

CompTox Chemicals Dashboard Virtual Training

Breakout Group Worksheet

Topic: Exposure/ADME-IVIVE

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](https://epa.gov/chemical-research/comptox-chemicals-dashboard-help) ([epa.gov/chemical-research/comptox-chemicals-dashboard-help](https://comptox.epa.gov/dashboard/releasenotes)) and [Release Notes](https://comptox.epa.gov/dashboard/releasenotes) (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 identify Exposure and ADME-IVIVE information and tools for a chemical of interest.

Directions

This session will focus on the Exposure and ADME-IVIVE 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 redoing 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. *In vitro* assays that measure the clearance (removal) of chemicals by hepatocytes (the primary cell of the liver) are used to estimate how fast a chemical is metabolized by the body. What is the human intrinsic hepatic clearance of Bisphenol A?
 - a. What is the source of the clearance data?

3. What is the predicted human steady-state plasma concentration of Bisphenol A for both 3 compartmentss and PBTK models, at the 95th percentile?
 - a. What is the value for the 50th percentile predictions?
4. Where can you find more information about the prediction model used?
 - a. What is the assumed daily chemical intake rate that causes the predicted concentrations?
5. Compare human and rat values for PK half-life.
6. What are the types of product or use categories recorded for Bisphenol A?
 - a. How many other chemicals share any particular General Use Category with Bisphenol A? (Multiple answers are possible.)
7. Use case information:
 - a. Which tab(s) can you find information on use cases for Bisphenol A?
 - b. What are some functional uses (known and predicted) for Bisphenol A?
8. How many facilities in your state reported releases of Bisphenol A in 2020?
9. Has disposal of Bisphenol A increased or decreased from 2003 to 2020?
10. According to 2014 biomonitoring data, what population had the highest calculated median exposure level (in mg/kg-bw/day) to Bisphenol A?

11. What is the predicted average exposure level (in mg/kg-bw/day) for the total population, according to the SEEM model, to Bisphenol A, with 95% confidence? What is the reference?
12. What are the median SHEDS Indirect and Direct exposure predictions?
13. Is Bisphenol A predicted to have a residential exposure?
14. What chemicals have been reported in wood polish in EPA's Chemical and Products (CPDat)?

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?

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Breakout Group Worksheet—**Answers** Topic: Exposure/ADME-IVIVE

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Goal

To identify Exposure and ADME-IVIVE information and tools for a chemical of interest.

Directions

This session will focus on the Exposure and ADME-IVIVE 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 redoing 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. *In vitro* assays that measure the clearance (removal) of chemicals by hepatocytes (the primary cell of the liver) are used to estimate how fast a chemical is metabolized by the body. What is the human intrinsic hepatic clearance of Bisphenol A?

19.90 $\mu\text{L}/\text{min}/\text{million hepatocytes}$. Navigate to ADME > IVIVE, then review data in the Measured column.

- a. What is the source of the clearance data?

Data source species is human. Reference is Wambaugh 2019. View table data.

3. What is the predicted human steady-state plasma concentration of Bisphenol A for both 3compartmentss and PBTK models, at the 95th percentile?

3compartmentss: 3.19 mg/L; PBTK: 2.35 mg/L predicted for 95th percentile. In ADME > IVIVE, view table data in the Predicted column. Use filters to display and hide relevant data.

- a. What is the value for the 50th percentile predictions?

3compartmentss: 0.48 mg/L; PBTK: 0.39 mg/L predicted for 50th percentile. In ADME > IVIVE, view table data in the Predicted column. Use filters to display and hide relevant data.

4. Where can you find more information about the prediction model used?

Hover over the “i” at the top of the page next to ADME - IVIVE, then click the link to the htk info page.

- a. What is the assumed daily chemical intake rate that causes the predicted concentrations?

1 mg/kg/day, available by hovering over the “Steady-State Plasma Concentration” row label.

5. Compare human and rat values for PK half-life.

Human: 39.61 hours; rat: 368.3 hours. In ADME > IVIVE, view table data in the Predicted column. Use filters to display and hide relevant data.

6. What are the types of product or use categories recorded for Bisphenol A?

Construction and building materials, furniture and furnishings, and not yet categorized. Navigate to Exposure > Product & Use Categories.

- a. How many other chemicals share any particular General Use Category with Bisphenol A? (Multiple answers are possible.)

Navigate to Exposure > Product & Use Categories, then click on any linked keyword in the General Use Keywords table. Count per general use type is on top of the table.

7. Use case information:

- a. Which tab(s) can you find information on use cases for Bisphenol A?

Product & Use Categories tab and Chemical Functional Use tab.

- b. What are some functional uses (known and predicted) for Bisphenol A?

The top 3 uses are as follows: antioxidant, UV absorber, and crosslinker. Navigate to Exposure > Chemical Functional Use, then review data in the Predicted Probability of Associated Functional Use table.

8. How many facilities in your state reported releases of Bisphenol A in 2020?

Navigate to Exposure > Toxics Release Inventory, then view and navigate around the map to find facilities in the relevant state.

- Has disposal of Bisphenol A increased or decreased from 2003 to 2020?

Yes. Navigate to Exposure > Toxics Release Inventory, scroll down to Production Related Waste Managed graph, and review data.

- According to 2014 biomonitoring data, what population had the highest calculated median exposure level (in mg/kg-bw/day) to Bisphenol A?

Children age 6-11. Navigate to Exposure > Biomonitoring Data, sort data by the Median column (click the Median header until there is a down arrow to the right of it).

- What is the predicted average exposure level (in mg/kg-bw/day) for the total population, according to the SEEM model, to Bisphenol A, with 95% confidence? What is the reference?

With 95% confidence it is below 2.04e-2 mg/kg-bw/day or 0.0204 mg/kg-bw/day. Navigate to Exposure > Exposure Predictions. Reference: Ring 2018.

- What are the median SHEDS Indirect and Direct exposure predictions?

Indirect: 7.15e-5 or 0.0000715 mg/kg/day; Direct: 0 mg/kg/day. Navigate to Exposure > Exposure Predictions. Use filters to reveal or hide relevant data.

- Is Bisphenol A predicted to have a residential exposure?

Yes. Navigate to Exposure > Exposure Predictions. Look at the General Predictions Data table.

- What chemicals have been reported in wood polish in EPA's Chemical and Products (CPDat)?

Navigate to the Products/Use Categories search tab, search for "wood polish," and select CPDat product category "wood polish." Of 12 chemicals, D-limonene is the first listed.

Reflection

- In what case example from your work environment would CompTox be useful?
- What have you learned about the process and workflow used to find information in CompTox?
- What challenges did you encounter, and how did you solve them?