Guidance document for using Chemical Mixture Calculator 2.0

Contents

Panoramix Portal

Login

To login into the Panoramix web portal complete the following steps:

1. Open a browser and enter the uniform resource locator (URL) for the Panoramix web portal login window.

URL= https://ssl.biomax.de/panoramix/cgi/login_token_2fa.cgi

The login page will be displayed.

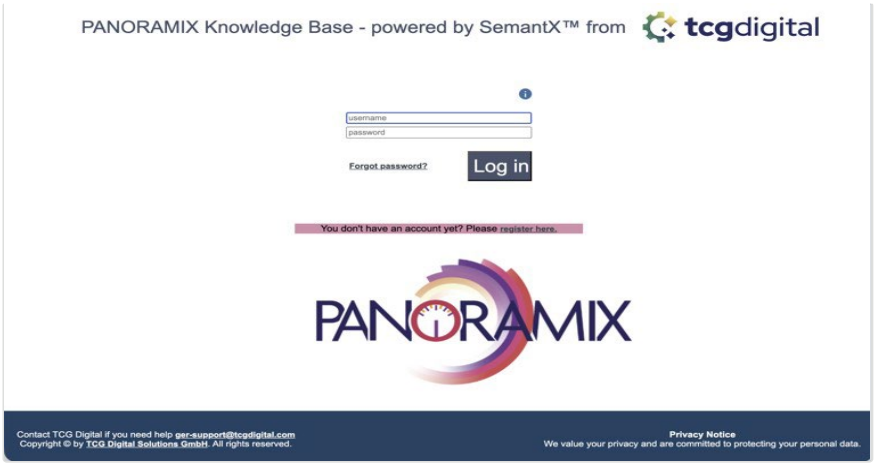

Figure 1: Login page of the Panoramix Project

2. Enter your username and password, then click the **Login** button. You will be directed to the token page (Figure 2), where you are required to enter the token sent to your registered email address associated with your portal access.

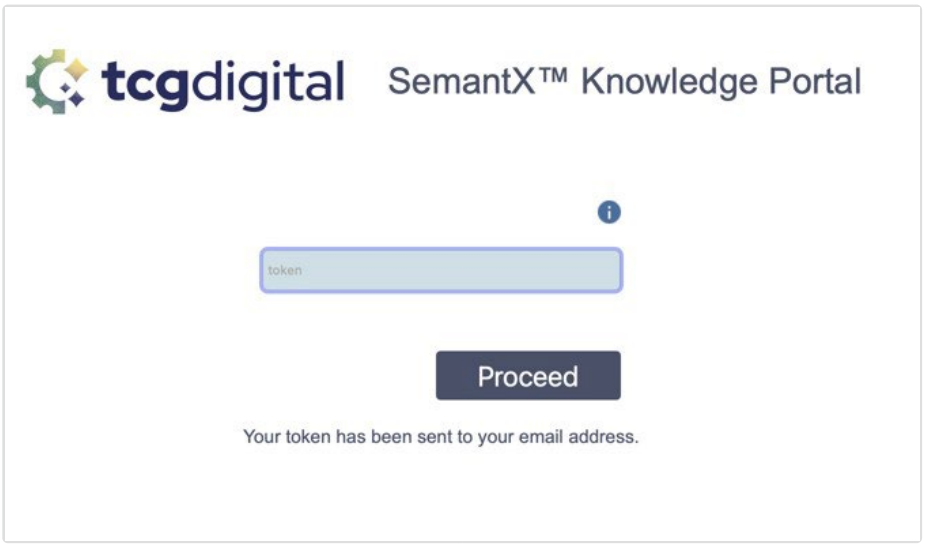

Figure 2: Token Page

Enter the token and click the **Proceed** button to access the Panoramix web portal **WebHome** (Figure 4).

3. If a user does not have account credentials, they can use the highlighted link below the Log in button to send an email request to the administrator, who can grant access to the portal.

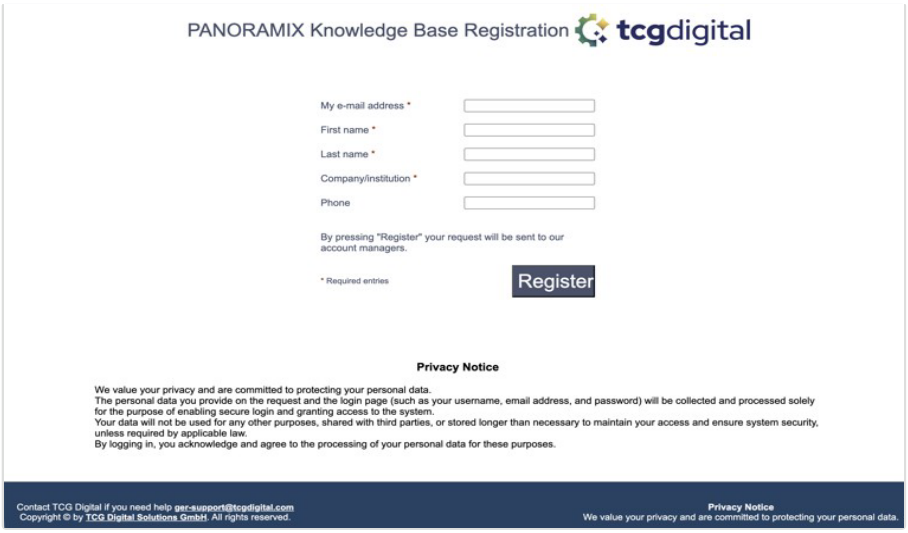

Figure 3: Request for access page

4. Enter the token and click the **Proceed** button to access the Panoramix web portal **WebHome.**

Homepage

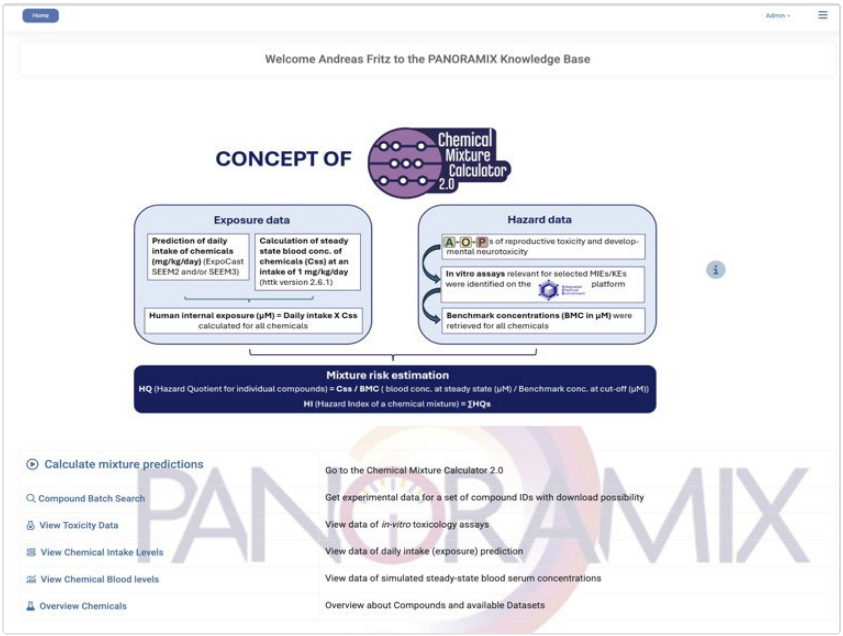

Figure 4: Homepage of the CMC

Navigation

Navigation Bar with **Home** button, Admin menu and SideBar

The **Home** button allows users to return to the start page at any time. The **Admin** menu is displayed only for users with administrative privileges. Navigation within the system is provided via the expandable menu on the right-hand side, in addition to the three sections presented as tiles.

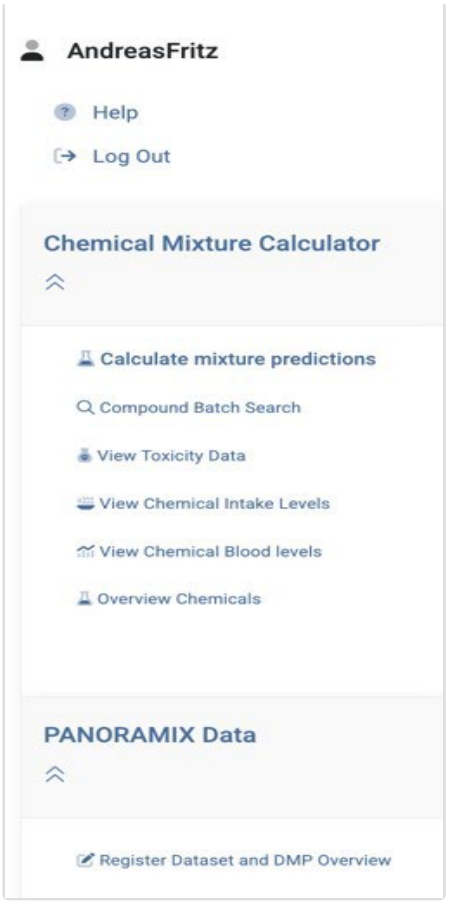

Figure 5: WebSide Bar for navigation

Breadcrumbs

Breadcrumbs represent your interaction trail, showing the concepts selected during refinement or filtering steps. Each time a concept is selected in a refiner, a new breadcrumb is added to the trail.

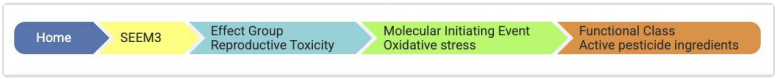

Figure 6: Example of the Bread Crumb Navigation Bar

To restart a search at any step, select that step in the Breadcrumb.
Select the last breadcrumb to view your complete journey, or select an earlier step to view its corresponding results.

Content

After clicking the CMC icon on the Home page, you will be taken to the overview page. The upper section explains the operating principle of the CMC (see Figure: xxx). Various options for searching within the system are available, including:

1. Calculate mixture predictions
2. Compound Batch Search

3. View Toxicity Data
4. View Chemical Intake levels
5. View Chemical Blood levels
6. Overview Chemicals

The info button on the right-hand side opens a modal window that provides information about the calculations and the datasets used.

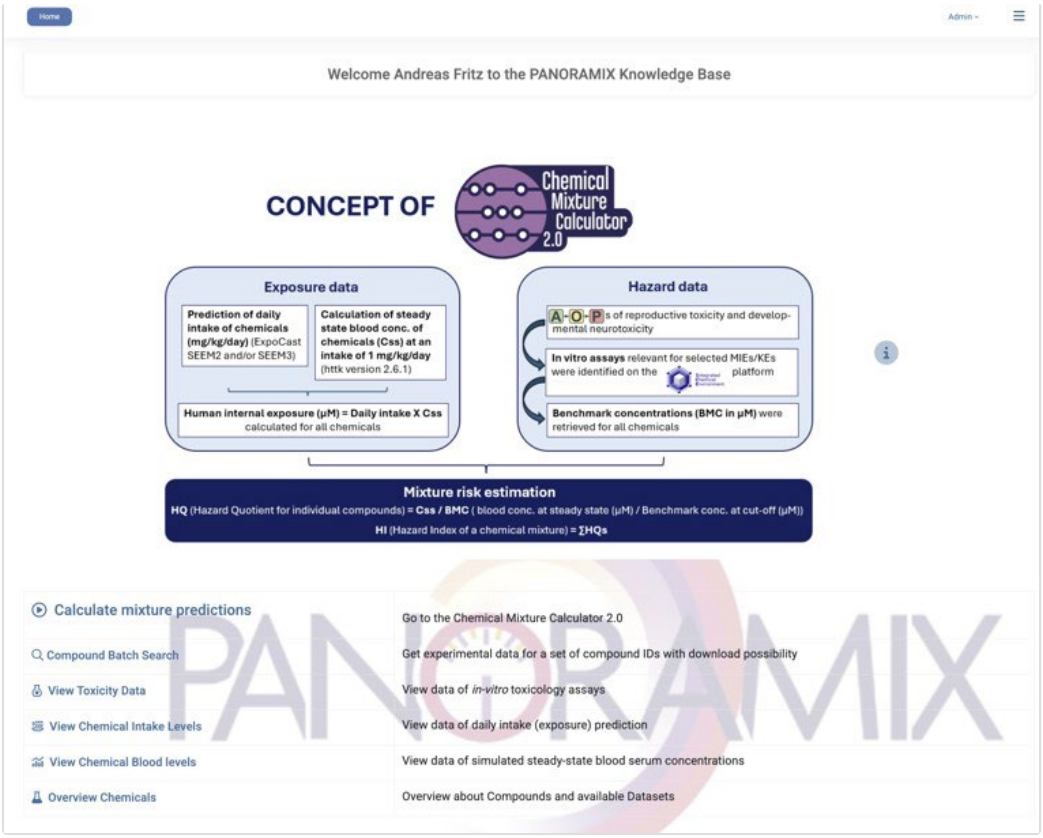

Figure 7: CMC Entry Page

Calculate mixture predictions

Exposure settings

By clicking the **Chemical Mixture Predictions** link, you will be directed to the CMC exposure settings. A description of the datasets is available via the **More Information** link and the information displayed on the left-hand side. After selecting a setting, you will directed to the CMC calculation page.

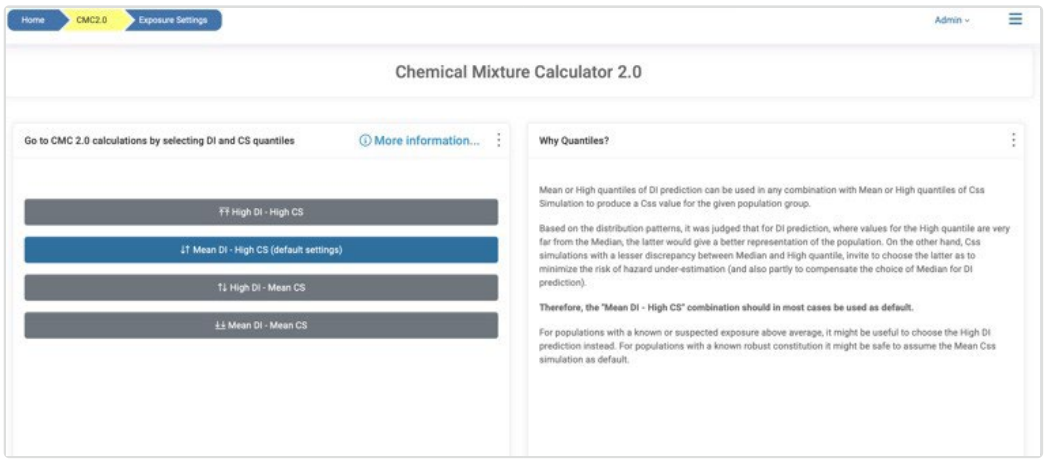

Figure 8: Exposure Settings Page

The calculator layout consists of several sections. In the top row, you can select the population for which the calculations are performed. Below this, an overview of the main three sections is provided, along with the actual calculation results, which are generated automatically.

The left panel contains the refiners, which act as filters to narrow down and further specify the dataset. The middle panel displays the compounds available for calculation can be performed. The right panel is initially empty and is populated as compounds are selected. These selected compounds are then used for the calculation, and the results are displayed above in the middle panel.

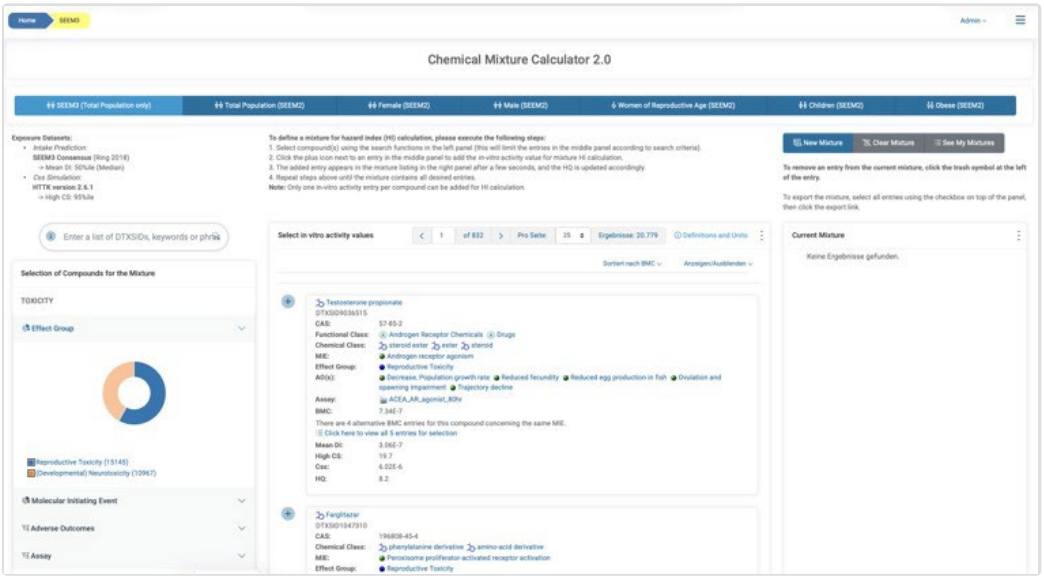

Figure 9: CMC 2.0 Page for Refinement and Mixture selection

Description of How to Perform a Calculation

To define a mixture for Hazard Index (HI) calculation, please follow these steps:

1. Use the search functions in the left panel to select the desired compound(s). This will filter the entries displayed in the middle panel according to your search criteria.

2. In the middle panel, click the **plus icon** next to a compound to add its *in vitro* activity value to the mixture.

3. The selected entry will appear in the mixture list in the right panel after a few seconds.

4. Repeat the steps above until all desired compounds have been added to the mixture.

5. Click the link to **Calculate and display the Hazard Index** to perform the calculation.

Note: Only one *in-vitro* activity entry per compound can be added for HI calculation.

By clicking the link "**calculate and display the Hazard Index**" the calculation is performed.

Once the calculation is executed, the results will be displayed as shown in the figure below.

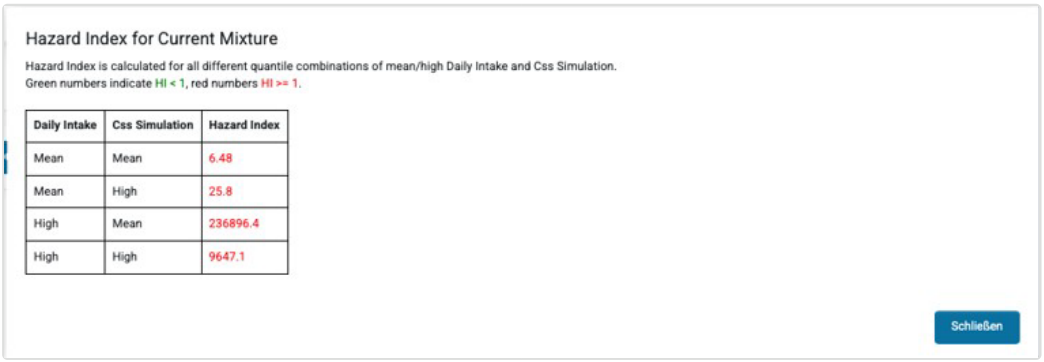

Figure 10: Modal window with results of a calculation

Left Panel – Refiners

Within the Panoramix Project, the following refiners are available. They can be used individually or in combination:

- Search Box (supports DTX IDs, CAS numbers in quotes, phrases and keywords)
- Toxicity
- Effect groups (e.g. Reproductive Toxicity, Developmental Neurotoxicity)
- Molecular Initiation Event
- Adverse Outcomes
- Assay
- Compound Classification
- ChEBI Ontology Classification
- Compound Data
- Hazard Data

The different types of refiners are described below, along with guidance on how to use them effectively.

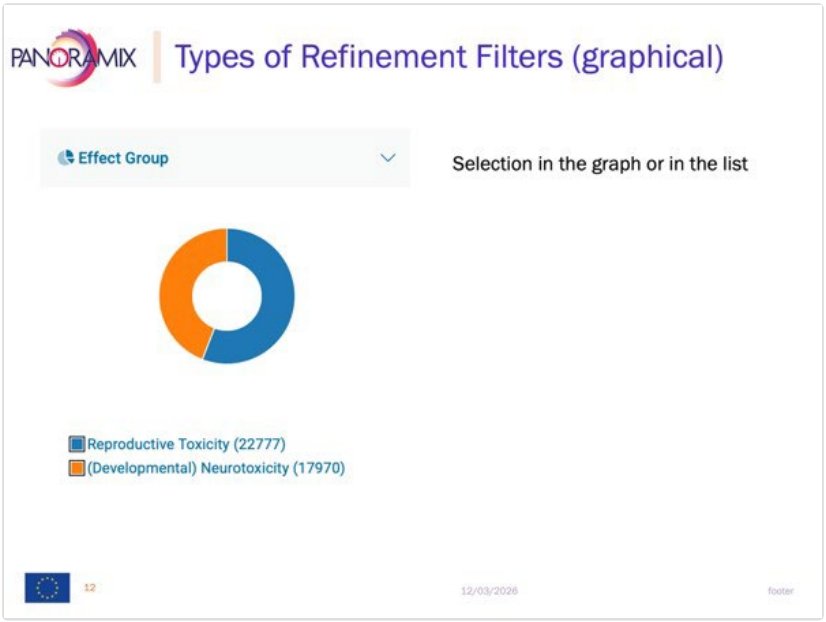

Figure 11: Graphical Filter example

Categorical Filters

Categorical filters allow users to select **specific categories or groups**. A search box can be used to quickly locate items in the list. Selections are made using checkboxes, and multiple items can be selected at once. After making your selections, click **Apply** to execute the search.

Use the **down arrow** to navigate through the list.

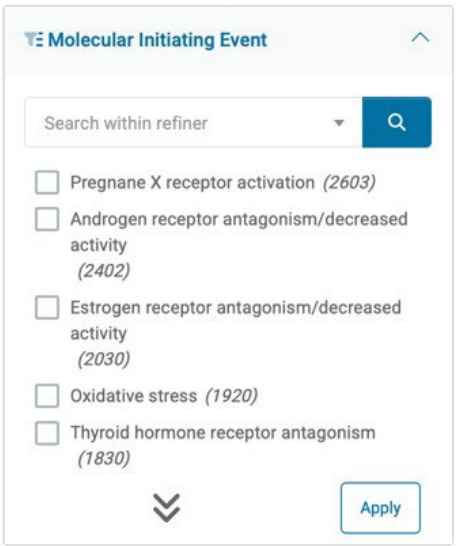

Figure 12: List Filter example

Sunburst Diagram

A **Sunburst diagram** is a **radial, hierarchical data visualization** used to display how categories are structured within larger categories. It represents hierarchical relationships using **concentric rings**, where each ring corresponds to a level in the hierarchy.

Figure 13: Sunburst Filter example

The **center circle** represents the **root node** (the top level of the hierarchy).
Each **outer ring** represents a deeper level of the hierarchy.
Segments (arcs) within each ring represent categories or nodes.
The **size of each segment** is typically proportional to a quantitative value (e.g., count, weight, or percentage).
Parent segments contain their **child segments** in the next outer ring.
Navigation Possibilities
Sunburst diagrams are often **interactive**, enabling several navigation techniques:

1. Drill-Down (Zoom-In)
Clicking on a segment focuses on that node, moving it to the center and displaying its children as new outer rings.
This helps users explore deeper levels of the hierarchy.

2. Drill-Up (Zoom-Out)
Users can return to higher levels by clicking the center node, a breadcrumb trail, or a “back” control.

Range Filter

Range Filters are used to select **numeric or continuous values**. They include slider controls, minimum–maximum input fields, and a range selector. After setting the desired range, click the **Apply** button to perform the search.

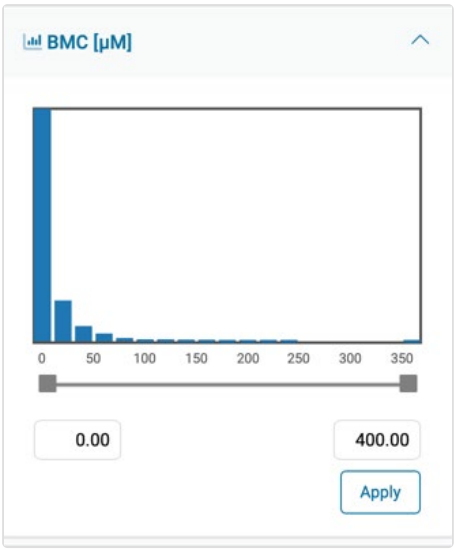

Figure 14: Range Filter example

Middle Panel

In the middle panel of the **Chemical Mixture Calculator**, displays the *in vitro* assay data for chemicals with available experimental results. Navigation through the results is provided via the pagination controls at the top of the panel, and the total number of results is shown to give an overview of the dataset.

Panel Navigation and Display

Results are presented across multiple pages. Use the pagination controls at the top of the panel to move between pages.

Users can customize the displayed information using the **show/hide** function. This option allows specific categories or variables to be shown or hidden depending on the user's preference.

Each result is presented in a structured display within the panel, enabling easy comparison and review of the available information.

The number of visible results and their arrangement may vary depending on active filters and sorting settings.

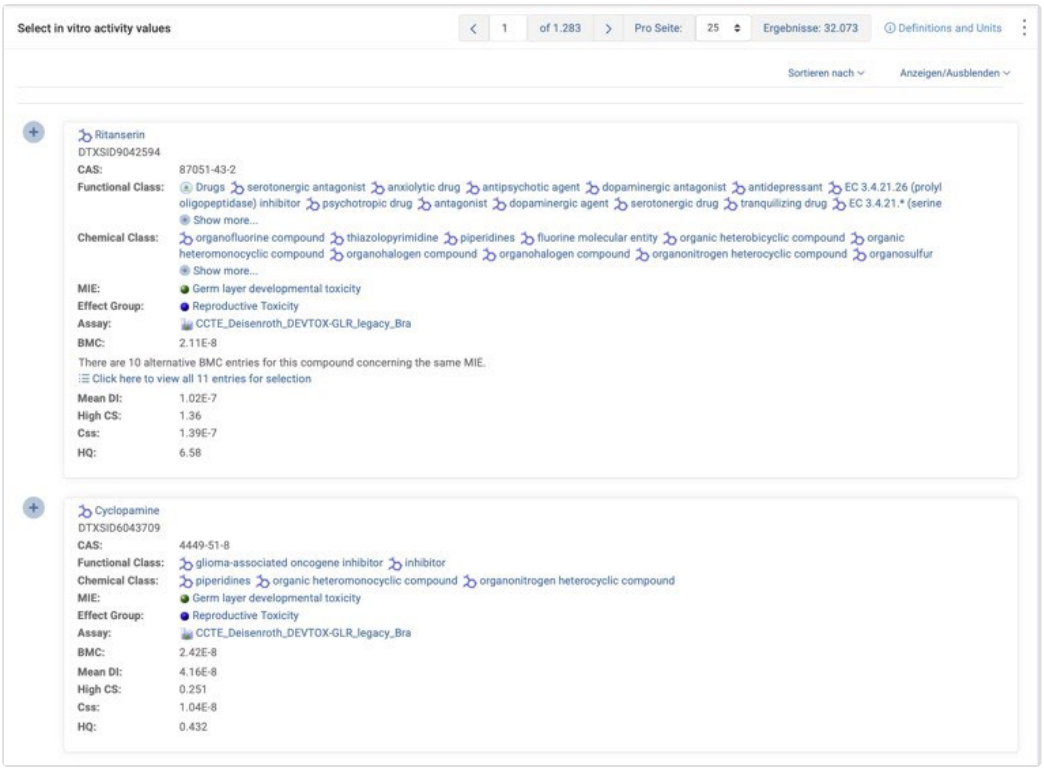

Figure 15: Middle Panel example with in vitro assy data for compounds.

A link provides access to the definitions of the terms and units used.

For each individual *in vitro* experiment, a card is displayed containing information on the chemical's classifications, its ontology assignment, and the corresponding experimental data and calculations:

The result list can be sorted according to their defined variables:

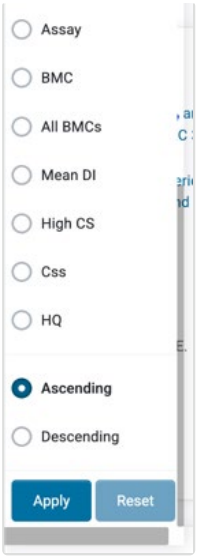

Figure 16: Sorting function in the pagination area of the middle panel

By clicking the **plus sign** on the left side of the card, the chemical is added from the middle panel to the Chemical Mixture and displayed in the right panel.

The display of categories and variables depends on the selected settings, which can be adjusted using the **show/hide** menu.

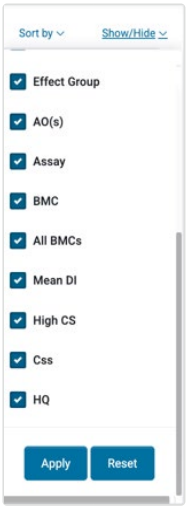

Figure 17: Show/Hide function in the pagination area of the middle panel

The number of results depends on the filter functions in the left panel as well as on the selected sorting.

Right Panel

In the right panel, the current selection used for calculating the Hazard Index is listed. Three tabs allow the user to display the current selection, delete it, or view previously saved selections. An export function is also available.

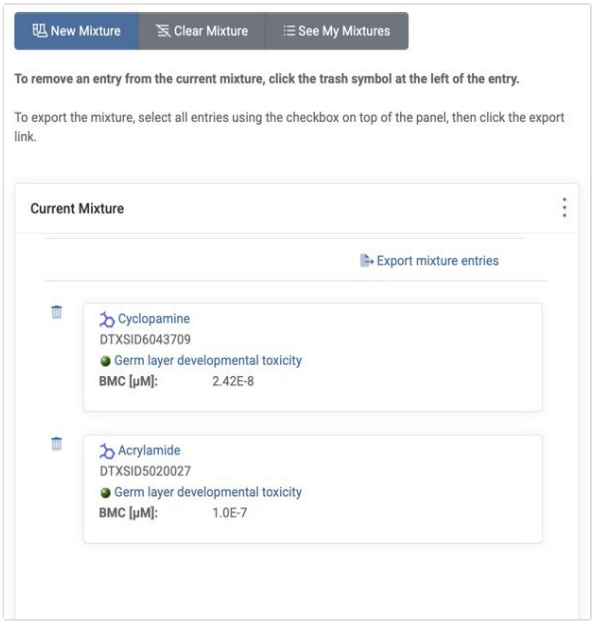

Figure 18: Right Panel with a selected chemical

How to see My saved selections:

- Go to the **"See my mixtures"** tab.
- Select an entry from the list by clicking the **check mark**, or remove it by clicking the **x**.

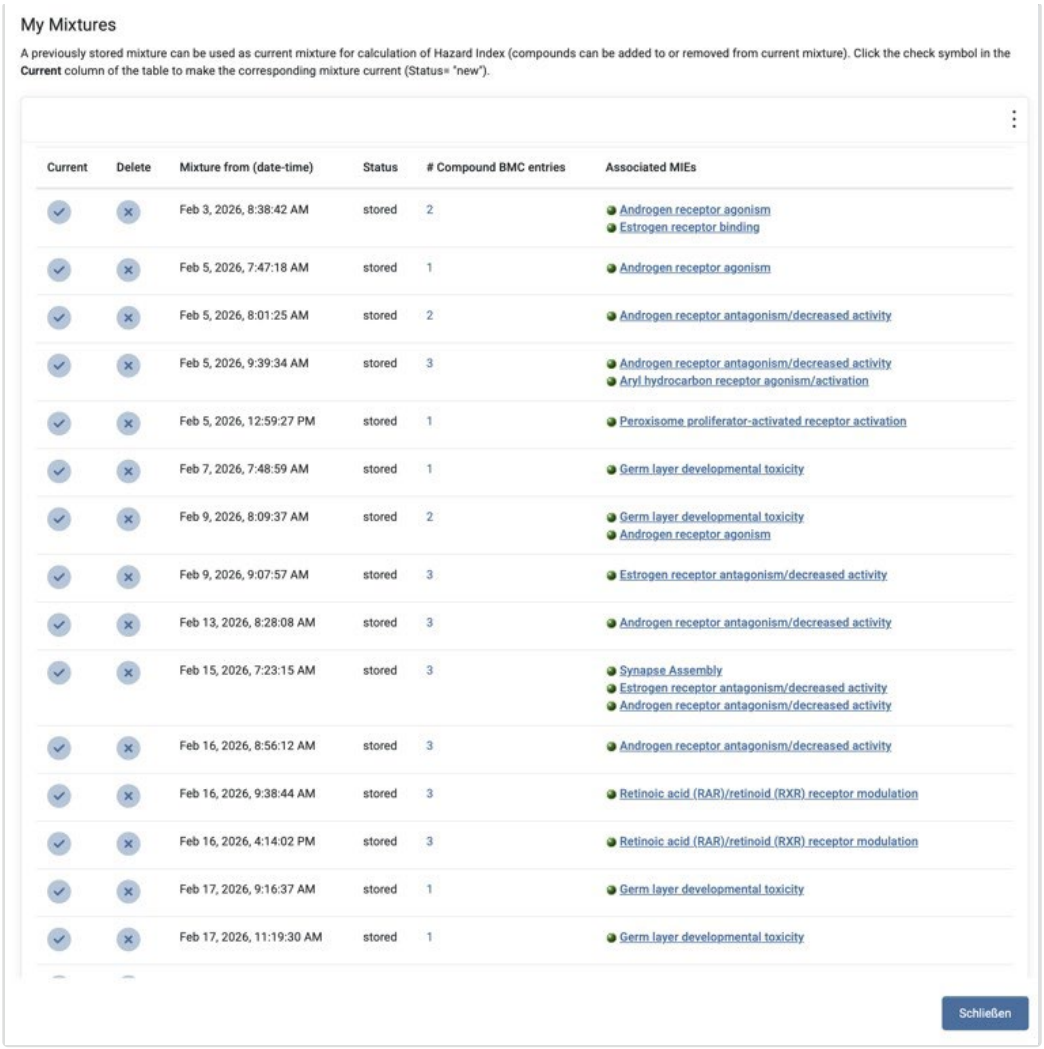

Figure 19: See My Mixtures Tab with a history of used mixtures

How to Export:

Press the **export link**.
A modal window will appear showing the progress of the process.
A message will appear in the modal window when the process is finished.
Download the file.
Open it in **Excel**

Figure 20: Example of the Export Modal Window which appears after pressing the export link

Compound Batch Search

The compound batch search allows users to query multiple compounds at once by submitting a list of identifiers, either CAS numbers or DTXS IDs. For demonstration purposes, two predefined ID lists are available: one containing DTXS IDs and one with CAS numbers.

Mixed lists containing both types of types are also supported.

To perform a batch search, paste the identifier list into the batch search input field and click **Search**.

Search results are displayed in a table view. The full result set can be exported, or a subset by selecting individual entries using the corresponding checkboxes.

Additional information for a specific compound can be accessed by clicking the **+ icon** to expand a panel displaying detailed compound data. The table layout can be customized by showing or hiding columns. Columns support sorting, and column-specific search functionality is available.

To export data, select the desired entries and click the **Export** button located in the toolbar above the table. An export status dialog is displayed to indicate progress. Once the export process is complete, the generated file can be downloaded to the local machine.

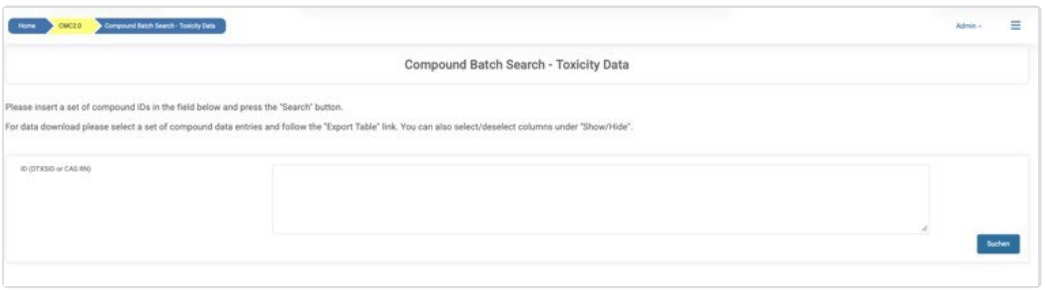

Figure 21: Compound batch Page

Examples of a batch search for

a) CAS numbers

101-61-1
101-77-9
10161-33-8
102-50-1
102676-31-3
103-56-0

b) DTOXS IDs

DTXSID6025513
DTXSID1045083
DTXSID1045085
DTXSID9040130

View Toxicity Data

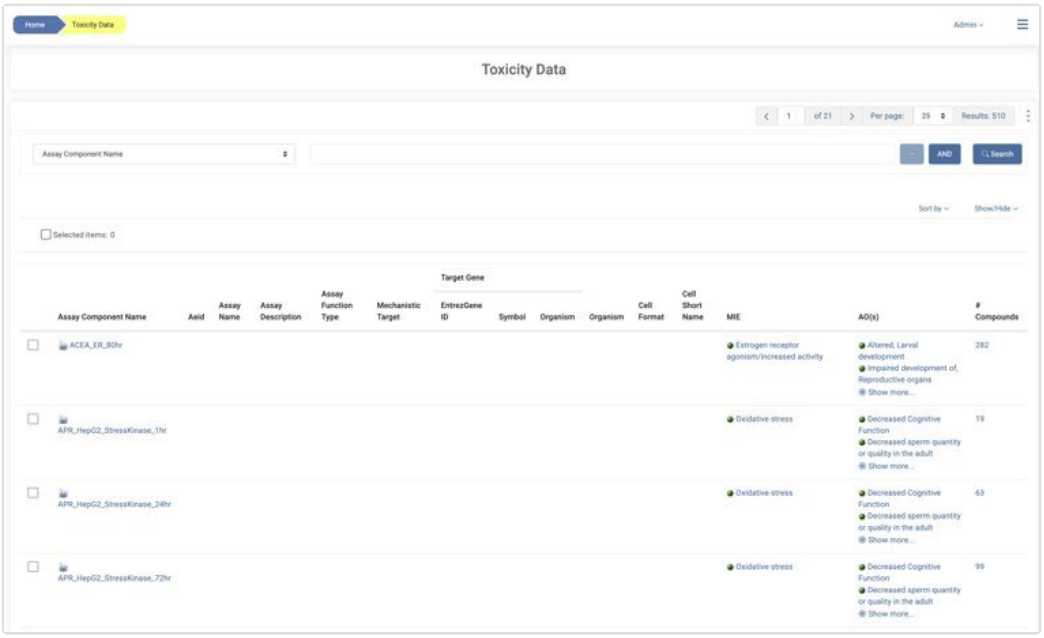

Figure 22: Results Page with a list view after a batch search

View Chemical Intake Levels

The **SEEM2 Exposure prediction study** includes a wide range of population groups:

- Total Population
- Women of Reproductive Age
- Males
- Females
- Children
- Teens
- Adults
- Seniors
- Obese
- Non-Obese

The dataset captures both the **median (50% quantile)** and the **upper limit of the 90% confidence interval (95% quantile)** for chemical intake.

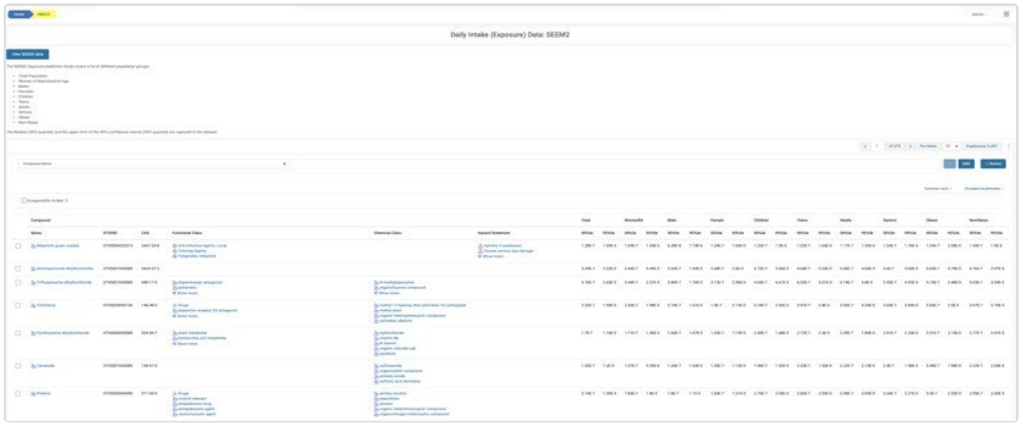

Figure 23: List View Page for the SEEM2 population data

In the list view, daily intake data from the SEEM2 population groups are displayed. The list can be **searched, sorted, and customized** using the **show/hide** function to display only the columns of interest

View Chemical Blood Levels

The list provides steady state concentrations for selected compounds. The dataset can be **searched, sorted** and **customized** by selecting or deselecting variables to show or hide them in the list view.

The **HTTK R package** calculates simulated serum steady-state concentration (**Css**) values [µM], based on an exposure of **1mg/kg body weight per day** of the corresponding substance.

The version **2.3.0** of the simulation covers several different population groups (corresponding table headers):

- Total Population (Total-v.2.3.0)
- Females (Female-v2.3.0)
- Males (Male-v2.3.0)
- Women of Reproductive Age (WomenRA-v2.3.0)
- Children (Children-v2.3.0)
- Obese (Obese-v2.3.0)

The dataset includes both the **median (50% quantile)** and the **upper limit of the 90% confidence interval (95% quantile)** for each group.

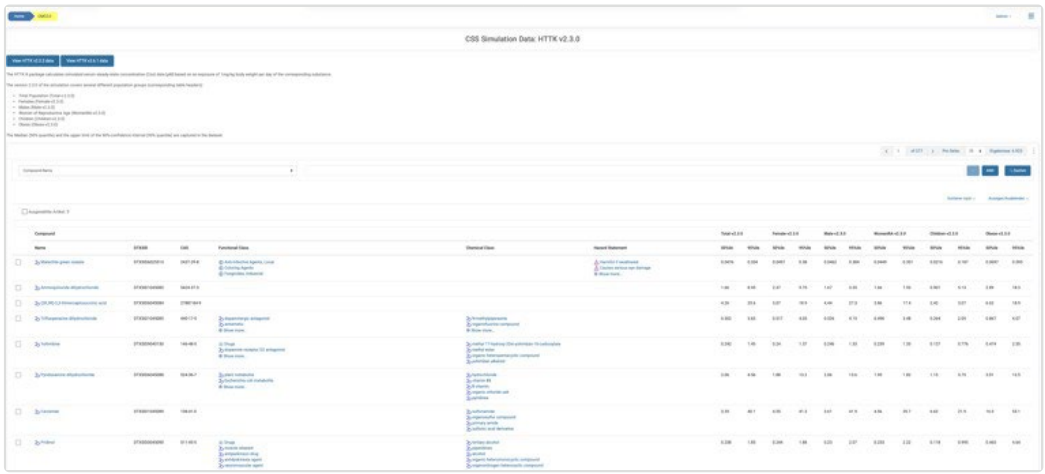

Figure 24: Blood Levels for chemicals

Overview - Chemicals

This is a list view containing DTX data for approximately **700,000 compounds**, including population information and hazard data. The dataset can be **searched, sorted, and customized** by selecting or hiding specific variables using the **show/hide** function.

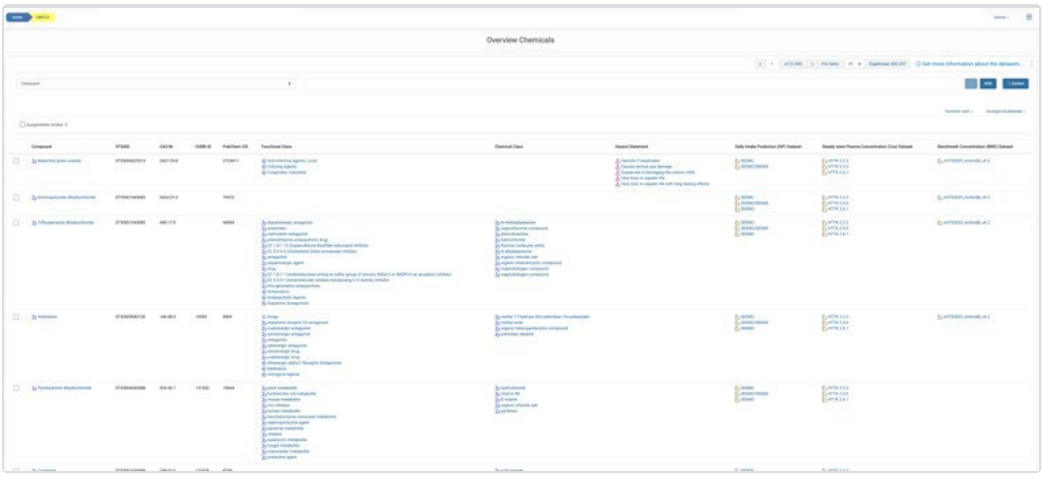

Figure 25: DTX Data for Chemical in List View

Panoramix Data

Register Dataset and DMP Overview

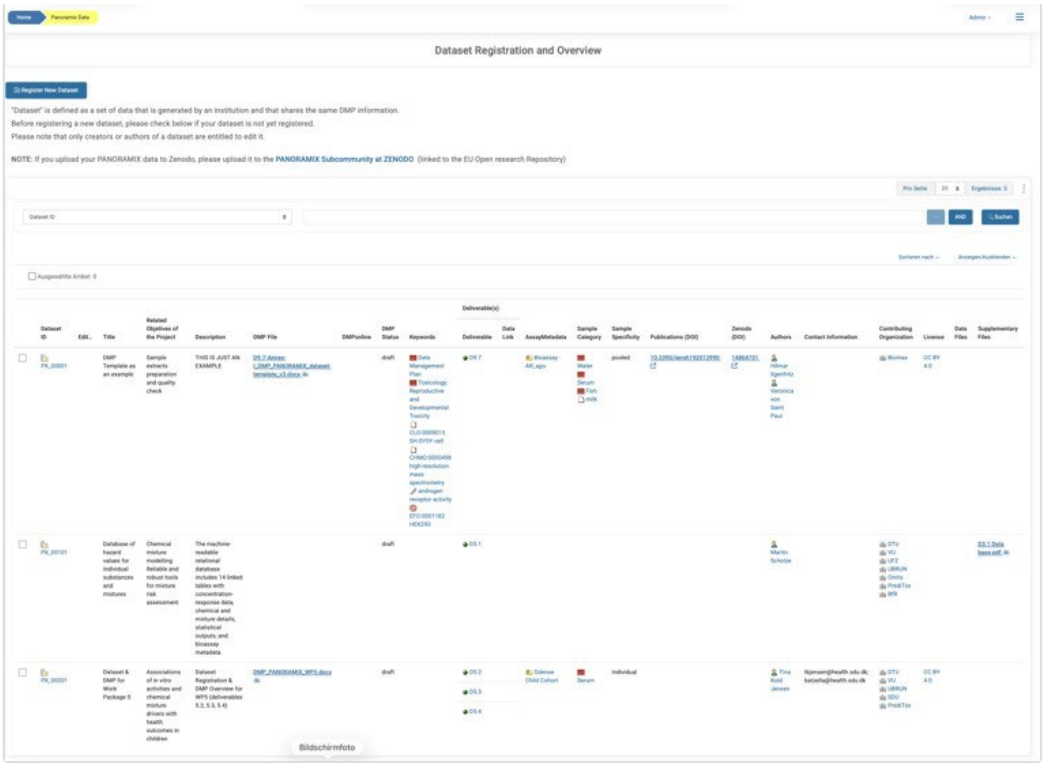

Figure 26: Entry Page for uploading DMP Data