ICE Search Tool

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ICE Search Intro (video one)

Welcome to the Integrated Chemical Environment, also known as ICE. In this video, we will show you how to build a query in the ICE search tool. A second video will help you understand and interpret ICE Search results.

The ICE Search tool allows you to integrate data from different models and testing systems to provide an overall view of chemical activity for regulatory endpoints of interest.

To compare or evaluate methods, users typically need to view data for chemicals of interest from multiple assays. Furthermore, combining biologically related datasets can support weight-of-evidence assessments of chemical safety and bioactivity.

However, the process of identifying desired data for multiple biologically relevant assays or datasets can be daunting for those without domain expertise in either biological endpoint or data processing.

You can use ICE to explore different properties and endpoints to get a summary view of a chemical's toxicity. The tool gives you access to data for over 800,000 chemicals.

Selecting Search on the top menu or from the icon below the graphics takes you to the ICE Search page.

Located throughout the tool are green information buttons to help you better understand key features and results. When you hover over a button, brief explanatory text will appear. When you click a button, more details will appear in a text box that can be resized and relocated on the screen.

If you encounter a problem using a tool, click the “Report an Issue” button on the left side of the display to generate an email to ICE Support

How to build a query

To run a search, you must specify at least one assay or chemical or a combination of both.

Chemical Input

ICE Search queries can access and integrate bioactivity data for over 10,000 chemicals as well as in silico predictions of properties and bioactivity for over 800,000 chemical structures from the U.S. Environmental Protection Agency's DSSTox database.

You can add chemicals to your query using one or both of two input methods in the Chemical Input field on the left side of the screen.

ICE gives you the option of using Chemical Quick Lists, which are lists of chemicals that have been found useful for evaluating specific types of toxicities. They are useful when you don't have a specific set of chemicals in mind to look at. For more information on these quick lists you can check the information boxes available in the selection box and also check the descriptions under the "Data" tab on the top right.

You can also enter your own list of chemical identifiers in the User Chemical Identifier box. You can do this by typing in one or more individual chemical identifiers. For this example, we can type in "50-28-2," the CASRN for the chemical estradiol.

You can also paste in a list of chemical identifiers. You can use any combination of the following identifiers: CASRNs, DTXSIDs, SMILES, and InChiKeys. An example of these identifiers are provided under the information box located in the Chemical Input field.

You can run a search in ICE without specifying chemicals. If you don't add any chemicals to your query, your results will include all chemicals with data for your selected assays.

Data Input

To select assays for your query, click on "Select Assays" from the Assay Input field

In the dialog box that appears, select a category of interest from the tabs, and then select the assays and endpoints of interest in the window that opens.

Data in ICE are organized in categories around toxicity or target endpoints of regulatory interest, such as acute lethality, irritation and corrosion, or developmental and reproductive toxicity, with additional categories allowing queries specific to curated high-throughput screening, or cHTS, and physicochemical property data.

This organization of assays makes it easy for users to identify and explore all data from both animal and non-animal tests relevant to that endpoint.

ICE also provides documentation with detailed information on endpoints, sources, and curation so that users have full provenance. Check the descriptions under the "Data" tab on the top right.

For this example, we are going to select the “Acute Lethality” assay type and select the all the “Dermal” and “Inhalation” endpoints.

We can also open the “Mode of Action” dropdown and select “p53 Signaling Pathway,” “Oxidative Stress,” and “Neuronal Transmission.” Use the check boxes to the left of each list to select or deselect assays in a category. You can select different assays from different categories. When you are done selecting assays and endpoints, select “Finished” on the bottom left of the dialog box.

You can run a search in ICE without specifying assays. If you don’t add any assays to your query, your results will include all assays with data for your selected chemicals.

Other parameters

Before we run the search, let’s look at two more options provided by ICE.

On the bottom you will see that we have the option "Add chemicals with identical QSAR structures." Checking this box will add chemicals available in ICE to your query that have the same QSAR structure as a chemical you have specified.

We provide this option because one of the challenges associated with identifying relevant data for a test chemical is that different salts of the chemical are often assayed. ICE provides the option to include results from chemicals with the same two-dimensional desalted structures based on the InChI keys of the “QSAR-ready” structures. The broader query based on the parent structure as opposed to a specific salt form can help expand the data returned for a specific structure.

ICE also gives you two options to define the scope of your search. The default option, “Union,” returns all assay results available in ICE for all chemicals specified in the search. The more restrictive option, “Intersection,” returns assay results only for chemicals that were tested in all the selected assays.

Now that we have built our query, we can run our search. See the results video for an overview of understanding and interpreting results.

Thank you for watching our video on how to build a search query in ICE. For more detailed information on the search tool, go to the “Help” top menu item and select “User Guides”.

Search Results (video two)

Welcome to the Integrated Chemical Environment, also known as ICE. In this video, we will show you how to understand and interpret results from the ICE search tool. We will be viewing the results of a search built in the previous video on building a query in ICE. If you have not yet viewed that video, you may want to do so before watching this one.

Summary Table

Once the Search query is run the “Results” tab will open. On the top there are three expandable headings. The first heading gives the names of the Chemical Quick Lists selected by the user, the second heading shows the names of the assays selected by the user, and the last heading gives the identifiers that were not returned by query. Identifiers may not be returned because the chemical had no data for the assays selected or the specific identifier was not available in the database.

Chemical search results are returned as a summary table. This table can be filtered; click the filter icon in a table heading to open a dialog box and select a subset of your results.

Click on the “Long View” button to view the assay–chemical pair data points. You’ll need to drag the scroll bar to the right to view the entire table.

You can interact with elements of the table. Click on the chemical’s CASRN to be directed to the available test article page about the chemical in the NTP Chemical Effects in Biological Systems (CEBS) database.

Or click on the DTXSID to be directed to the U.S. Environmental Protection Agency’s CompTox Chemical Dashboard entry for the chemical.

The first column of the results table displays a "View Details" button for each chemical.

This view contains two tabs, “Substance or Mixture Details” and “Curve Surfer.” Let’s look at the details for the substance 17beta-Estradiol.

Under “Substance Details” you can find the chemical structure, physicochemical properties, and a plot of bioactivity results if any cHTS assays were selected. The pie chart presents the bioactivity of the chemicals in all assays combined. The stacked bar plot on the right displays assay call count for each cHTS assay.

You can change the format of this plot from stacked bar to pie chart and display assay call count as percentages by selecting the different options under "Plot Type."

Click on the graph legend to remove or add bioactivity from the graph view or specify what assay types be included in the graph view.

In either the single chemical or mixture detail view, the “Curve Surfer” tab allows you to view and interact with concentration-response curves from cHTS data. You can use the dropdowns

to filter the view or reorder the graphs. The Curve Surfer is also a stand-alone tool. You can check the user guide and help page to learn more about it.

To see how this works for a mixture, click on the Detail View for Bengal Dry Roach Spray. Under "Mixture Details" on the top left, we have information on the active ingredients of the mixture and on the right, we get the chemical structure if available and the physicochemical properties for each active ingredient. On bottom left we have the box-and-whiskers plot that shows the AC50 and LD50 values for each active ingredient.

Download Results

You can download your search results to your desktop. When you click "Download" you are given three options.

"Summary Data" includes a single row for each chemical, with a summary of all assays run on that chemical given in the columns.

A second option, "Wide Format," returns summary data with the individual cHTS assays if there is a cHTS assay group specified in the query.

"Long Format" view returns data as one row for each unique chemical-assay combination. This view provides additional experimental detail and can be useful for those wanting to analyze the data further.

Each format is available for download as a tab-delimited text file or Excel file. Any filters applied to the displayed data will also be applied to the download. So if you need all the data, make sure you clear any filters before downloading.

Send results to other tools

Use the "Send filtered results to" dropdown list next to the download button to send Search parameters to other ICE tools to run additional queries. For details on the use and outputs of these tools, refer to their user guides.

You can also send chemicals to query the EPA CompTox Chemicals Dashboard or copy the CASRNs or DTXSIDs to the clipboard. Same as downloading results, any filters applied to the table would be carried over here.

Bioactivity Graphs

The last item on the "Results" tab is the bioactivity results graphs for all selected chemicals and any selected cHTS assays presented in two plots.

The pie chart, which appears below the legend, presents the bioactivity of all assays combined, and the stacked bar plot displays call count for each cHTS assay.

As with the detailed view, the format of this plot can be changed to pie charts, with the counts displayed as percentages. You can click on the graph legends to remove or add data from the view and select which assay types are included in the graph.

Thank you for watching our video on Search Results in ICE. For more detailed information on the search tool, go to the “Help” top menu item and select “User Guides”.