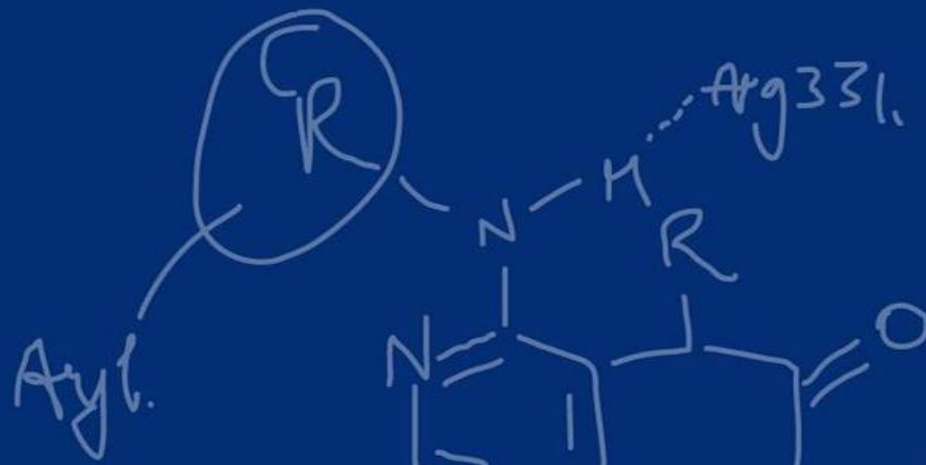
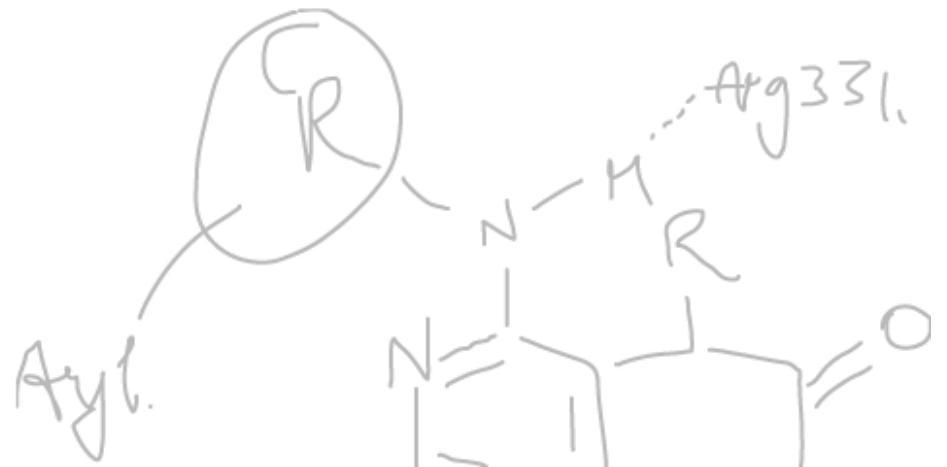

Instant JChem: Linking Chemistry & Biology

Creating integrated drug discovery
innovation alliances



Agenda

- **Overview**
- Project data flow
- Schemas
- Data model
- User security
- Deployment
- Integrating Oracle views
- Conclusion



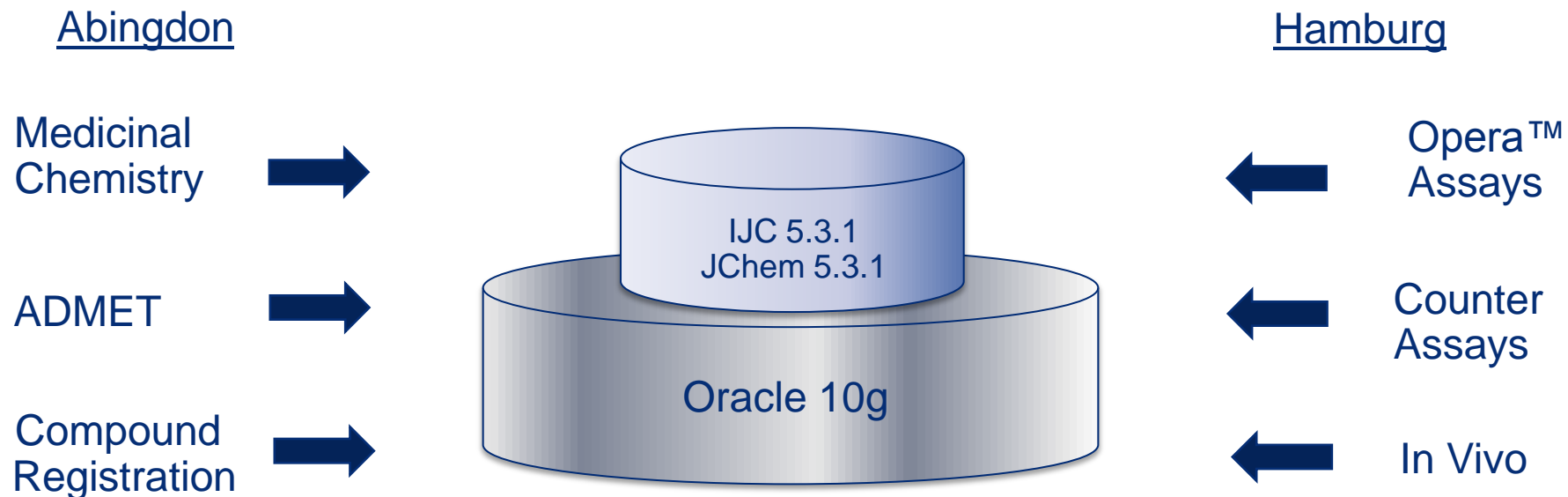
Overview

Shared IJC project database setup at Evotec

- Enterprise licenses for server use shared across Abingdon and Hamburg sites
- Dedicated IJC server at Abingdon with Oracle 10g and JChem cartridge
- One Oracle schema per drug discovery project containing project data (currently used 7 live IJC shared projects)
- A project IJC schema is connected to each Oracle schema
- Built-in IJC security & roles used for user management
- Deployment to project users via web server URLs

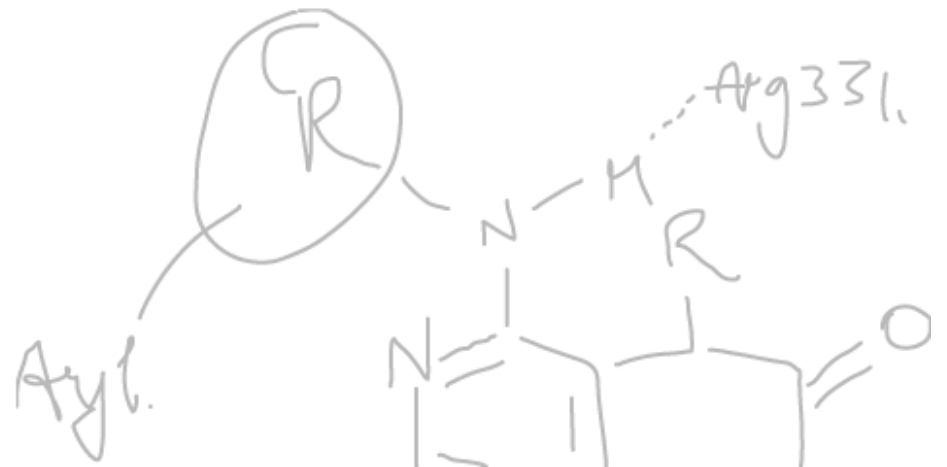
Project data flow

Drug discovery IJC project at Evotec



Agenda

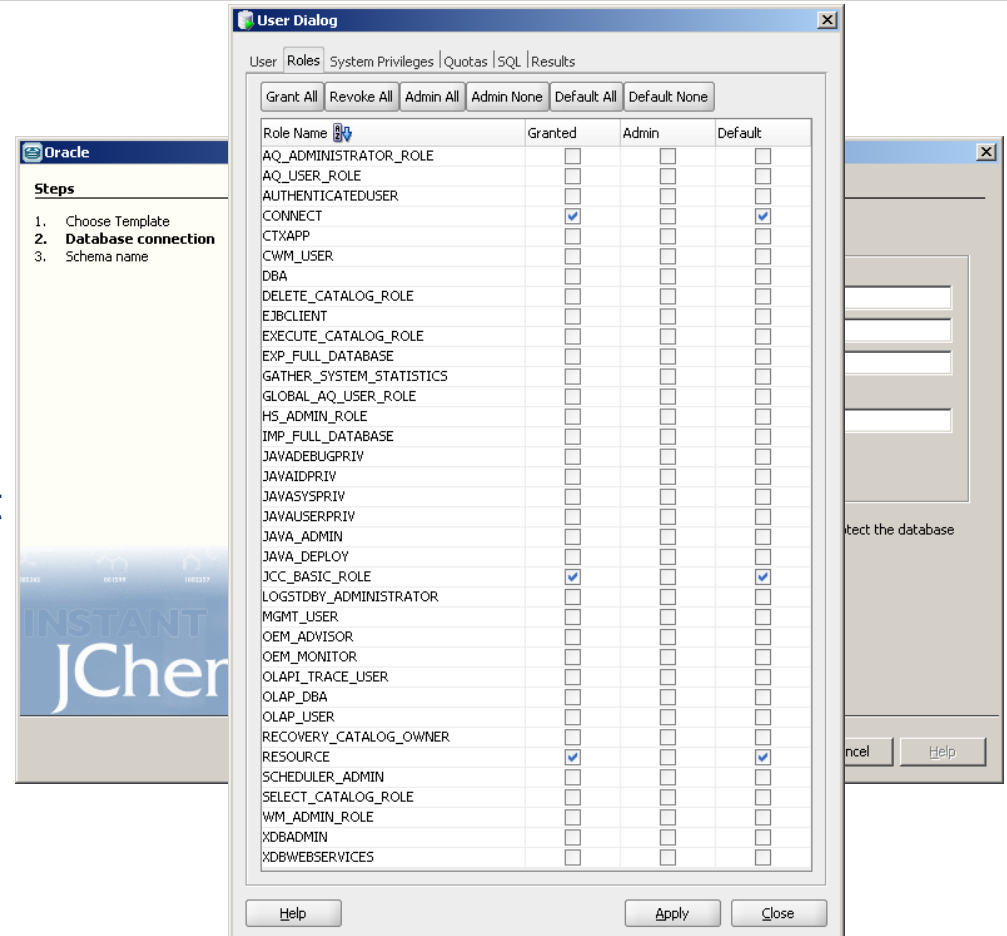
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Schemas

Create Oracle & IJC schemas

- Create project Oracle user
- Grant JCC_BASIC_ROLE to Oracle user
- Create a new empty IJC project
- Create a new schema in IJC & connect to the Oracle project schema



The screenshot shows the Oracle User Dialog window with the 'Roles' tab selected. The 'Grant All' button is active. The table below shows the roles and their status for the user.

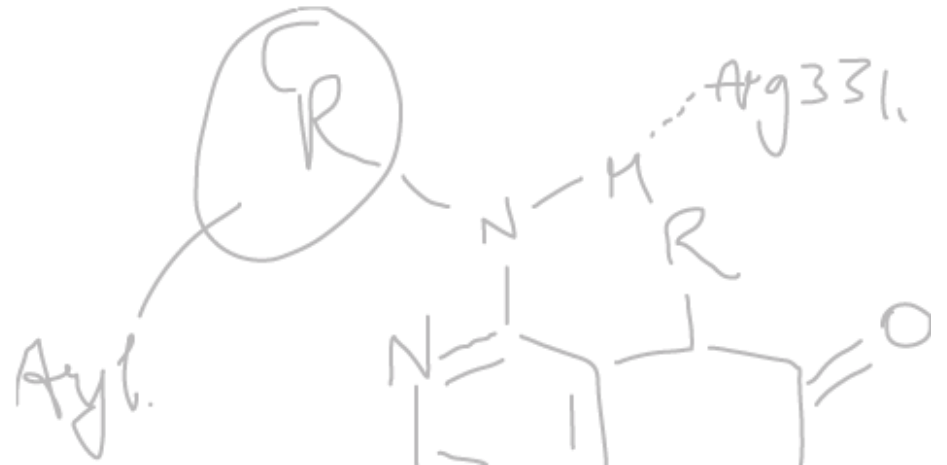
Role Name	Granted	Admin	Default
AQ_ADMINISTRATOR_ROLE	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
AQ_USER_ROLE	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
AUTHENTICATEDUSER	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
CONNECT	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
CTXAPP	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
CWM_USER	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
DBA	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
DELETE_CATALOG_ROLE	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
EJBCLIENT	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
EXECUTE_CATALOG_ROLE	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
EXP_FULL_DATABASE	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
GATHER_SYSTEM_STATISTICS	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
GLOBAL_AQ_USER_ROLE	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
HS_ADMIN_ROLE	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
IMP_FULL_DATABASE	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
JAVADEBUGPRIV	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
JAVAIIDPRIV	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
JAVASYSPRIV	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
JAVAUERPRIV	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
JAVA_ADMIN	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
JAVA_DEPLOY	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
JCC_BASIC_ROLE	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
LOGSTDBY_ADMINISTRATOR	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
MGMT_USER	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
OEM_ADVISOR	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
OEM_MONITOR	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
OLAPI_TRACE_USER	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
OLAP_DBA	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
OLAP_USER	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
RECOVERY_CATALOG_OWNER	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
RESOURCE	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
SCHEDULER_ADMIN	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
SELECT_CATALOG_ROLE	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
WM_ADMIN_ROLE	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
XDBADMIN	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
XDBWEBSERVICES	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

The Instant JCher interface shows the 'Steps' section with the following instructions:

1. Choose Template
2. Database connection
3. Schema name

Agenda

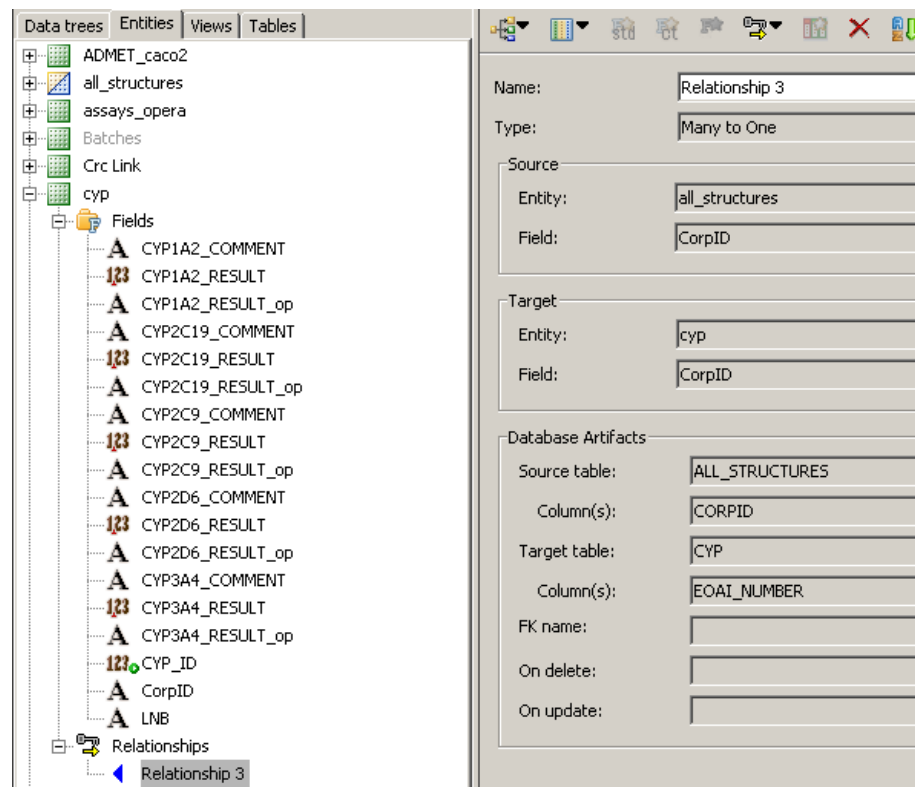
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Data model

Build project databases in IJC

- Create tables
 - SDFFile import of existing data is a convenient method
 - Choose cartridge-indexed type for structure tables
- Create relationships, indexes, edges & datatrees
- Link tables on CorpID field
- Set constraints on tables & fields
- Create grid & form views
- Create project users and assign roles



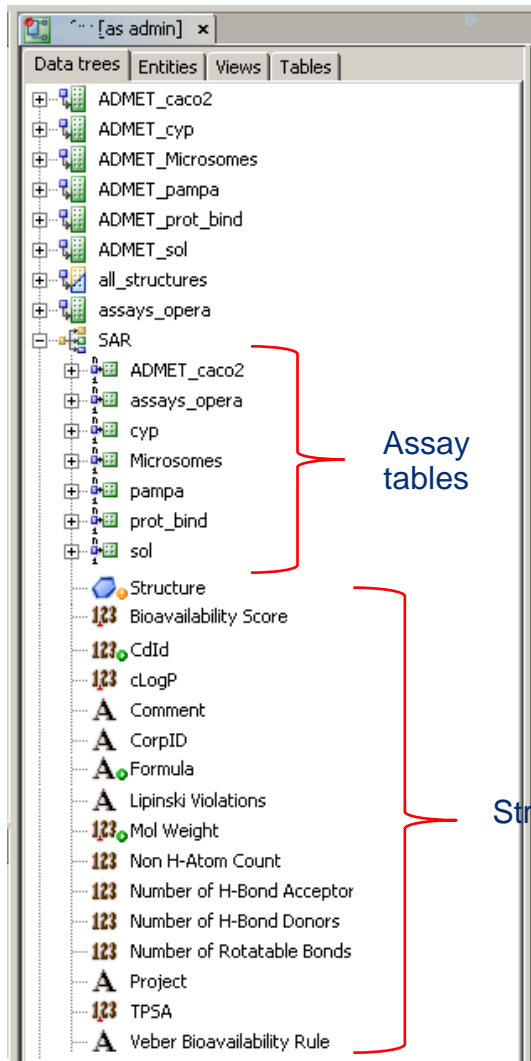
The screenshot displays the IJC software interface. On the left, a tree view shows the data model structure under 'Entities'. The 'Fields' folder is expanded, listing various tables and their fields, such as CYP1A2_COMMENT, CYP1A2_RESULT, CYP1A2_RESULT_op, CYP2C19_COMMENT, CYP2C19_RESULT, CYP2C19_RESULT_op, CYP2C9_COMMENT, CYP2C9_RESULT, CYP2C9_RESULT_op, CYP2D6_COMMENT, CYP2D6_RESULT, CYP2D6_RESULT_op, CYP3A4_COMMENT, CYP3A4_RESULT, CYP3A4_RESULT_op, CYP_ID, CorpID, and LNB. At the bottom of the tree, the 'Relationships' folder is expanded, showing 'Relationship 3' selected.

On the right, a configuration window for 'Relationship 3' is open. It shows the following details:

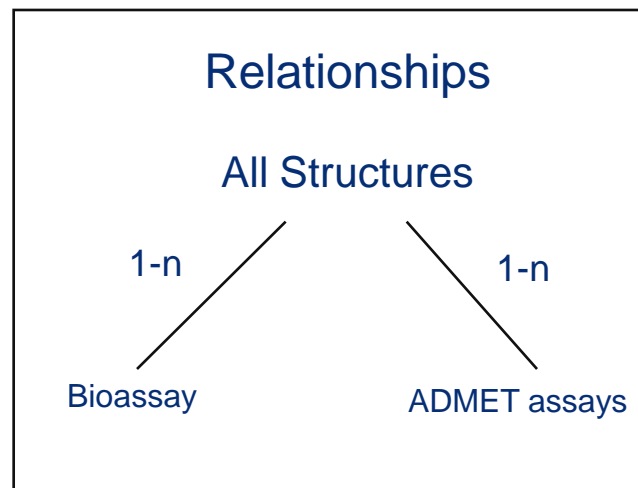
- Name: Relationship 3
- Type: Many to One
- Source:
 - Entity: all_structures
 - Field: CorpID
- Target:
 - Entity: cyp
 - Field: CorpID
- Database Artifacts:
 - Source table: ALL_STRUCTURES
 - Column(s): CORPID
 - Target table: CYP
 - Column(s): EOAI_NUMBER
 - FK name:
 - On delete:
 - On update:

Data model

Schema Editor view: Data trees

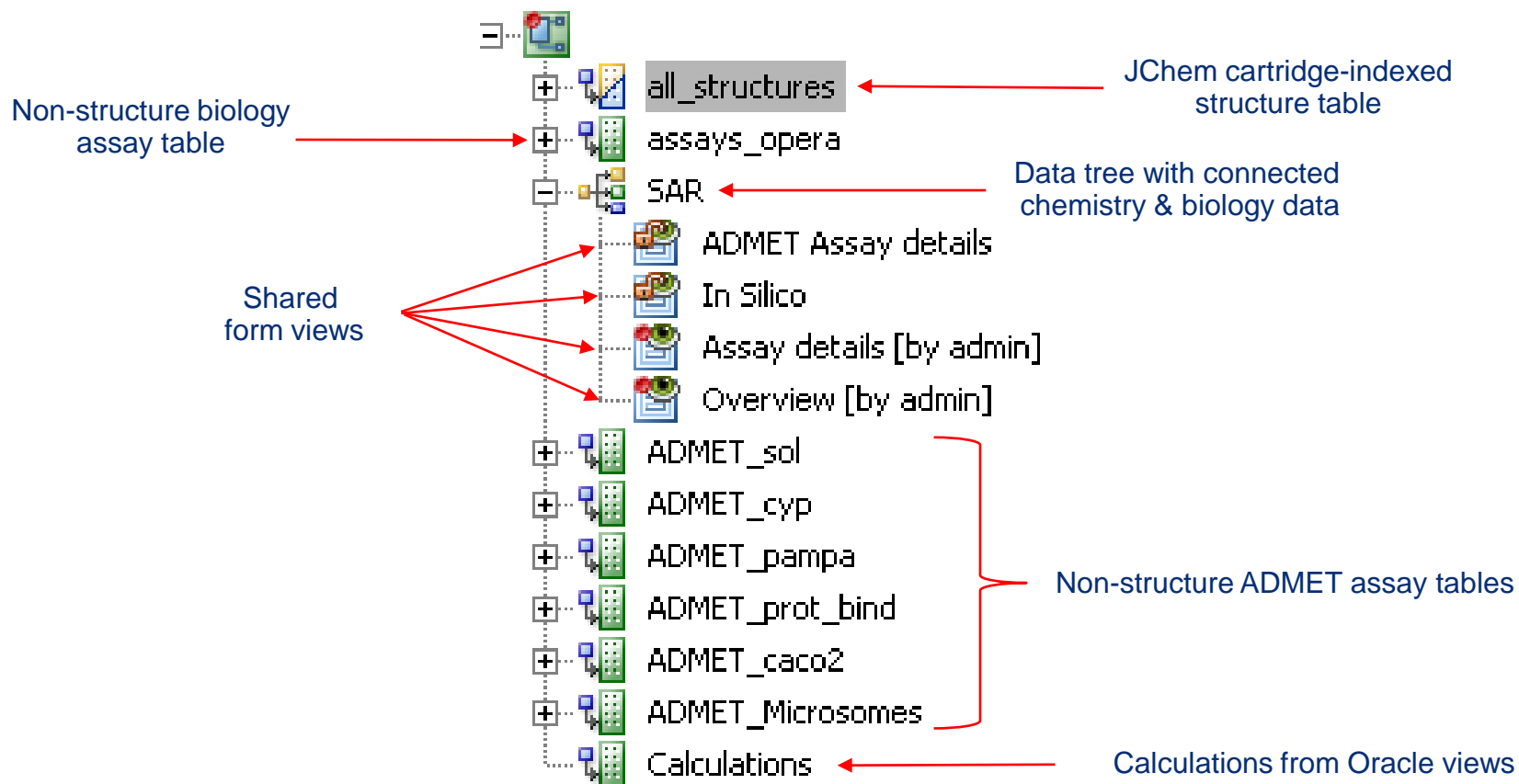


- SAR data tree contains joined chemistry & biology tables, allowing many assay results for each assay type per compound structure



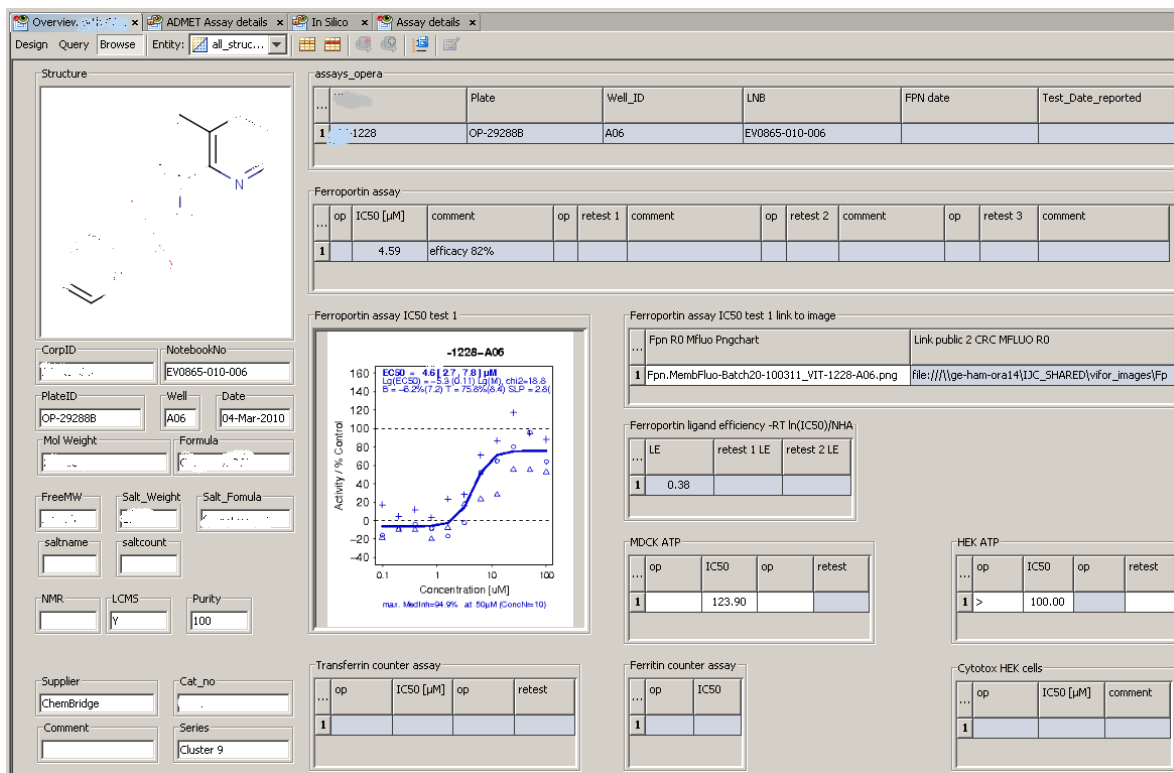
Data model

User view



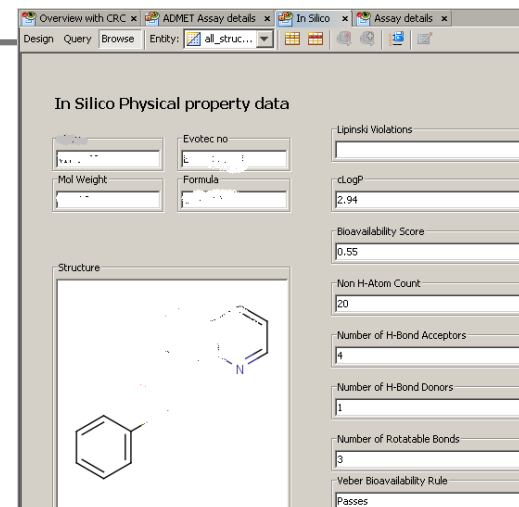
Data model

User view

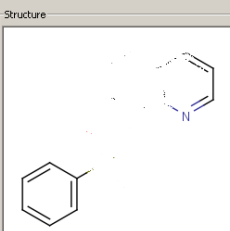


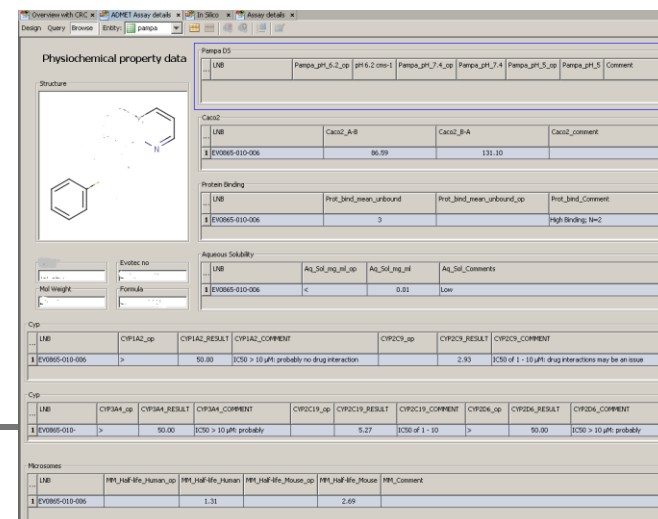
The screenshot displays a comprehensive user interface for data management. It includes a top navigation bar with tabs for 'Overview with CRC', 'ADMET Assay details', 'In Silico', and 'Assay details'. The main area is divided into several sections:

- Structure:** A 3D ball-and-stick model of a chemical structure.
- assays_opera:** A table listing assay operations with columns for Plate, Well_ID, LNB, FPN date, and Test_Date_reported.
- Ferroportin assay:** A table with columns for op, IC50 [µM], comment, and retest information.
- Ferroportin assay IC50 test 1:** A graph showing 'Activity / % Control' vs 'Concentration [µM]' with a fitted sigmoidal curve. Parameters include EC50 = 4.6 [2.7; 7.8] µM, SLP = -2.8, and others.
- Ferroportin assay IC50 test 1 link to image:** A table linking assay results to image files.
- Ferroportin ligand efficiency -RT ln(IC50)/NHA:** A table with columns for LE, retest 1 LE, and retest 2 LE.
- MDCK ATP:** A table with columns for op, IC50, and retest.
- HEK ATP:** A table with columns for op, IC50, and retest.
- Cytotox HEK cells:** A table with columns for op, IC50 [µM], and comment.
- Transferrin counter assay:** A table with columns for op, IC50 [µM], and retest.
- Ferritin counter assay:** A table with columns for op and IC50.
- Metadata:** Fields for CorpID, NotebookNo, PlateID, Well, Date, Mol Weight, Formula, FreeMW, Salt_Weight, Salt_Formula, saltname, saltcount, NMR, LCMS, Purity, Supplier, Cat_no, Comment, and Series.



This section displays 'In Silico Physical property data' for a molecule. It includes a 'Structure' view and a table of properties:

Evotec no		Lipinski Violations	
Mol Weight		cLogP	2.94
Formula		Bioavailability Score	0.55
Structure		Non H-Atom Count	20
		Number of H-Bond Acceptors	4
		Number of H-Bond Donors	1
		Number of Rotatable Bonds	3
		Veber Bioavailability Rule	Passes



This section displays 'Physicochemical property data' for a molecule, including a 'Structure' view and several data tables:

LNB	Pampr_pH_5_2_op	pH 6.2 cmo-1	Pampr_pH_7_4_op	Pampr_pH_7_4	Pampr_pH_5_op	Pampr_pH_5	Comment
1	EV0665-010-006	86.59	131.10				

LNB	Prot_Bind_mean_unbound	Prot_Bind_mean_unbound_op	Prot_Bind_Comment
1	EV0665-010-006	3	High Binding: H=2

LNB	Aq_Sol_mg_op	Aq_Sol_mg_op	Aq_Sol_Comments
1	EV0665-010-006	<	0.01 Low

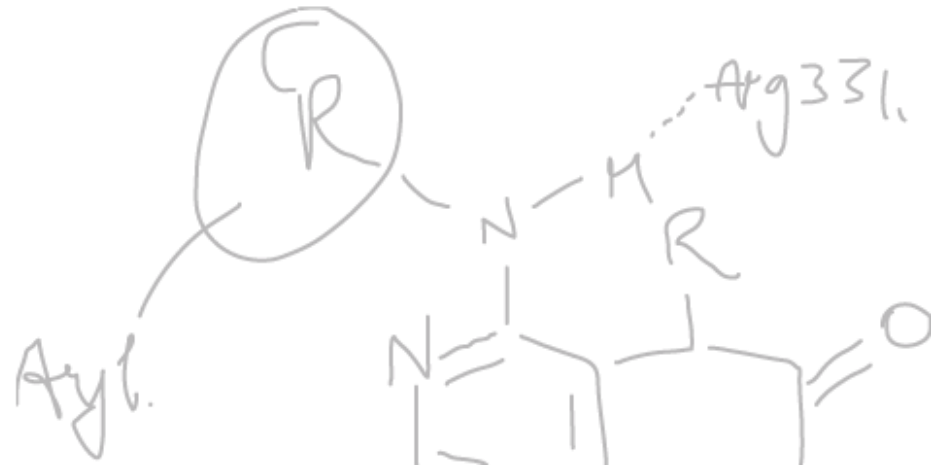
LNB	CYP3A4_op	CYP3A4_RESULT	CYP3A4_COMMENT	CYP3C_op	CYP3C_RESULT	CYP3C_COMMENT
1	EV0665-010-006	>	IC50 > 10 µM probably no drug interaction	2.93	IC50 of 1 - 10 µM drug interactions may be an issue	

LNB	CYP3A4_op	CYP3A4_RESULT	CYP3A4_COMMENT	CYP3C19_op	CYP3C19_RESULT	CYP3C19_COMMENT	CYP3D6_op	CYP3D6_RESULT	CYP3D6_COMMENT
1	EV0665-010-	>	IC50 > 10 µM probably	5.27	IC50 of 1 - 10	>	50.00	IC50 > 10 µM probably	

LNB	PP1_half-life_human_op	PP1_half-life_human	PP1_half-life_mouse_op	PP1_half-life_mouse	PP1_Comment
1	EV0665-010-006	1.31	2.69		

Agenda

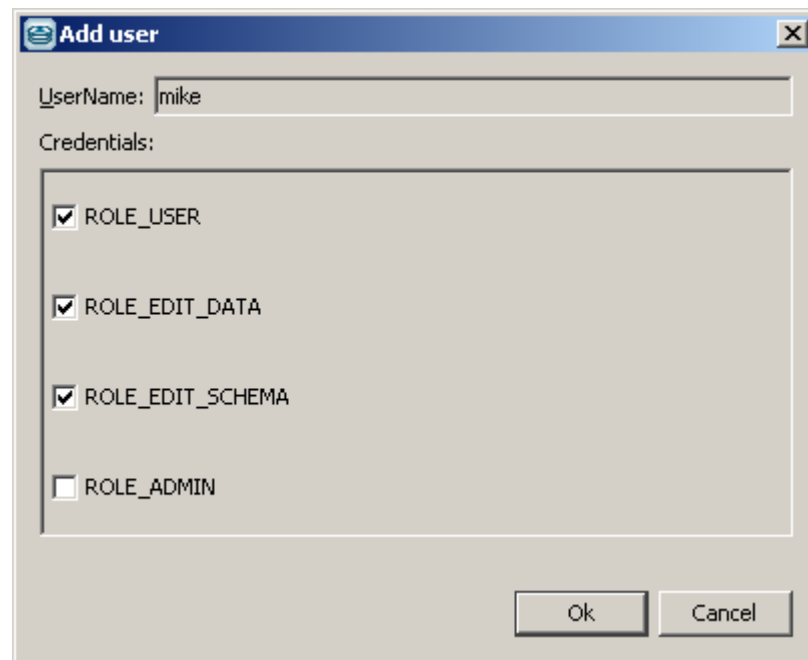
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User security

Typical IJC setup for a small drug discovery project

- 4 Scientists with Edit Data Role (2 in Abingdon & 2 in Hamburg)
- Updates made via SDfile (Edit Data Role) with auto mapping (SDfiles for loading formatted in the Evotec CCD)
- 14 Scientists with Read Only Role (ROLE USER) across Abingdon and Hamburg
- 2 Administrators (1 in Abingdon & 1 in Hamburg) with Edit Schema Role
- Built in Admin user used for rebuilding JChem tables after software updates & managing users and roles



Add user

UserName: mike

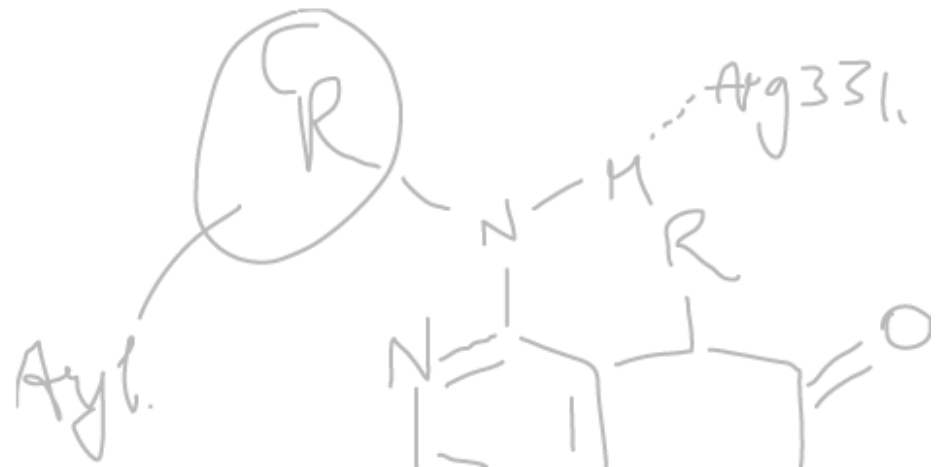
Credentials:

- ROLE_USER
- ROLE_EDIT_DATA
- ROLE_EDIT_SCHEMA
- ROLE_ADMIN

Ok Cancel

Agenda

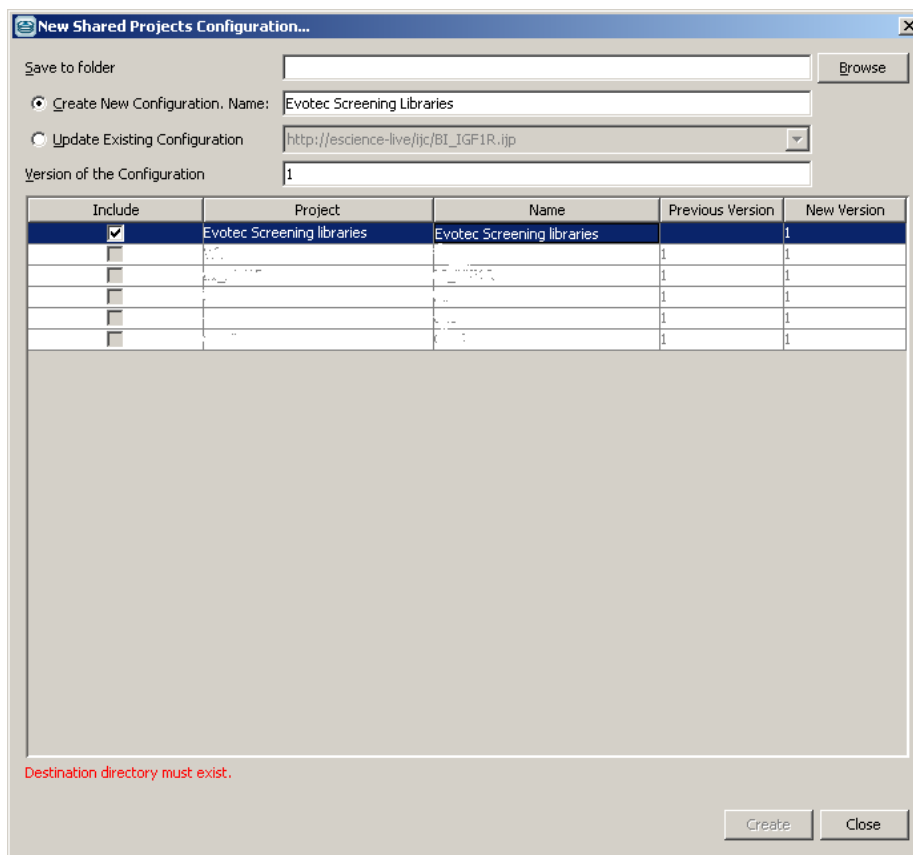
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Deployment

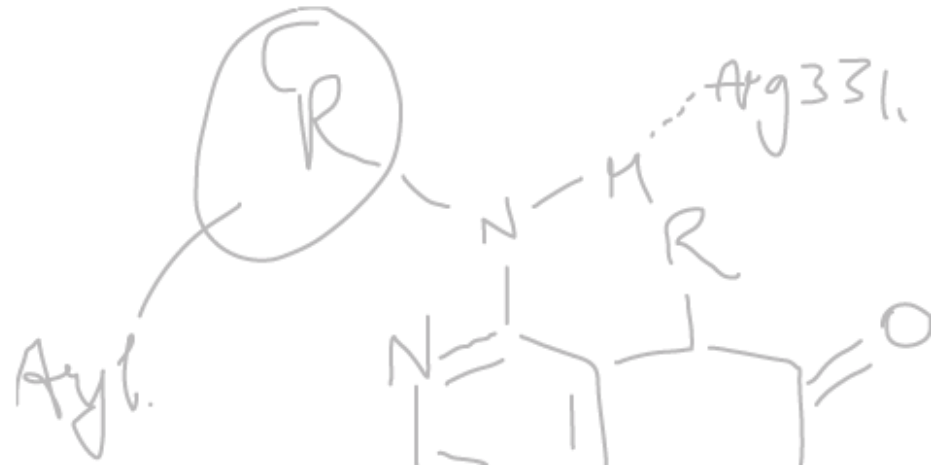
Via shared URLs

- Create users and roles & make all views you want to deploy shared
- Use Create Shared Projects wizard to generate new configuration files (.ijp and .zip files)
- Place configuration files on a web server: <http://escience/ijc/>
- Provide user account with initial password and URL e.g. <http://escience/ijc/project.ijp> to all of the users



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Integrating Oracle views

Useful for calculations across multiple tables

e.g. Ligand Efficiency of a compound = $RT \ln(IC50)/NHA$

Where:

R = molar gas constant = 0.0019859 kcal K⁻¹ mol⁻¹

T = Assay temperature in Kelvin = 273.15+37

IC50 in Molar units → Database field in **assays opera** table

NHA = Non-H atom count → Database field in **structure** table

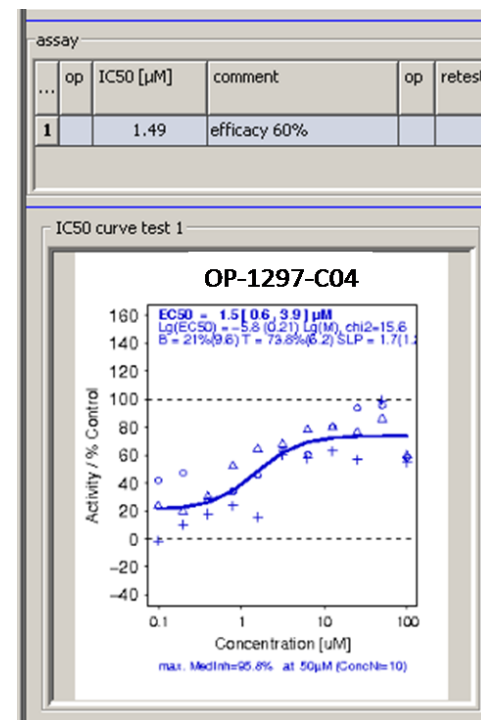
- Create or replace view Calculations as select **a.compound_id**, **b.IC50**, **a.NHA**, ... from **all_structures a**, **assays_opera b** where **a.compound_id = b.compound ID**
- Promote the Oracle view Calculations to a new entity in the IJC schema. Add relationships & data edges and integrate the Ligand Efficiency field into the IJC form for viewing and querying.

ligand efficiency -RT ln(IC50)/NHA			
...	LE	retest 1 LE	retest 2 LE
1	0.45	0.32	0.46

Integrating Oracle views

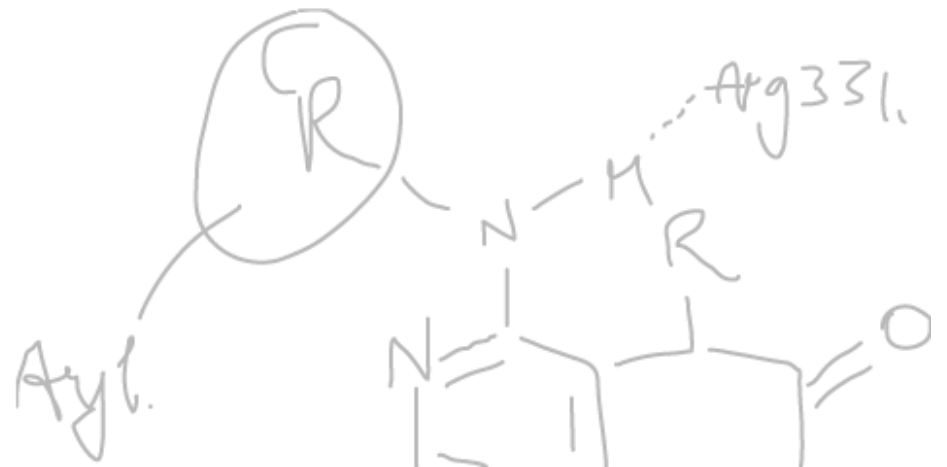
Useful for viewing Dynamic URLs when the related table needs to be updated

- Data imports into tables containing dynamic URL fields is not yet possible. A workaround is with Oracle views:
 - The data is updated in table A, e.g. IC50, ID's, Filename etc.
 - Create the Oracle view selecting the Compound ID & Filename
 - Promote the Oracle view to a new entity in the IJC schema -> table B
 - Define a dynamic link on table B, e.g. root path + table B.filename
 - Create a 1-1 relationship on tables A & B in IJC and incorporate into the data tree
 - Integrate the dynamic link into the IJC form
 - Can now do IJC imports into table A and get the dynamically linked images of concentration response curves from table B



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Conclusion

Overview and future

- IJC is providing Evotec a valuable resource for storing and sharing Chemistry and Biology data for our client projects
- We are using IJC as a replacement for ISIS/Base databases with positive feedback from the users
- We are still finding new uses for it!

Future Plans

- Integrate our own calculators & methods into Marvin / IJC
 - Integrate more ways of displaying results (graphing, etc.)
 - Implement user dependent permissions on viewing & editing entities would be nice
 - Improved ways of sharing IJC data with our clients
-

Thank yous

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