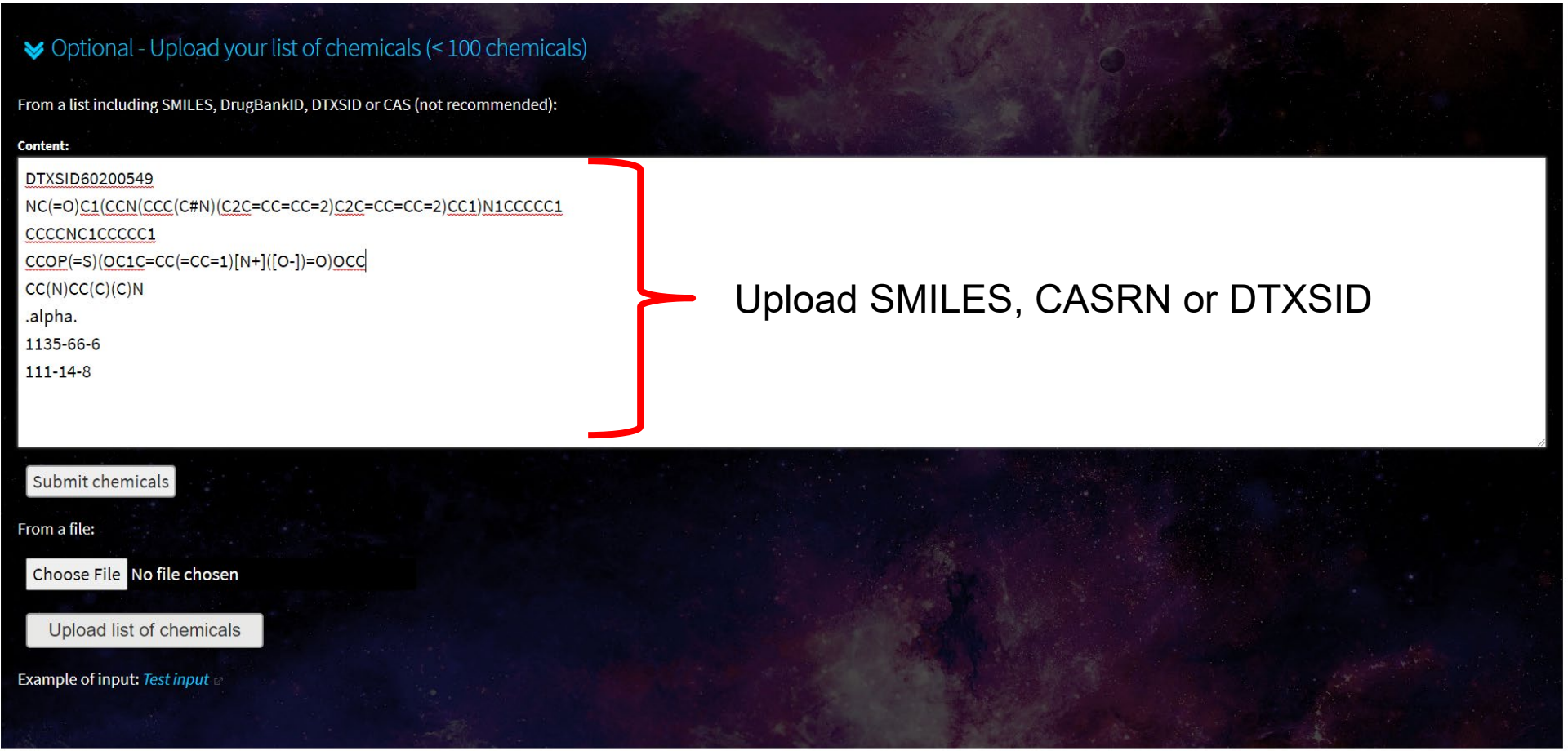
- Choose up to 5 properties to put on the map
  - Toxicity values/predictions
  - Physicochemical properties

ChemMaps: Visualizing the Chemical Universe

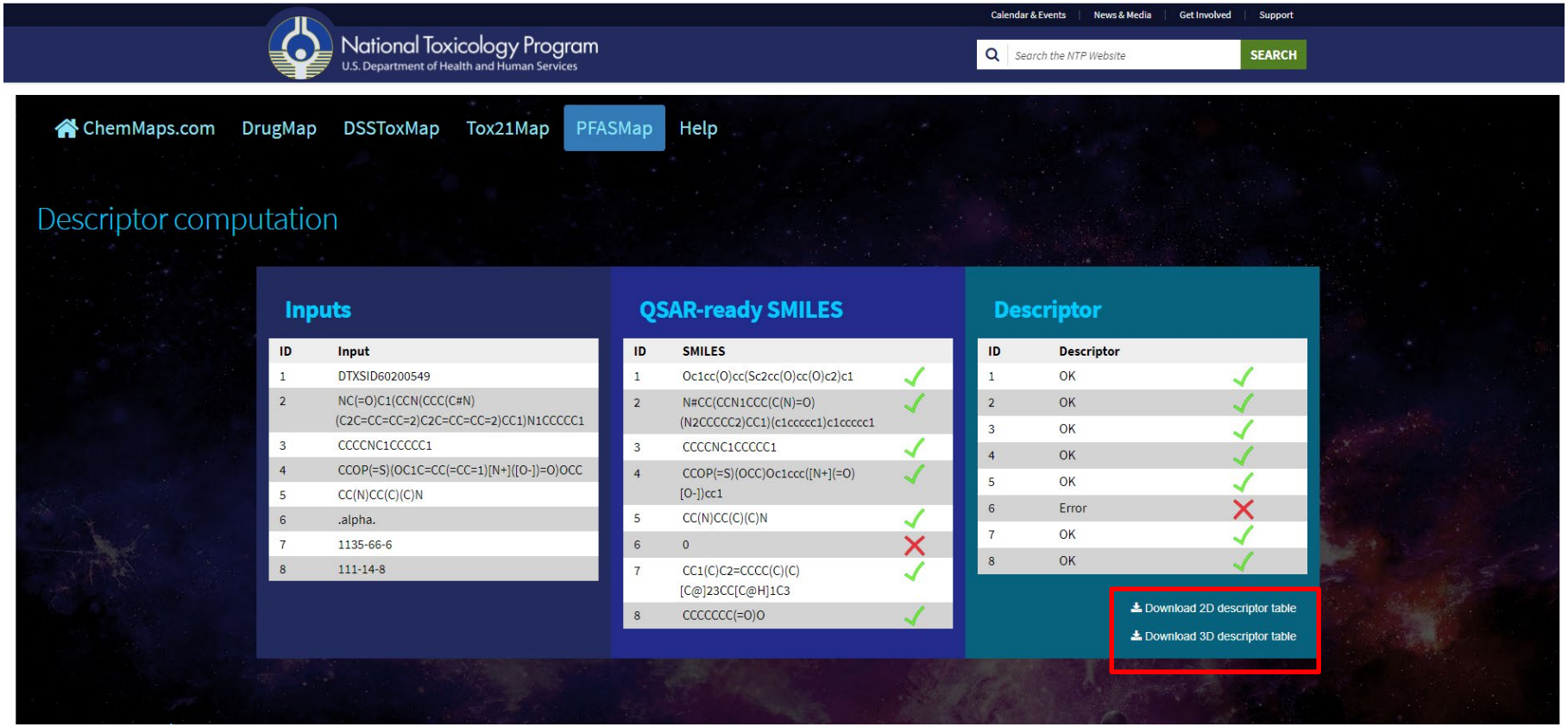


- Chemicals are represented using a planet (default) or a star (based on tox/property information)

ChemMaps: Project New Chemicals

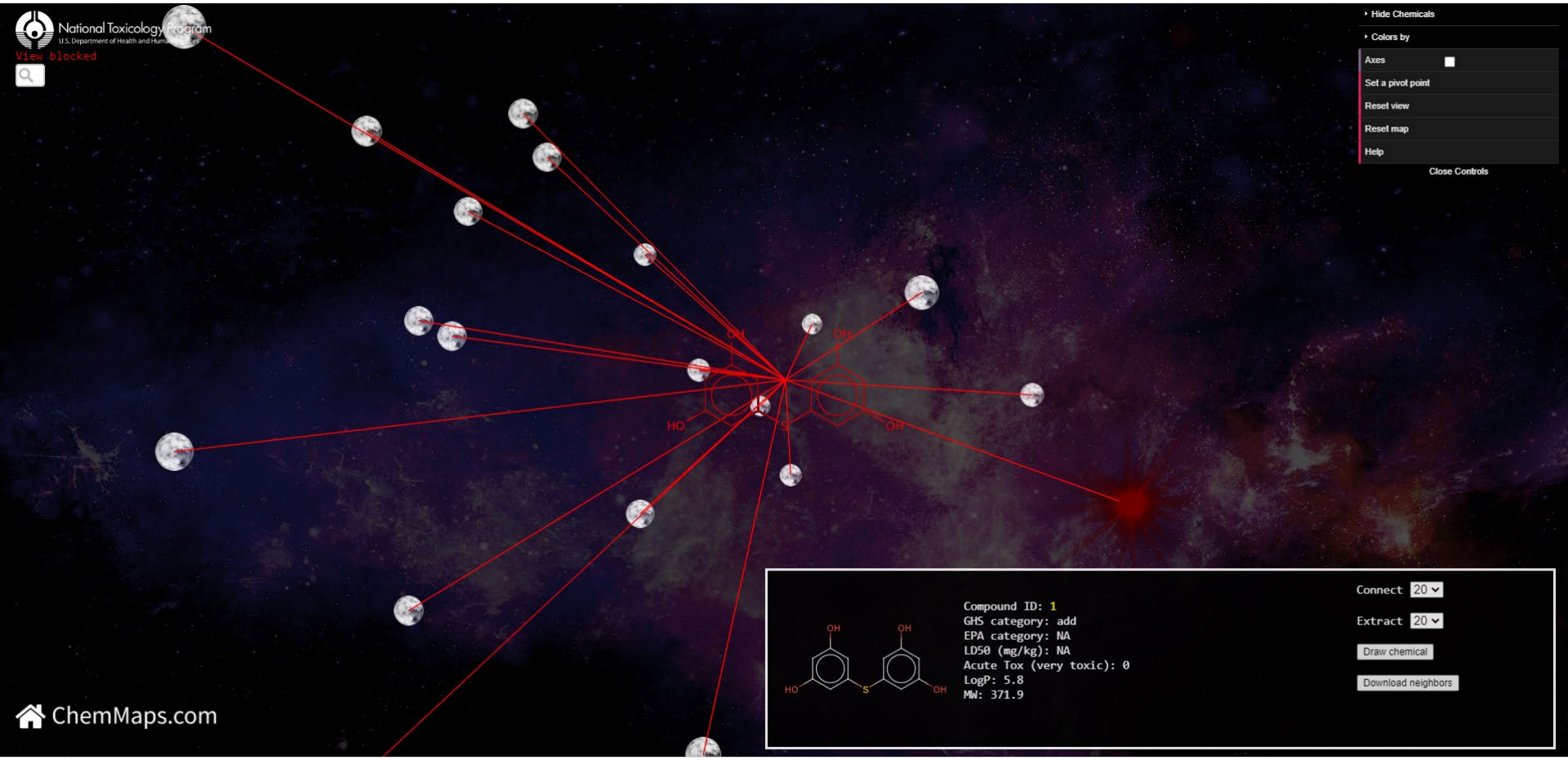


ChemMaps: Project New Chemicals



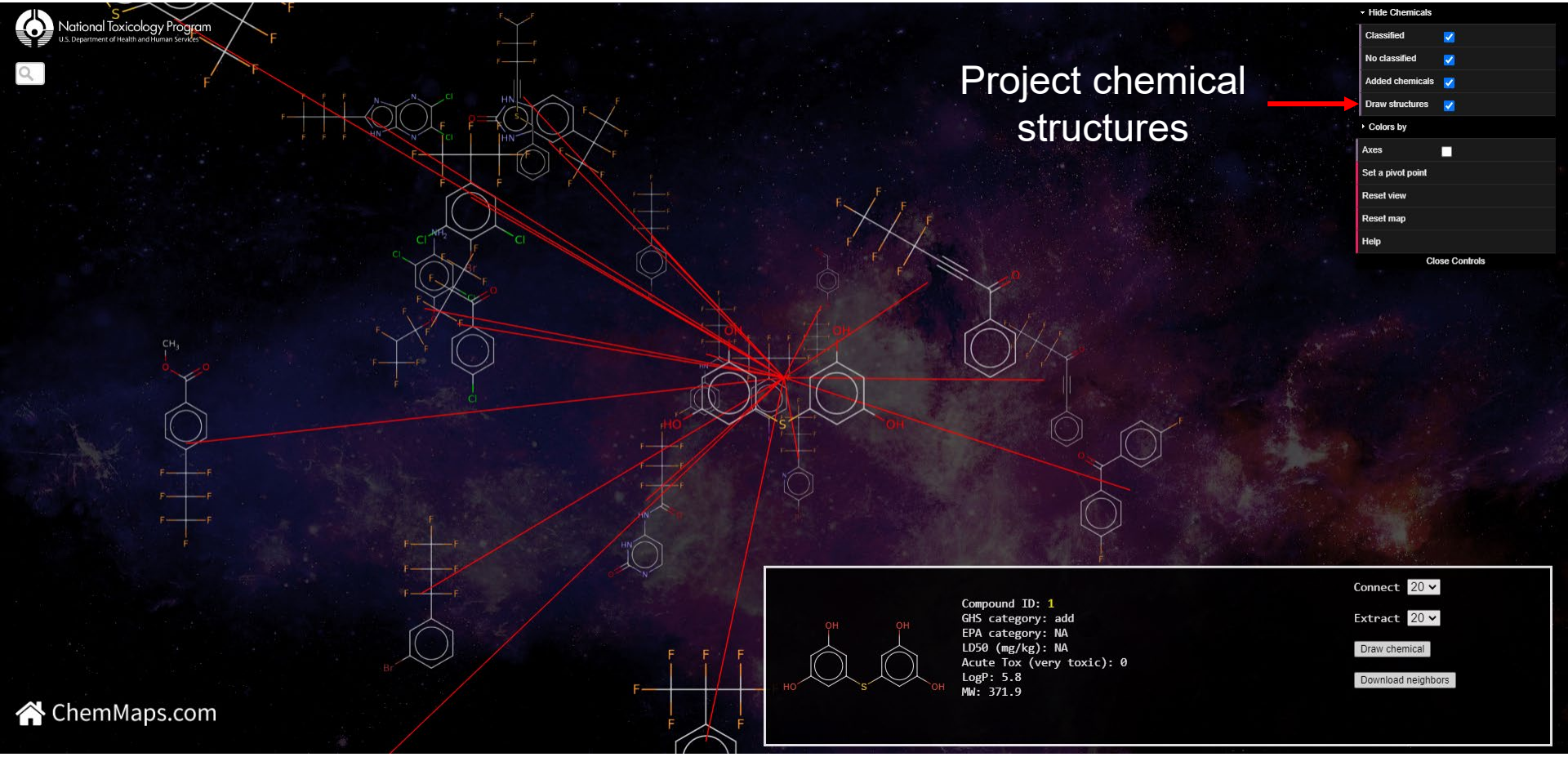
- Automated structure preparation
  - Clean structures
  - Prepare SMILES in QSAR ready form
  - Compute descriptors (downloadable)

ChemMaps: Project New Chemicals



- Analyze new chemical neighborhood

ChemMaps: Project New Chemicals



- Analyze new chemical neighborhood