

1001 Configurations

A potpourri of popular extensions, add-ons and configurable options in D360

Dr. Fabian Rauscher | D360 UGM 2019



Preface

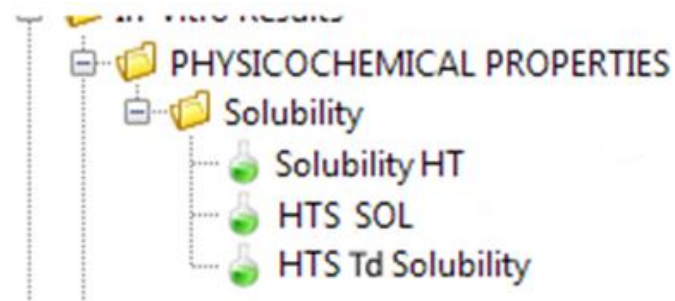
- D360 flexible configurable system
 - Core product installer for all customers
 - Customer specific configuration & plugins
- Data catalog mapping customer data sources into D360
- Extendable through configuration, scripting, coding

A ... like Assays



The Evergreens: Super Assays & Assays Groups

- Results from multiple, equivalent assays represented in more columns than necessary.

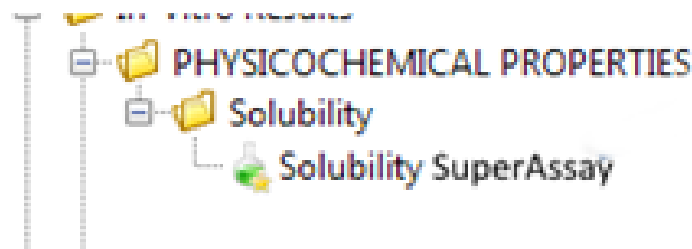


Spreadsheet View [1]

	CHEMBL Id	Structure	Solubility HT Mean SOL (ug/ml) pH 4.500	Solubility HT Mean SOL (ug/ml) pH 6.800	HTS SOL Mean Solubility (ug/ml) pH 4.500	HTS SOL Mean Solubility (ug/ml) pH 7.400	HTS Td Solubility Mean Sol (ug/ml) pH 4.500	HTS Td Sol Mean Sol (ug/ml) pH 6.800
1:	CHEMBL1241676		0.130	0.110				
2:	CHEMBL1242568				0.650	2.050		
3:	CHEMBL1242656						320.000	221

The Evergreens: Super Assays & Assays Groups

- Same assays combined into a Super Assay so they appear as single assay

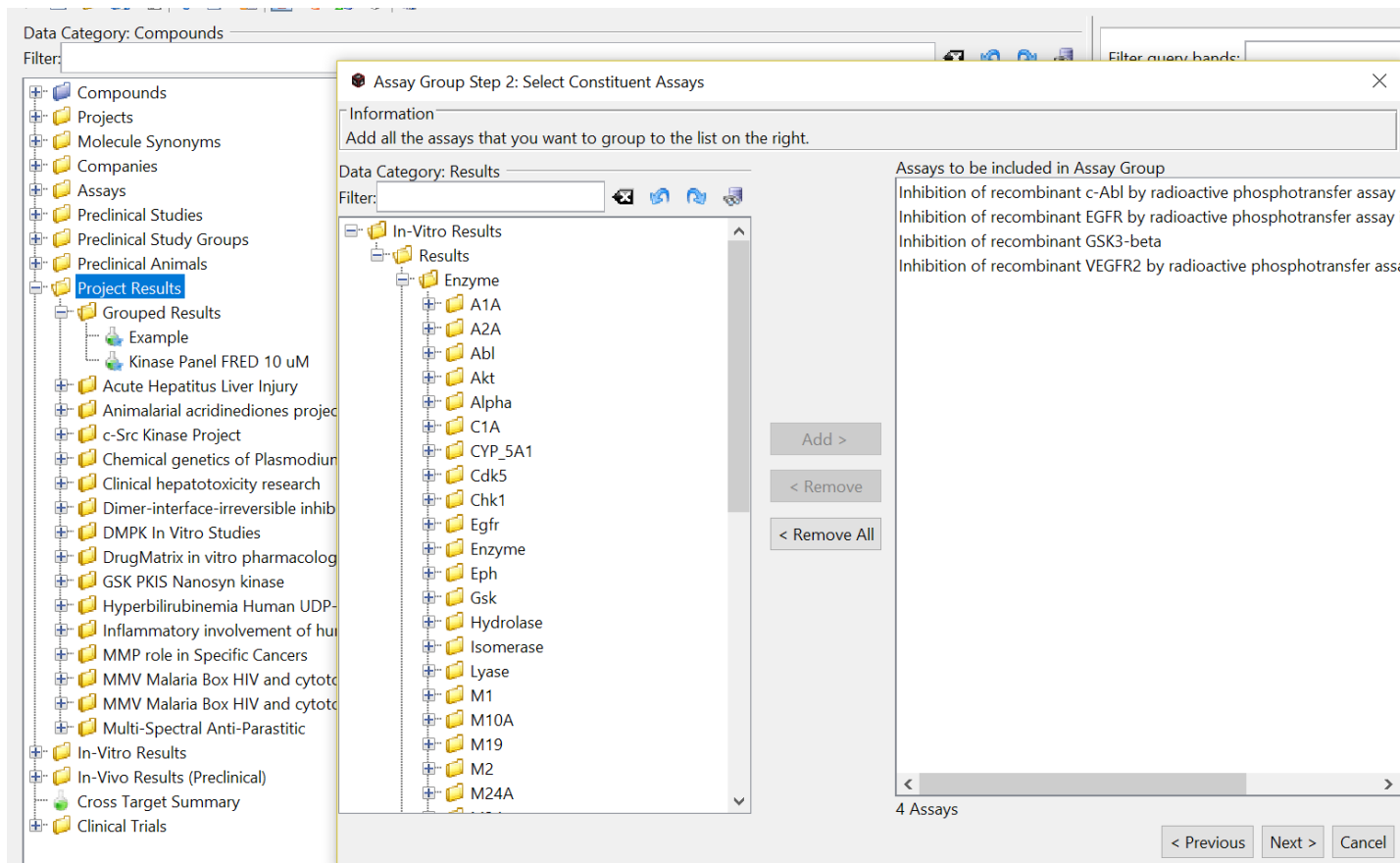


Spreadsheet View [1]

	CHEMBL Id	Structure	Solubility SuperAssay Mean Solubility (ug/ml) pH 4.500	Solubility SuperAssay Mean Solubility (ug/ml) pH 6.800	Solubility SuperAssay Mean Solubility (ug/ml) pH 7.400
1:	CHEMBL1241676		0.130	0.110	
2:	CHEMBL1242568		0.650		2.050
3:	CHEMBL1242656		320.000	2200.000	

The Evergreens: Super Assays & Assays Groups







- An Assay Group is a “fake” assay that allows retrieval of the results of multiple assays much more easily and keeps the results from individual assays separate



NKOTB - Negative log Results

- Negative log Results

Query Bands

Inhibition of recombinant c-Abl by radioactive phosphotransfer assay in presence of 10 uM ATP (Results) Show   
IC50 (nM) (GMean), pIC50 (Mean) 
Constraint(s) A: pIC50 > 6 


Inhibition of recombinant c-Abl by radioactive phosphotransfer assay in presence of 10 uM ATP (Results)

Retrieve everything tested

Retrieve everything tested from:

Last N Days

7

Results & Conditions

Analysis Information

Results

IC50 (nM) [\(GMean\)](#)

pIC50 [\(Mean\)](#)

Graphical Result IC50

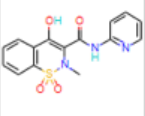
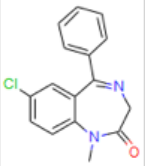
[Add Criterion](#)

A: > 6 

Conditions

NKOTB - BioProfile Summary

- Most important assay results for all the assays that a compound has been tested in using a compact table representation.

Spreadsheet									
	ChEMBL Id	Structure	Summarized Test ID	Summarized Test Short Name	Summarized Princ. Result Type	Summarized Princ. Result Value	Count Used Princ. Result Value	Summarized Condition Names	Summarized Condition Values
1:	CHEMBL527		33	Inhibition of human Prostaglandin G/...	Mean Inhibition (%)	-7.000	1	Dose (ug/mL) : Enzyme sub-type	0.1 : PGHS-1
			33	Inhibition of human Prostaglandin G/...	Mean Inhibition (%)	25.000	1	Dose (ug/mL) : Enzyme sub-type	0.1 : PGHS-2
			33	Inhibition of human Prostaglandin G/...	Mean Inhibition (%)	10.000	1	Dose (ug/mL) : Enzyme sub-type	1 : PGHS-1
			33	Inhibition of human Prostaglandin G/...	Mean Inhibition (%)	58.000	1	Dose (ug/mL) : Enzyme sub-type	1 : PGHS-2
			33	Inhibition of human Prostaglandin G/...	Mean Inhibition (%)	35.000	1	Dose (ug/mL) : Enzyme sub-type	10 : PGHS-1
			33	Inhibition of human Prostaglandin G/...	Mean Inhibition (%)	62.000	1	Dose (ug/mL) : Enzyme sub-type	10 : PGHS-2
2:	CHEMBL12		20	Inhibition of [3H]-Ro-15-1788 binding...	Mean Ki (nM)	6.600	1	Receptor sub-type	alpha-2-beta-3-gamma-2
			20	Inhibition of [3H]-Ro-15-1788 binding...	Mean Ki (nM)	13.000	1	Receptor sub-type	alpha-1-beta-3-gamma-2
			20	Inhibition of [3H]-Ro-15-1788 binding...	Mean Ki (nM)	33.000	1	Receptor sub-type	alpha-3-beta-3-gamma-2
			20	Inhibition of [3H]-Ro-15-1788 binding...	Mean Ki (nM)	11.000	1	Receptor sub-type	alpha-5-beta-3-gamma-2
			28	Binding affinity to human recombina...	Mean Ki (nM)	> 3000.000	1	Receptor sub-type	alpha-6-beta-3-gamma-2
			28	Binding affinity to human recombina...	Mean Ki (nM)	14.000	1	Receptor sub-type	alpha-1-beta-3-gamma-2
			28	Binding affinity to human recombina...	Mean Ki (nM)	20.000	1	Receptor sub-type	alpha-2-beta-3-gamma-2
			28	Binding affinity to human recombina...	Mean Ki (nM)	15.000	1	Receptor sub-type	alpha-3-beta-3-gamma-2
			28	Binding affinity to human recombina...	Mean Ki (nM)	11.000	1	Receptor sub-type	alpha-5-beta-3-gamma-2
			10021	Half-maximal inhibition of [125I]-CCK...	GMean IC50 (nM)	> 100000.000	1		
			10022	Half-maximal inhibition of [125I]-CCK...	GMean IC50 (nM)	> 100000.000	1		
10058	Inhibition of binding of Batrachotoxin...	Mean Inhibition (%)	15.200	1					

Concatenated Aggregation, Result Type, Unit

Concatenated Condition Names

Concatenated Condition Values (same order as the concatenated Condition Names)

Test ID

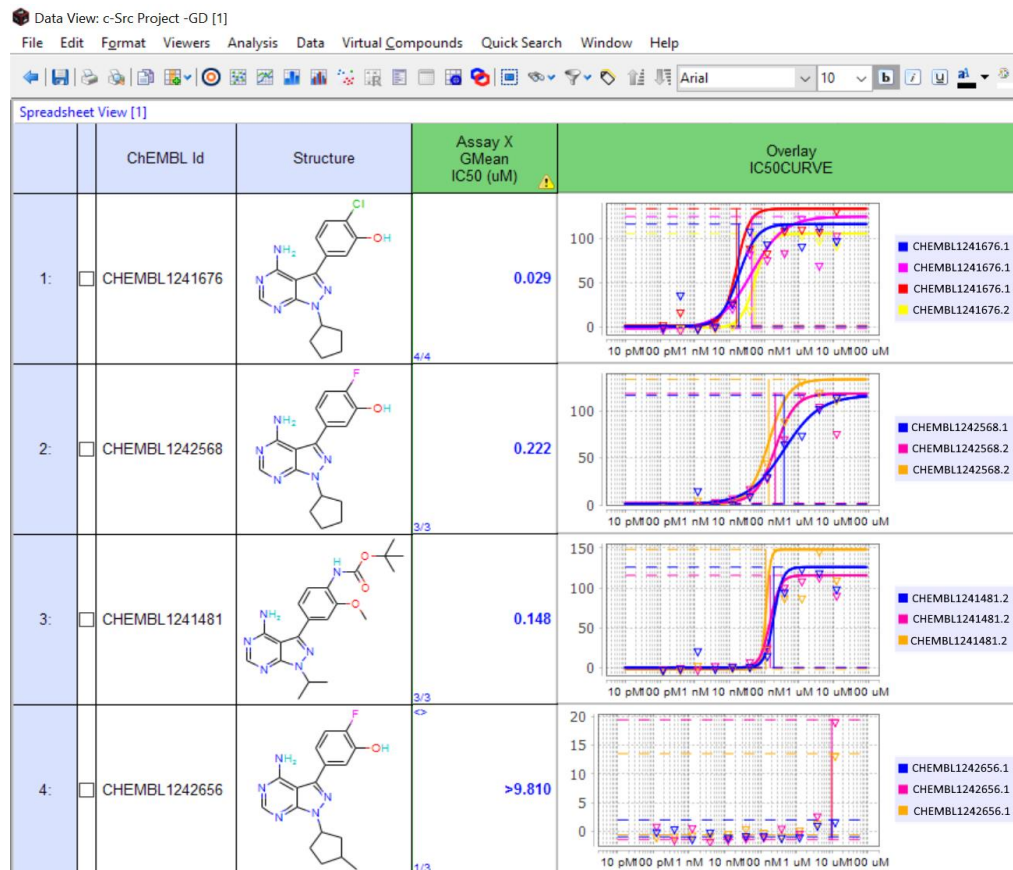
Test Name

Aggregated Value

Number of values used for aggregation

Dose-response curves rendering

- Curve renderer that reproduces fitted dose response curves from result parameters



Drilldown templates

- Default drilldown table content can be modified and extended.
 - Change order of columns
 - Pull in additional result types & data fields

Drilldown: Agonist activity at human PPAR ligand binding domain expressed in human 293T cells cotransfected with Gal4-DBD by luciferase transa... X

Drilldown Source

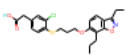
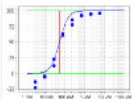
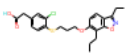
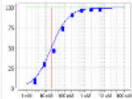
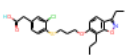
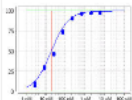
Field Name: Agonist activity at human PPAR ligand binding domain expressed in human 293T cells co Field Value: 1300

Mean 12

EC50 (nM) 100

< >

Drilldown Data

CHEMBL Id	Structure	Agonist ac... EC50 (nM)	Agonist activit... EC50 (nM) Receptor sub-t...	Image Result	Agonist activity... Target Class	Agonist ac... Target Sub...	Agonist ac... Target	Agonist acti... PubMed ID
CHEMBL279053		1.30E+03	alpha		Transcription Fa...	Nuclear Rec...	Peroxisome...	19928766
CHEMBL279053		100	gamma		Transcription Fa...	Nuclear Rec...	Peroxisome...	19928766
CHEMBL279053		12.0	delta		Transcription Fa...	Nuclear Rec...	Peroxisome...	19928766

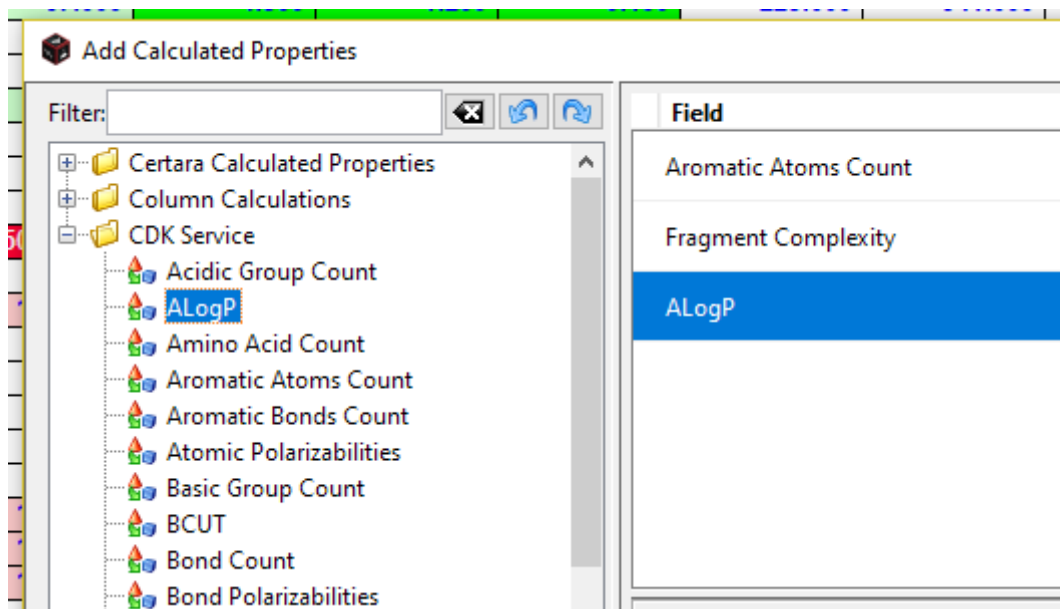
Print Table... Print Preview... Copy Table Add to Dataset Close ?

Web Services

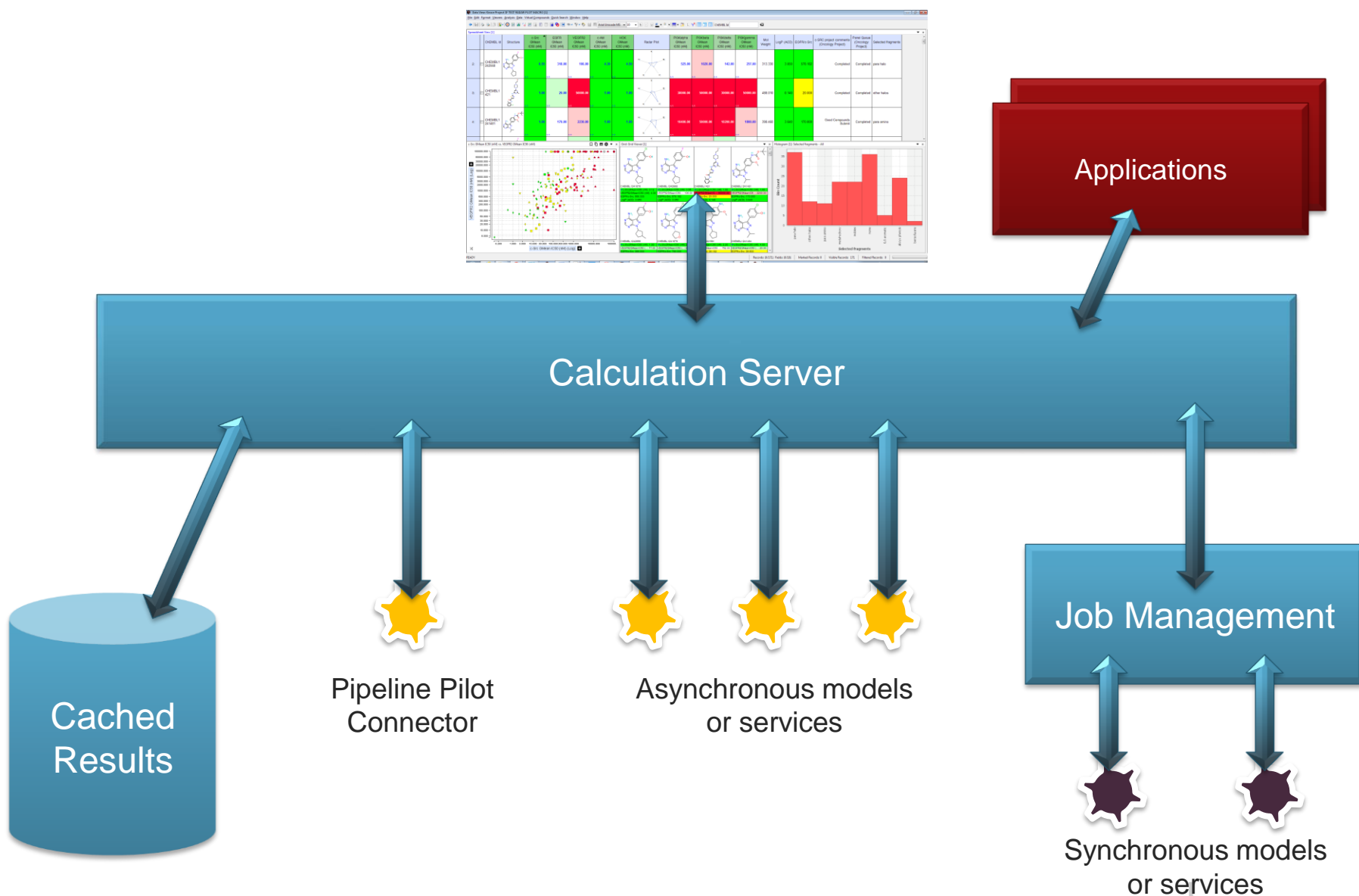


Integration with Web Services

- Direct integration into D360 client
 - Property calculations
 - Compound lookup
 - Support for async. and sync. services.



Calculation Caching Server

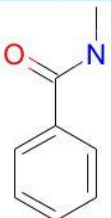


Web Services as Data Source in D360

- Web services can be configured to some extent to act like a virtual database table/view in D360's middle layer.
 - A search within such a virtual table leads to a web service call.
 - Example: Matched Molecular Pair workflows


MMP Transform Matched Molecular Pairs (MMP)

Reference (MMP Transform WS):



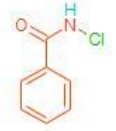

MMP Input Structure Edit

Substructure (MMP Transform WS):



MMP Input Structure Edit

Property (MMP Transform WS):
Select Specific

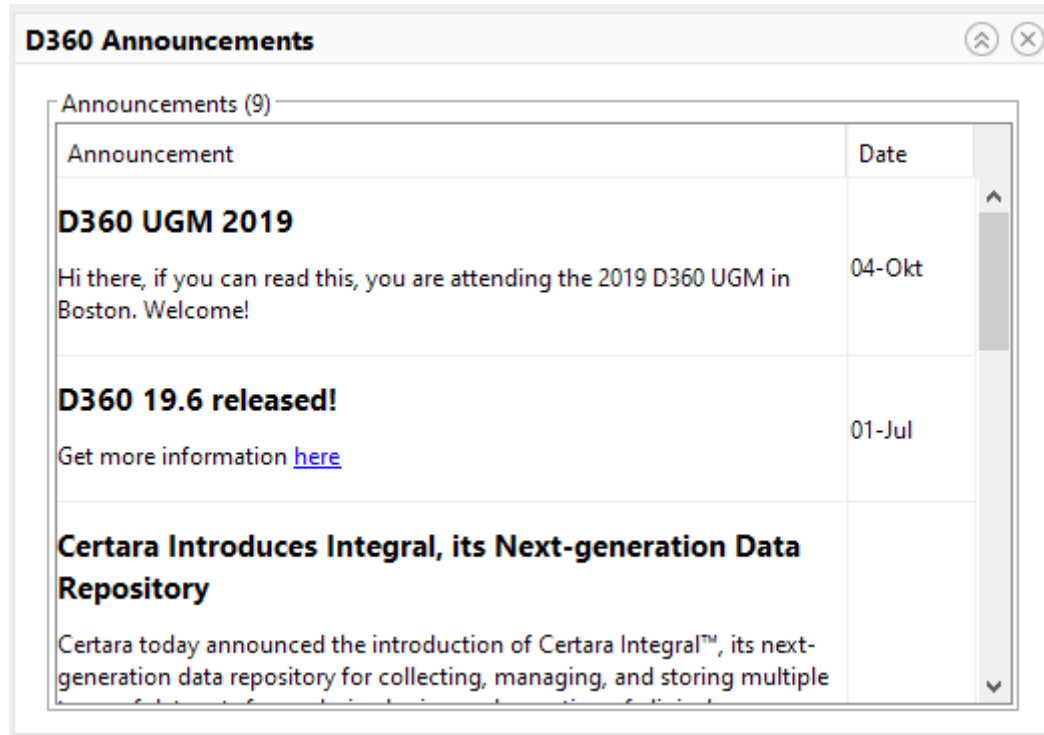
	Product	Count Property	Delta Property	Sigma Property	SMILES_from Property	SMILES_to Property
1:		1594 1/1	0.211 1/1	0.402 1/1	—R1	Cl-R1
2:		1144 1/1	-0.153 1/1	0.388 1/1	—R1	F-R1

**Usability
& Security**



Announcement/News widget

- Database-backed announcement widget displaying the last n announcements to users.



Usability & Security

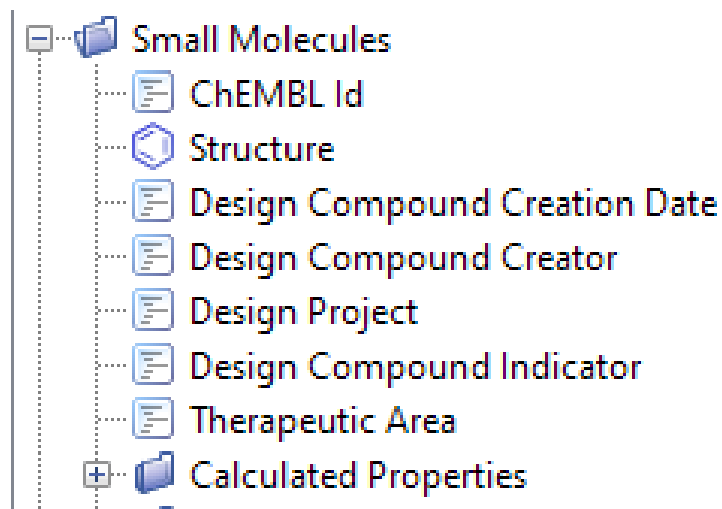
- Interfaces to manage research projects in D360
- TLS encrypted traffic D360 client-server
- Restricting access to data

Chemistry



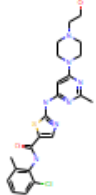
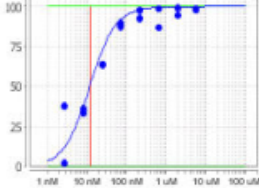
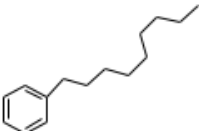
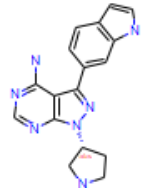
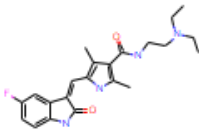
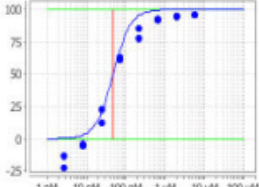
Integration with Virtual/Design Compounds

- Existing virtual compound repository data can be integrated into the standard “Compound” data category such that:
 - Standard queries can retrieve both real and captured virtual compounds.
 - Additional data can be stored about virtual compounds using D360’s annotation system



Integration with Virtual/Design Compounds

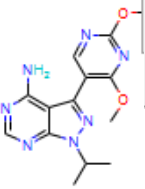
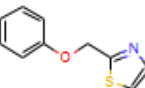
Spreadsheet

	ChEMBL Id	Structure	Design Compound Indicator	c-Src project comments (Oncology Project)	c-Src Mean IC50 (nM)	c-Src Mean pIC50	c-Src Graphical Result IC50
1: <input type="checkbox"/>	CHEMBL1421		N	Completed	1 1/1	9 1/1	
2: <input type="checkbox"/>	DC-00011147		Y	Not interesting			
3: <input type="checkbox"/>	DC-00011143		Y	Prioritize for synthesis			
4: <input type="checkbox"/>	CHEMBL535		N	Sutinib;Submit	400 1/1	6.40 1/1	

Capturing Compound Ideas

- A D360 dataset may contain real and virtual compounds
 - Sketched into the dataset or imported from a file.
- D360 Capture allows virtual compounds in the dataset to be captured as design ideas.

The screenshot shows the D360 software interface. The 'Virtual Compounds' menu is open, displaying options: 'Add Record from Sketch...', 'Import Data Records...', 'Enumerate Virtual Compounds from R-Groups...', 'Capture Virtual Compounds as Design Compounds...', 'Delete Virtual Compounds in Dataset...', and 'Delete Design Compounds from Database...'. Below the menu is a table with columns for 'ChEMBL Id' and 'Structure'. The table contains two rows: Row 171 with ChEMBL Id 'CHEMBL1242846' and a complex heterocyclic structure; Row 172 with ChEMBL Id 'VC~00000001' and a simpler structure. The table has a grid of colored cells (red, grey, blue) below the structure column, with '1/1' and '0/1' labels.

	ChEMBL Id	Structure
171:	<input type="checkbox"/> CHEMBL1242846	
172:	<input type="checkbox"/> VC~00000001	

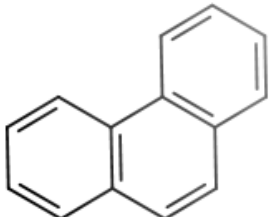
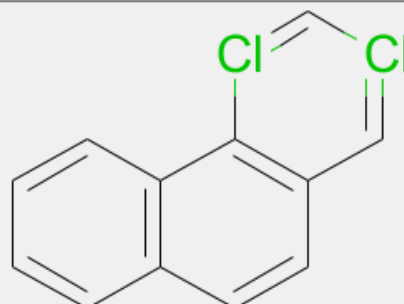
The dialog box 'Capture Virtual Compounds as Design Compounds' is shown. It contains an 'Information' section explaining that capturing virtual compounds as design compounds persists chemical structures for annotation and retrieval by D360 queries. It notes that design compounds are assigned a new identifier and must be associated with a shared workspace. The 'Design Compound Capture' section has three radio buttons: 'Selected Virtual Compounds (0)', 'Marked Virtual Compounds (0)', and 'All Virtual Compounds in Dataset (1)'. The 'All Virtual Compounds in Dataset (1)' option is selected. A 'Design Project' dropdown menu is set to 'Choose Workspace...'. At the bottom are 'Capture Virtual Compounds as Design Compounds' and 'Cancel' buttons.

Custom Sketch & Calculate interface

Sketch and Calculate

Reference Get ID:

Sketch Get ID:

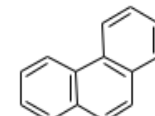


Calculated Properties

Property	Reference	Sketch	Delta
ALogP (ALogP)	3.18	4.05	0.87
Mol Weight (Mol Wei...	223.10	178.23	-44.87
H Bond Donors (H B...	0	0	0
H Bond Acceptors (H...	0	0	0
Heavy Atoms (Heavy...	14	14	0

Add calculations to the dataset

Structure cart (1 structures in cart)



And so ends our story ...

- Wait ... are there more stories you can tell? Yes, of course:
 - Custom follow on actions, involving scripting and widget-like interfaces
 - Custom menu entries and right click menus, such as an assay lookup facility
 - Plugins that fetch structures from extra databases for firewalled projects based on the user id
 - ...
- The D360 services team is at your disposal to entertain you with more stories of 1001 configurations and help you to bring them to life in your D360 environment.