United States Environmental Protection Agency

CompTox Chemicals Dashboard Virtual Training

Breakout Group Worksheet
Topic: Hazard/Bioactivity

This worksheet was developed for the Breakout Group session of the CompTox Chemicals Dashboard Virtual Training, hosted by the U.S. Environmental Protection Agency's Center for Computational Toxicology and Exposure on October 18, 2022.

For more information about the CompTox Chemicals Dashboard tool, visit the CompTox Chemicals Dashboard at comptox.epa.gov/dashboard. Users also are welcome to review the Help page (epa.gov/chemical-research/comptox-chemicals-dashboard-help) and Release Notes (comptox.epa.gov/dashboard/releasenotes). Starting from the CompTox Chemicals Dashboard, click on the About drop-down menu. The Help page link is third from the top, and the link for Release Notes is at the bottom.

Goal

To investigate *in vivo* animal data (both human and ecology focused) and *in vitro* data focusing on the Hazard, Bioactivity and Lists of Assays tabs using case examples.

Directions

This session will focus on the Hazard and Bioactivity tabs of the Dashboard using the suggested example chemical of Bisphenol A (CAS RN 80-05-7). When you finish, we encourage you to explore the Dashboard by re-doing the worksheet with other chemicals of interest to you.

Individual Chemical Search

1. Enter a chemical name or CASRN in the main search bar and select the chemical of interest from the automatically populated options that appear under the search bar. For this exercise, facilitators will be using Bisphenol A (BPA) (CAS RN 80-05-7).

2. From the Hazard tab, what are some of the Sources and Risk Assessment types for the available Exposure Limits?

3. What sources provide LOAELs for the compound? What is an example of a LOAEL for reproductive effects in rats?

4. From the Bioactivity tab, select the ToxCast: Summary option. What is the cytotoxic lower bound and cytotoxic median concentrations? How many assay endpoints are active at an AC50 below the cytotoxic lower bound concentration? (Note: If the ToxCast: Summary menu item is unavailable, try a searching for a different compound.)

5. From the Toxcast: Conc. Response Data page under the Bioactivity tab, how many active assay endpoints (active hit calls) include PPARg in the endpoint name?

6. Where can the tissue or cell type be viewed for various assay endpoints? What cell types were used for the PPARg assay endpoints?

7. From the Toxcast: Conc. Response Data page, click the link for *Analytical Data on Tox21 Browser* option to view analytical QC data. Are the identity and purity confirmed for the compound? (Keep this tab open for the subsequent question.)

8. From the Toxcast: Conc. Response Data page, view concentration-response curves for the "TOX21 AR_BLA_Antagonist_ratio" assay endpoint by typing the assay endpoint into Endpoint Name column filter and clicking the icon within the data row in the *All plots* column. What is the difference in the AC50 between the multiple runs of the data?

    a. Looking at the Sample ID annotated in the left upper corner on the conc-response curves in the *All plots* view, match the Sample ID with the Tox21 analytical QC data identified in Question #7. Was one sample ID used for both runs in this assay, or different sample IDs?

9. Does the chemical perturb the estrogen or androgen receptors?

    a. Individual assay(s): Is the chemical active for affecting estrogen receptor 1, or androgen receptor? Is the activity species-specific, or across cells from various species?

    b. Model predictions: Is the chemical an estrogen receptor agonist or antagonist, and/or does it bind the estrogen receptor? List AUC values for each model, as available.

10. From the HTTr: Summary option under the Bioactivity tab, how many rows of data are related to breast cancer?

11. From the HTPP: Summary option under the Bioactivity tab, what is the most sensitive endpoint?

12. What file types can be downloaded for ToxCast data from the Dashboard?

    a. From the Toxcast: Conc. Response Data page under the Bioactivity tab, export all active assay endpoint data in breast or mammary cells.

Chemical Lists

13. Using the Chemical Lists option under the Lists tab in the top banner of the Dashboard, locate and navigate to the ATSDRMRLS list (ATSDR: Minimal Risk Levels (MRLs) for Hazardous Substances). Filter to show all chemicals that are active in ≥30% of ToxCast assays, then export using the "Send To Batch Search" button. Add the following to the export:
    - Metadata: IRIS and PPRTV
    - Enhanced Data Sheets: ToxValDB Details

    a. Within the exported file—

        i. How many chemicals have IRIS data? PPRTV data?

        ii. How many rows of data are available for the hazard component (Toxval Details tab)?

14. Using the Chemical Lists option under the Lists tab in the top banner of the Dashboard, identify the chemical that is active in the most assays in the latest InvitroDB data version (ToxCast_invitroDB_v3_5, which is the text that can be used in the filter search bar for the List Acronym column).

15. Where can the current (and previous) complete version of the ToxCast data be downloaded?

Reflection

1. In what case example from your work environment would CompTox be useful?

2. What have you learned about the process and workflow used to find information in CompTox?

3. What challenges did you encounter, and how did you solve them?

CompTox Chemicals Dashboard Virtual Training

Breakout Group Worksheet—Answers
Topic: Hazard/Bioactivity

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Goal

To investigate *in vivo* animal data (both human and ecology focused) and *in vitro* data focusing on the Hazard, Bioactivity and Lists of Assays tabs using case examples.

Directions

This session will focus on the Hazard and Bioactivity tabs of the Dashboard using the suggested example chemical of Bisphenol A (CAS RN 80-05-7). When you finish, we encourage you to explore the Dashboard by re-doing the worksheet with other chemicals of interest to you.

Individual Chemical Search

1. Enter a chemical name or CASRN in the main search bar and select the chemical of interest from the automatically populated options that appear under the search bar. For this exercise, facilitators will be using Bisphenol A (BPA) (CAS RN 80-05-7).

   Bisphenol A

2. From the Hazard tab, what are some of the Sources and Risk Assessment types for the available Exposure Limits?

   Select Exposure Limits from the drop-down menu. Answers: FDA CEDI, EFSA, DOE PAC.

3. What sources provide LOAELs for the compound? What is an example of a LOAEL for reproductive effects in rats?

   Select Point of Departure from the drop-down menu, list any sources in the Source column. Example answers: IRIS, ECHA eChemPortal 2020, ToxRefDB, etc.

   Enter *LOAEL* into the Type column filter, *reproduction* into the Risk Assessment column filter, and *rat* into the Species column filter. Example answers: ToxRefDB LOAEL: 500 mg/kg -day; ECHA POC 2013, 2014, 2016 LOAEL: 100 mg/kg-day.

4. From the Bioactivity tab, select the ToxCast: Summary option. What is the cytotoxic lower bound and cytotoxic median concentrations? How many assay endpoints are active at an AC50 below the cytotoxic lower bound concentration? (Note: If the ToxCast: Summary menu item is unavailable, try a searching for a different compound.)

   View graphic to identify the cytotoxic concentrations. Enter the Cytotox lower bound concentration (9.509 for BPA) into the AC50 field, and assign the filter to "less than": 92 endpoints.

   Note that the Dashboard will default to only showing active Hit Call assay endpoints and filtering out "background" assays. The number 92 assumes those defaults were not changed.

5. From the Toxcast: Conc. Response Data page under the Bioactivity tab, how many active assay endpoints (active hit calls) include PPARg in the endpoint name?

   Enter *PPARg* in the Endpoint Name filter, then filter to Active. Answer for BPA: 2.

6. Where can the tissue or cell type be viewed for various assay endpoints? What cell types were used for the PPARg assay endpoints?

   View the Cell Line column. For PPARg, the Cell Line types are liver, kidney, and NA.

7. From the Toxcast: Conc. Response Data page, click the link for *Analytical Data on Tox21 Browser* option to view analytical QC data. Are the identity and purity confirmed for the compound? (Keep this tab open for the subsequent question.)

   Search for the chemical in the search bar in the new tab, and select the chemical of interest from the automatically populated options that appear under the search bar. BPA has two sample IDS:

   Tox21_202992, MW Confirmed, Purity > 90% at both T0 and T4 (approximately 0 and 4 months, respectively)

   Tox21_400088, MW Confirmed, Purity > 90% at both T0 and T4 (approximately 0 and 4 months, respectively)

8. From the Toxcast: Conc. Response Data page, view concentration-response curves for the "TOX21 AR_BLA_Antagonist_ratio" assay endpoint by typing the assay endpoint into Endpoint Name column filter and clicking the icon within the data row in the *All plots* column. What is the difference in the AC50 between the multiple runs of the data?

   There are two rows in this example, and both give the same data: 1.46 vs. 1.71.

a. Looking at the Sample ID annotated in the left upper corner on the conc-response curves in the *All plots* view, match the Sample ID with the Tox21 analytical QC data identified in Question #7. Was one sample ID used for both runs in this assay, or different sample IDs?

   For BPA for this assay endpoint, both of the samples listed in the Tox21 QC data were used: Tox21_400088 and Tox21_202992.

9. Does the chemical perturb the estrogen or androgen receptors?

   a. Individual assay(s): Is the chemical active for affecting estrogen receptor 1, or androgen receptor? Is the activity species-specific, or across cells from various species?

      From Bioactivity tab → Toxcast: Conc. Response Data, then enter *Esr1* in the Gene field; clear and enter *AR* in the Gene field.

   b. Model predictions: Is the chemical an estrogen receptor agonist or antagonist, and/or does it bind the estrogen receptor? List AUC values for each model, as available.

      From Bioactivity tab → Toxcast: Models, then review estrogen receptor model predictions.

10. From the HTTr: Summary option under the Bioactivity tab, how many rows of data are related to breast cancer?

    Enter *Breast Cancer* into the filter bar for the Target column. For BPA: 35 rows.

11. From the HTPP: Summary option under the Bioactivity tab, what is the most sensitive endpoint?

    Filter Hitcall 0.9 greater than or equals, sort by lowest BMD. For BPA: f_157.

12. What file types can be downloaded for ToxCast data from the Dashboard?

    ToxCast Summary: CSV, Excel

    ToxCast Conc. Response Data: CSV, Excel for either representative plots or all plots

    ToxCast Models: CSV, Excel

    a. From the Toxcast: Conc. Response Data page under the Bioactivity tab, export all active assay endpoint data in breast or mammary cells.

       Enter *breast* into the Cell Line field. Click the box in the top left of the table to select all rows. In the export drop-down menu, select *Representative Plots Only* for one of the file types. View export for additional assay information, once downloaded.

Chemical Lists

13. Using the Chemical Lists option under the Lists tab in the top banner of the Dashboard, locate and navigate to the ATSDRMRLS list (ATSDR: Minimal Risk Levels (MRLs) for Hazardous Substances). Filter to show all chemicals that are active in ≥30% of ToxCast assays, then export using the "Send To Batch Search" button. Add the following to the export:
    - Metadata: IRIS and PPRTV
    - Enhanced Data Sheets: ToxValDB Details

    Filter the table by the % Active column, selecting the "Greater than or equals" option for the filter and typing 30. This results in 21 chemicals. Once in the Export screen, click the Choose Export Options button, then the Choose Export Format button to display all options in the Customize Export Results screen.

    a. Within the exported file—

        iii. How many chemicals have IRIS data? PPRTV data?

        IRIS data: 11. PPRTV data: 2.

        iv. How many rows of data are available for the hazard component (Toxval Details tab)?

        8627 rows of data.

14. Using the Chemical Lists option under the Lists tab in the top banner of the Dashboard, identify the chemical that is active in the most assays in the latest InvitroDB data version (ToxCast_invitroDB_v3_5, which is the text that can be used in the filter search bar for the List Acronym column).

    Click the hyperlink for the list once the filter search bar has been appropriately filled out, and filter the list by the # Active column. The answer is Tributyltin chloride with 567 active assay endpoints.

15. Where can the current (and previous) complete version of the ToxCast data be downloaded?

    Find link within ToxCast Summary info icon: www.epa.gov/chemical-research/exploring-toxcast-data-downloadable-data.

Reflection

4. In what case example from your work environment would CompTox be useful?

5. What have you learned about the process and workflow used to find information in CompTox?

6. What challenges did you encounter, and how did you solve them?