

Generate a SAR table from the Experimental Pharmacology Knowledge Area

Do you need to predict or compare pharmacological activity of in-house compounds?

Clarivate Analytics Integrity enables you to compare the measured pharmacological activity values of a series of related compounds to identify those with the greatest activity and to predict biological activity of in-house compounds. With help of Integrity you can quickly create a Structure Activity Relationship (SAR) table for compounds based on the mechanism of action and easily work with the data and draw insight from your findings by using data management options in the Experimental Pharmacology knowledge area. **Example Scenario:** you are developing an inhibitor of type 4 phosphodiesterase B (PDE4B) and are searching for compounds that exhibit the same mechanism of action.

Retrieve data:

Run your search

The screenshot shows the 'Advanced Search' interface. At the top, there are tabs for 'Advanced Search' and 'Session History', along with 'Clear Form' and 'Start' buttons. Below this, the 'Experimental Pharmacology' section is active. Two checkboxes, 'Include Literature Results' and 'Include Patent Results', are checked. There are three input fields for 'Optional Value' with 'Index' and 'AND' buttons to the right. Under the 'Product' section, there are two radio buttons: 'Lead Compounds' (selected) and 'Under Active Development'. Below this is a dropdown menu for 'Select Value' with a list of options. 'Mechanism of Action' is highlighted in green. To the right of this dropdown are three 'Index' buttons. At the bottom of the dropdown list, 'Development Status', 'Milestone', and 'Natural Source' are also visible.

Within Integrity go to the **Experimental Pharmacology** knowledge area.

Note that **Include Literature Results** and **Include Patent Results** are checked by default.

Under the **Product** section select **Mechanism of Action** as the search field.

Click the **Index** button on the right to open the **Browse Index** box for this field.

Type "Phosphodiesterase" or "PDE4" in the Lookup box and click **Lookup**.

Tip:

- Click **Order Alphabetically** to obtain a short list of all the search terms that contain your lookup term and make your selection from here.

Select the mechanism of action of your interest (Phosphodiesterase PDE4B Inhibitors in this example).

Click **Start** to run your search.

Results appear in the table format.

The screenshot shows the 'Browse Index' dialog box. On the left, there is a 'Lookup' field containing 'PDE4' and a 'Lookup' button. Below it, there are instructions on how to use the search and navigation buttons. On the right, a list of search terms is displayed. The terms are: 'Phosphodiesterase PDE4 Inhibitors', 'Phosphodiesterase PDE4B Inhibitors', 'Phosphodiesterase PDE4C Inhibitors', 'Phosphodiesterase PDE4D Inhibitors', 'Phosphodiesterase PDE7 Inhibitors', 'Phosphodiesterase PDE8 Inhibitors', 'Phosphoenolpyruvate Carboxykinase (PEPCK) Inhibitors', 'Phosphoethanolamine/Phosphocholine Phosphatase (PHOSPHO1) Inhibitors', 'Phosphoglycerate Mutase 1 (PGAM1) Inhibitors', 'Phospholipase Inhibitors', 'Phospho-N-acetylmuramoyl-Pentapeptide-Transferase (Mra Y Transferase) Inhibitors', 'Phosphopantetheine Adenylyltransferase (PPAT) Inhibitors', 'Phosphoribosylpyrophosphate Synthase Inhibitors', '6-Phosphofructo-2-Kinase/Fructose-2,6-Biphosphatase 3 (PFKFB3) Inhibitors', 'Platelet-Activating Factor Acetylhydrolase 1B Subunit Beta (PAFAH1B2) Inhibitors', 'poly(ADP-ribose) Glycohydrolase (PARG) Inhibitors', 'Polyamine Oxidase Inhibitors', 'Prenyl Transferase Inhibitors', 'Probable Proline Dehydrogenase 2 (PRODH2; HsPOX1) Inhibitors', 'Prolyl 4-Hydroxylase (Protein Disulfide-Isomerase) Inhibitors', 'Protease Inhibitors', and 'Protein ABHD16A Inhibitors'. The first two terms are highlighted in green.

Working with your data:

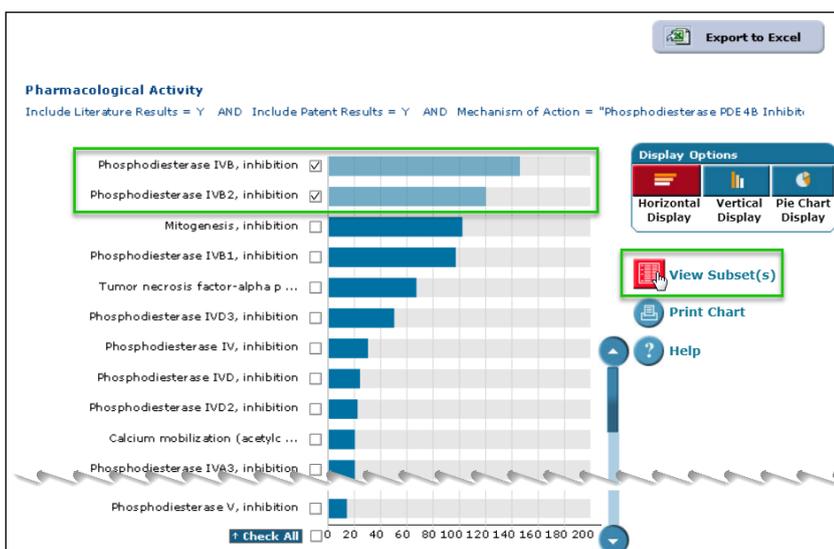
Refine by pharmacological activity

You can view the data retrieved by categories and refine them using the **Filter by Statistics** tool (at the right of the table results).

Click **Pharmacological Activity** to open this chart, review the data categories and select subsets of data.

Tip:

- Use the chart scroll bar to view and select categories below the scroll line in the chart. Click the **Export to Excel** button at the top to export all categories and their corresponding numeric values to spreadsheet format for easy visualization and sorting.



Click the checkboxes to select the top two pharmacological activity categories – Phosphodiesterase IVB, inhibition and Phosphodiesterase IVB2, inhibition.

To return results for these two categories only click **View Subset(s)**.

Unify parameters so values are directly comparable

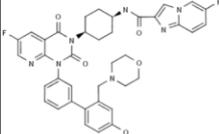
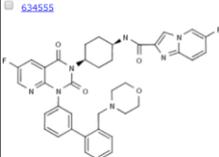
To facilitate comparison of data represented by different parameters – in this case, IC50 and pIC50, open the **Options** pull-down menu. Select **Unify Parameters to Non-Log Form**. Results are displayed as IC50 values.

*Tip: You can click the underlined column header **Value** to display data in ascending numeric order.*

Display SAR table

Records Retrieved: 206 in Experimental Pharmacology				Options			
Drug Name	Biomarker	Mechanism of Action	Experimental Activity	Pharmacology Activity	Parameter	Value	Details
634553		Phosphodiesterase PDE4B Inhibitors	cAMP-Specific 3',5'-cyclic Phosphodiesterase 4B (PDE4B) Inhibition, IN VITRO	Phosphodiesterase IVB2, inhibition	vity assay	IC-50	1.58 pM Pat. 12
634560		Phosphodiesterase PDE4B Inhibitors	cAMP-Specific 3',5'-cyclic Phosphodiesterase 4B (PDE4B) Inhibition, IN VITRO	Phosphodiesterase IVB2, inhibition	vity assay	IC-50	3.16 pM Pat. 12
634558		Phosphodiesterase PDE4B Inhibitors	cAMP-Specific 3',5'-cyclic Phosphodiesterase 4B (PDE4B) Inhibition, IN VITRO	Phosphodiesterase IVB2, inhibition	vity assay	IC-50	3.16 pM Pat. 12
634555		Phosphodiesterase PDE4B Inhibitors	cAMP-Specific 3',5'-cyclic Phosphodiesterase 4B (PDE4B) Inhibition, IN VITRO	Phosphodiesterase IVB2, inhibition	vity assay	IC-50	3.16 pM Pat. 12
634559		Phosphodiesterase PDE4B Inhibitors	cAMP-Specific 3',5'-cyclic Phosphodiesterase 4B (PDE4B) Inhibition, IN VITRO	Phosphodiesterase IVB2, inhibition	vity assay	IC-50	3.16 pM Pat. 12
634557		Phosphodiesterase PDE4B Inhibitors	cAMP-Specific 3',5'-cyclic Phosphodiesterase 4B (PDE4B) Inhibition, IN VITRO	Phosphodiesterase IVB2, inhibition	vity assay	IC-50	3.98 pM Pat. 12

Open the **Options** pull-down menu and select **Structure-Activity** to generate the SAR table as shown.

Experimental Activity: cAMP-Specific 3',5'-cyclic Phosphodiesterase 4B (PDE4B) Inhibition, IN VITRO						
Pharmacological Activity: Phosphodiesterase IVB2, inhibition						
Parameter: IC-50						
Drug Name & Structure	Mechanism of Action	Material	Method	Value	Details	
<input type="checkbox"/> 634553 	Signal Transduction Modulators Phosphodiesterase PDE4B Inhibitors	Recombinant human enzyme	Radioactivity assay	1.58 p	Pat. 1	
<input type="checkbox"/> 634555 	Signal Transduction Modulators Phosphodiesterase PDE4B Inhibitors	Recombinant human enzyme	Radioactivity assay	3.16 p	Pat. 1	

Tip:

- You can return to the Experimental Pharmacology data display format (via the **Options** menu or by using the **Back** button of your browser) and further refine data using **Filter by Statistics** feature should you wish to compare data for a specific material or method.

If you have any questions please contact us at: DTStraining@clarivate.com