APPLICATION NOTE

ACD/LABS [ADVANCED CHEMISTRY DEVELOPMENT, INC.]

Predictive Software for Cost Effective Lead Optimization in Virtualized R&D

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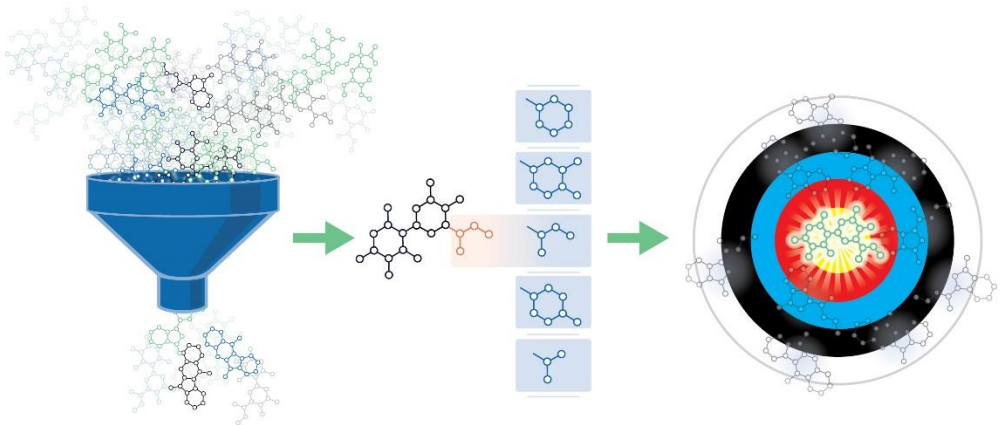
Focus Lead Optimization with Predictive Software

Virtual R&D companies commercialize their technology or intellectual property by one of two methods: applying a foundational capability in the discovery and development of new chemical entities or licensing that capability to others.

Figure 1 represents a common sequence of events in early discovery.



Screen diverse chemical space to identify a lead series

Confirm and optimize pharmacophore(s) through analog synthesis and testing

Enhance potency while minimizing off-target effects

Figure 1: The typical lead identification, analog synthesis, and optimization workflow.

To limit the cost of investigating the broad scope of off-target effects (ADME, toxicity, dosage, formulation, etc.) successful organizations invest in predictive modelling software. This *in silico* approach helps to reduce trial-and-error experimentation to:

- → Balance expenditure and lead optimization success
- → Prioritize a "minimally viable" set of synthetic and assay activities

Minimize the Opportunity Cost of *In Silico* Approaches

What do you sacrifice by choosing prediction over experimentation?

A concern for those considering predictive software for lead optimization is the possibility of overlooking a compound. Either due to inaccurate prediction or because the chemical space of interest is under-represented or lacking from the training database.

To avoid missing the "rough diamond", choose predictive software that provides results along with:

- → Published experimental data for structurally similar analogs and/or
- → A measure of certainty in predicted results

Percepta® Property Predictions for Lead Optimization

Percepta provides a full portfolio of predictive models and algorithms to support lead optimization. In addition to physicochemical, ADME, and toxicity predictions, the modules provide:

- → A list of similar structures from the database with experimental results from peer-reviewed literature
- → Indicators of prediction accuracy—reliability index, probability, calculation protocols, etc.

A Workflow for Externalized Lead Optimization

1. Import your "Hit List" of lead series to calculate properties of interest.
2. Review and sort predictions and add structure analogs for calculation.

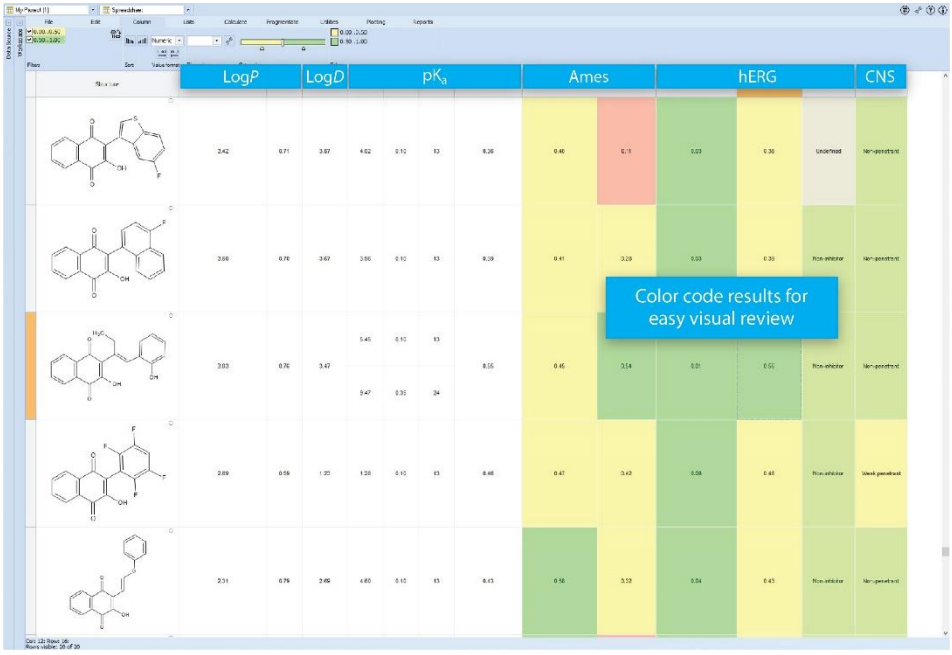


Figure 2: Spreadsheet view in Percepta allows you to view, sort, and filter results.

3. Review details in individual prediction modules.

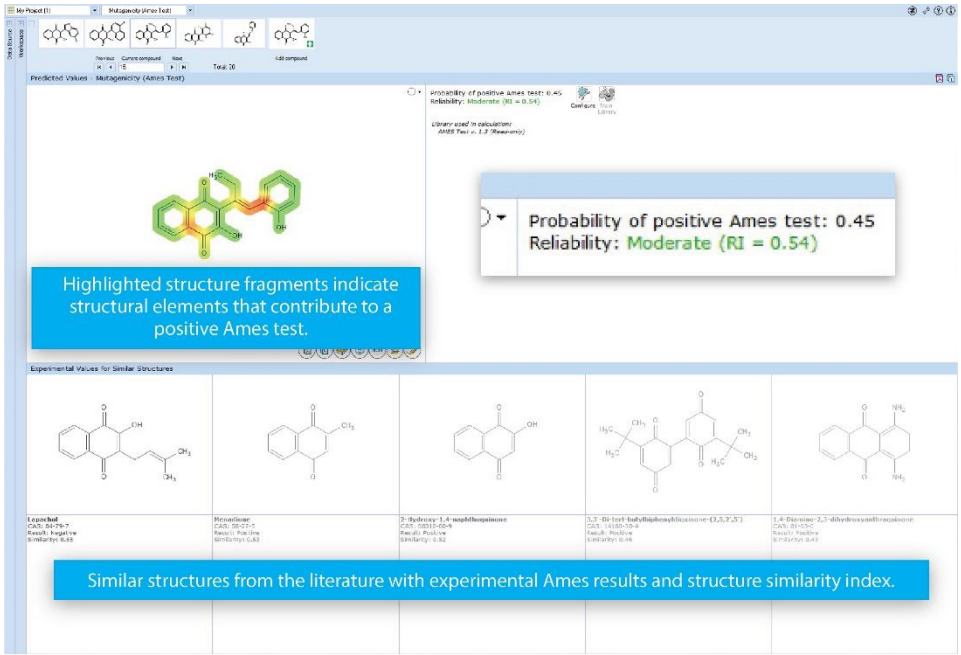


Figure 3: The Mutagenicity module in Percepta. Review predicted results along with reliability and similar structure information for confident decisions.

4 Annotate the spreadsheet with comments and indicate which analogs are to be synthesized.
5 Report your final target analog list as an SDfile for submission to synthesis resources (internal or CRO).

Software Deployment Options

Whether you and your collaborators work in a shared office space, or you're distributed across the country (or the world), we have a deployment that will suit your needs.

Client Installation on the Cloud

The Percepta thick client offers rich functionality so you can understand your results to great depth. It is architecturally simple for deployment, so you don't need an IT expert to install or support it. Installing Percepta on a private cloud ensures access for everyone, regardless of their physical location

Browser-Based Application.

Browser-based deployment of Percepta is a more complex installation. It delivers most of the functionality of the thick client with faster, easier access for a geographically scattered team with better tools for making collaborative decisions.