> Side Effect Database (SED) Comparative Pharmacology Services

This program is designed for clients who wish to have their compound(s) tested through the same SED assay set. Once tested, Caliper 'compares' the compound profile with those compounds included in our SED. This service is available to you, the user, in several steps, the first of which is the PROFILEing of your compound(s) through the set of 65 assays outline in the SED. Caliper uses the same set of criteria and stringent QA/QC measures when testing the client compound(s) as was done for the SED data set including: assay conditions, concentration(s), tube replicates, and percent inhibition parameters. Once the client compound(s) are assayed, Caliper employs proprietary data mining tools and statistical analysis to compare the screening data with the profiles of the compounds comprising the SED set.

**STEP 1 - Compound screening at 10 μM (Pass 1)**

Screening of client compound(s) through SED assay set (SED PROFILE) through Pass 1 (10 μM in duplicate)

**STEP 2 - Followup on active compounds from Pass 1 evaluation**

IC50/Ki followup (9 concentrations in duplicate) on compounds exhibiting >75% inhibition

**STEP 3 - Caliper performs Comparative Pharmacology analysis using proprietary data mining tools**

Data mining program identifies and ranks up to 5 compounds in the SED compound set with the greatest degree of similarity with the client compound profile. Summary report for each of the similar compounds is provided to the client detailing: Compound name, commercial use(s), known bioactivities & adverse properties.

**STEP 4 (Optional)**

Follow-on to Step 3 where the client receives percent inhibition and IC50/Ki values for the compounds identified from the step 3 analysis.

Pharmacology profiling has become an invaluable tool for lead compound selection, optimization and candidate prioritization. Analysis of PROFILE data identifies off-target interactions that can help predict potential side effects, efficacy and safety of compounds under development before they progress to the more costly stages of preclinical and clinical trials.

Caliper offers a major addition to the PROFILE toolbox through the creation of our pharmacoinformatics program, the Side Effect Database (SED).

Our SED contains the profile data for more than 2,300 compounds which have been screened through 65 assays. The result is a highly enriched, full-rank compound dataset of more than a half a million datapoints to assist in identifying and eliminating side effect and safety concerns which improves and sharpens drug discovery and development programs.
The SED is designed to help you query and determine patterns of chemical - molecular target interactions that are correlated with specific biological activities or clinical outcomes. By employing the SED, empirical interpretation of data is replaced with statistical predictability, resulting in greater speed, efficiency and precision in your drug development efforts. With the SED, you can select lead compounds at an early stage with increased confidence and accuracy.

Uses of the SED include:
- Support of medicinal chemistry for lead optimization
- Support of computational chemistry for rational drug design
- Support of high throughput screening for chemical series selection
- In silico screening strategies

THE SED FEATURES

The SED is designed to provide the client with profile data for any of the 2,300 compound(s) listed in our SED data set. The following information is included when choosing SED:
- Percent inhibition values for each receptor or enzyme tested at 10 μM
- IC50/Ki values are available upon request for specific receptors or enzymes where our criteria for compound activity were met

Pricing structure for the SEDSelect
- Percent inhibition data of 10 μM = $2,000/compound
- IC50/Ki values (includes percent inhibition values at the 9 concentrations) = $400/compound/assay

THE SED COMPOND SET

To construct the SED, Caliper has assembled and profiled an extensive library of 2,300 compounds resulting in a full-rank, information-rich pharmacoinformatics resource. Caliper captures several key characteristics of the compounds in the SED including: common name, JUPAC name, chemical formula, salt form, molecular weight, CAS number, vendor identification, and compound structure in MOL file or SMILE string formats.

THE ASSAYS

Our Side Effect Database (SED) incorporates a broad array of well characterized and validated in vitro screens which are important mediators of drug side effects or drug actions. Assay categories include:
- GPCRs
- Voltage-gated ion channels
- Ligand-gated ion channels
- Neurotransmitter transporters
- Nuclear receptors
- CNS-related enzymes

All assays are performed at the Novascience laboratories using consistent reagents, assay conditions, and reference agents. Compounds exhibiting ≥ 30% inhibition at 10 μM (duplicate) in the pass 1 are automatically verified at 3 concentrations in duplicate (pass 2). Those compounds demonstrating activity ≥ 75% inhibition in either the pass 1 or pass 2 are tested at 9 concentrations in duplicate to determine IC50/Ki values.

Applications of the SED

> Full SED database

Access to the full SED database is designed for those companies with their own data mining tools and statistical analysis programs
- 2,300 compounds
- 65 assays
- Full rank data set including IC50/Ki values for compounds exhibiting ≥ 75% inhibition at 10 μM
- Over a half a million datapoints

Pricing available upon request

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- **GPCR**
  - Voltage-gated ion channels
  - Ligand-gated ion channels
  - Neurotransmitter transporters
  - Nuclear receptors
  - CNS-related enzymes

All assays are performed at the NovoScreen laboratories using consistent reagents, assay conditions, and reference agents. Compounds exhibiting > 30% inhibition at 10 μM (duplicate) in the pass 1 are automatically verified at 3 concentrations in duplicate (pass 2). Those compounds demonstrating activity > 75% inhibition in either the pass 1 or pass 2 are tested at 9 concentrations in duplicate to determine IC50/Ki values.

#### Applications of the SED

**> Full SED database**

Access to the full database is designed for those companies with their own data mining tools and statistical analysis programs.

- 2,300 compounds
- 65 assays
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