

Implementation of an Integrated Cheminformatics System at RTI: Fine Grained Security

Private Data Vaults(Lab)

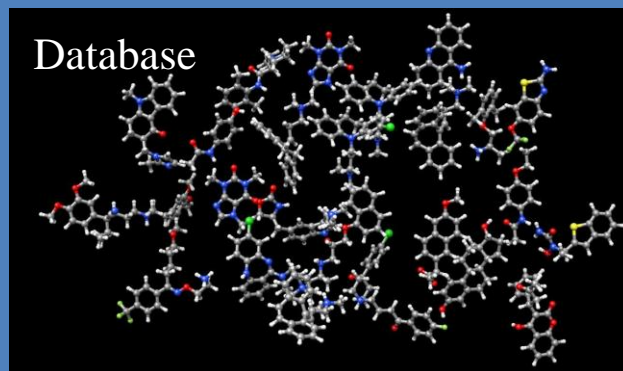
PostDoc-Entry

ChemAxon Properties Found in IJC.

Challenges

- Implementation of an Institutional compound registration system for mining 50-years of GPCR structural/synthetic-scheme/bioanalytical data against diverse targets.
- Import data from sources as diverse as IJC, Microsoft Filemaker PRO, Excel spreadsheets, and PAPER!
- Replace out of the box DeltaSoft access/permissions with fine-grained security based on roles in the institution, lab and collaboration status. Collaborator access must be based on project-level granularity.

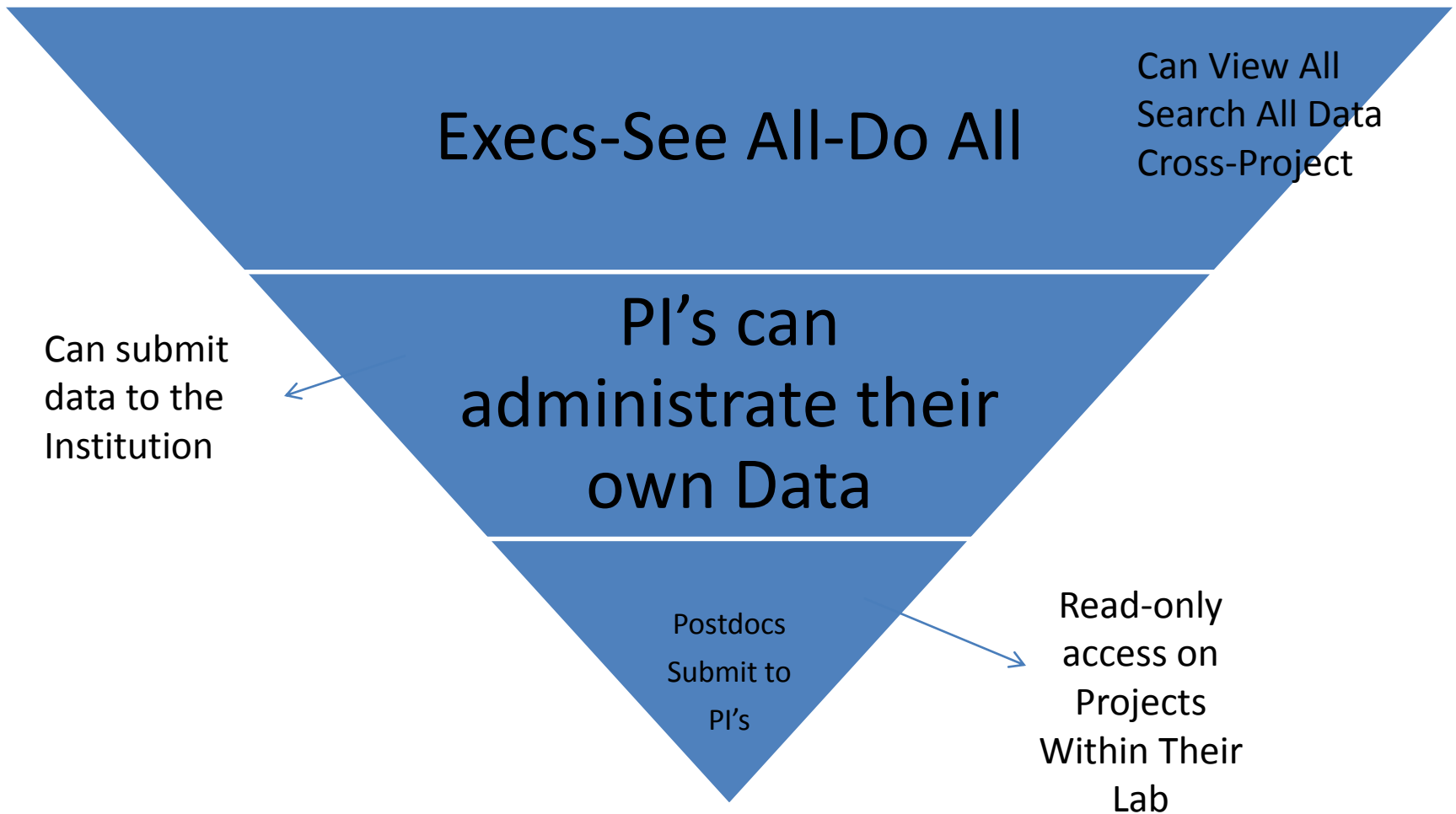
Before-customization....



Institutional Database

Prior to customization ---all your structural/ synthesis/ bioassay/analytical data would have been in ONE big 'pot' . All data seen by all employees. Violates CDA's with external clients and offer's insufficient protection for internal intellectual authorship and IP.

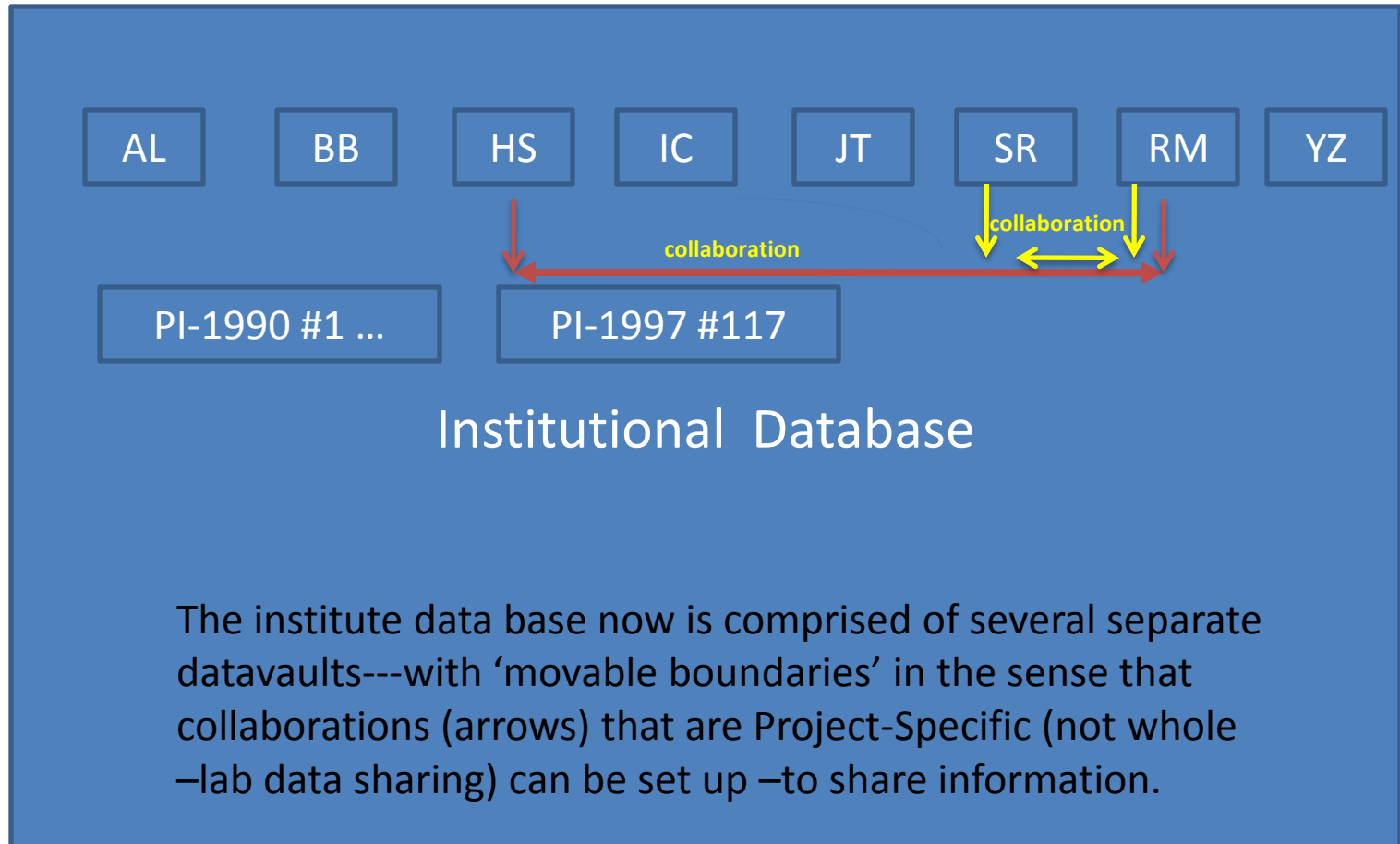
Role Based Permissions



Roles within Institution

- PostDocs/Students:
 - Allow viewing of data based on their lab membership
 - Allow them to input structural/bioanalytical/bioassay data for review by PI prior to committing data for compound registration and bioassay recording.
- PI's early on can act as lab-compound registrar to facilitate getting data in rapidly.
- PI's can see all data within their lab and data on shared projects.

After Customization: DataVaults



By Introducing a Views and Triggers we Customized Access to both View and Review Data

```
CREATE OR REPLACE TRIGGER chemreg_document_trg_upd before
update ON CHEMREG_DOCUMENTS referencing old as old new as new
for each row
begin

IF DBMS_SESSION.IS_ROLE_ENABLED ('chemreg_flag') THEN
    raise_application_error (-20001, 'User is not allowed to commit
the insert. ');
END IF;
```

```
CREATE OR REPLACE FORCE VIEW project_view_pi
AS
SELECT *
FROM chemregrti.project
WHERE UPPER (active) = 'Y'
AND project.pi_group IN (SELECT personnel.pi_group
FROM personnel
WHERE username = USER)
ORDER BY project_name;
```

Example of a Trigger-
Restricting Registration
to PI's or a Registrar
Based on Roles.

Example of a View-
Restricting Access to Shared
Data Based on Personnel
Listings in Project-
Collaboration Tables.



Chemreg_Admin

Update Mode

Personnel Administration

Person ID	Person Name	PI Group	Oracle Username	Active	Created By	Created Date
7	JAMES THOMAS	JT	JTHOMAS	Y	CHEMCART	24-Apr-2011
5	SCOTT RUNYON	SR	SRUNYON	Y	CHEMCART	24-Apr-2011
6	RANGAN (RONNIE) MAITRA	RM	RMAITRA	Y	CHEMCART	24-Apr-2011
8	ANITA LEWIN	AL	ALEWIN	Y	CHEMCART	24-Apr-2011
9	YANAN ZHANG	YZ	YZHANG	Y	CHEMCART	24-Apr-2011
10	BRUCE BLOUGH	BB	BBLOUGH	Y	CHEMCART	24-Apr-2011
11	H. SELTZMAN	HS	HSELTZMAN	Y	CHEMCART	24-Apr-2011
14	DANNI HARRIS	DH	DANNIHARRIS	Y	CHEMREG	13-Jun-2011
18	FLAG_BB	BB	FLAG_BB	Y	DANNIHARRIS	19-Jun-2011
20	FLAG_JT	JT	FLAG_JT	Y	DANNIHARRIS	19-Jun-2011
21	FLAG_RM	RM	FLAG_RM	Y	DANNIHARRIS	19-Jun-2011
1	TEST	TT	CHEMCART	Y	CHEMCART	10-Feb-2011
16	FLAG_IC	IC	FLAG_IC	Y	DANNIHARRIS	19-Jun-2011
4	IVY CARROLL	IC	ICARROLL	Y	CHEMCART	24-Apr-2011
17	FLAG_AL	AL	FLAG_AL	Y	DANNIHARRIS	19-Jun-2011
19	FLAG_HS	HS	FLAG_HS	Y	DANNIHARRIS	19-Jun-2011
22	FLAG_YZ	YZ	FLAG_YZ	Y	DANNIHARRIS	19-Jun-2011
13	CHEMREGPI	SR	CHEMREGPI	Y	CHEMREG	03-Jun-2011
15	FLAG_SR	SR	FLAG_SR	Y	DANNIHARRIS	19-Jun-2011

New: Access to your data is now determined by whether a listed user is recorded as being in your PI group.

NEW

A User in the group defined by your PI initials can view your data sets.

Or if they are PI collaborators and are listed with the same project number in the Project Administration Table- they can also update/insert or delete compounds and biodata.

ChemCart - COMPOUND_REGISTRATION_ADMIN - Windows Internet Explorer

http://10.172.10.48:8080/chemcart/chemcart.jsp?app=COMPOUND_REGISTRATION_ADMIN&datasource=default

File Edit Form List Search Sort Pivot Update Tools Options Help

Hit List: 1 of 1 (ADMIN)
Selected: 22 of 25 (PROJECT)
Searching: All

Project Administration

Project ID	Project Name	PI Group	Active	Created By	Created Date
35	165096.001	RM	Y	DANNIHARRIS	21-Jun-2011
25	165096.001	SR	Y	CHEMREG	03-Jun-2011
18	165112	YZ	Y	CHEMCART	24-Apr-2011
4	207568	IC	Y	CHEMCART	24-Apr-2011
19	207690	BB	Y	CHEMCART	24-Apr-2011
15	209702	AL	Y	CHEMCART	24-Apr-2011
6	209736	IC	Y	CHEMCART	24-Apr-2011
12	210941	RM	Y	CHEMCART	24-Apr-2011
22	211435	HS	Y	CHEMCART	24-Apr-2011
5	211882	IC	Y	CHEMCART	24-Apr-2011
21	212099	HS	Y	CHEMCART	24-Apr-2011
17	212156	YZ	Y	CHEMCART	24-Apr-2011
13	212174	RM	Y	CHEMCART	24-Apr-2011
3	212251	IC	Y	CHEMCART	24-Apr-2011
23	212455	HS	Y	CHEMCART	24-Apr-2011
7	212654	SR	Y	CHEMCART	24-Apr-2011
11	212661	RM	Y	CHEMCART	24-Apr-2011
26	212661	HS	Y	CHEMREG	03-Jun-2011
9	271100.068	SR	Y	CHEMCART	24-Apr-2011

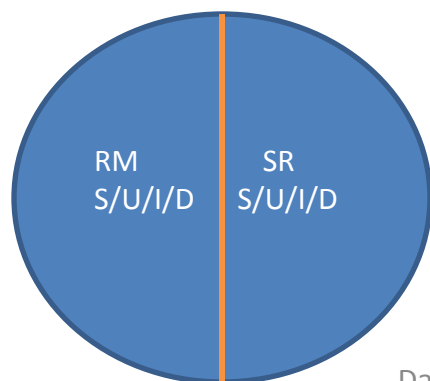
Scott and Bonnie are collaborating on Apelin project as co-PI's Therefore they both

Different Privileges....for Collaborations of different types

- Example: Either Scott and Ronnie, with the same Project # for Apelin---could have the same Privileges on the Apelin Project if I enter the PROJECT NO with both their Initials on the PI/GROUP column –then they both have Insert/Update/Select/Delete privileges on the Project/Compound/Bioassay Registrations.
- or, Ronnie as a collaborator could just be granted an overriding PI Role and Scott might have collaborator privileges analogous to the privileges accorded PostDocs (i.e. can select/read but not insert/update/delete a record on the project).

TYPE I

Collaborators as “Co-PI”

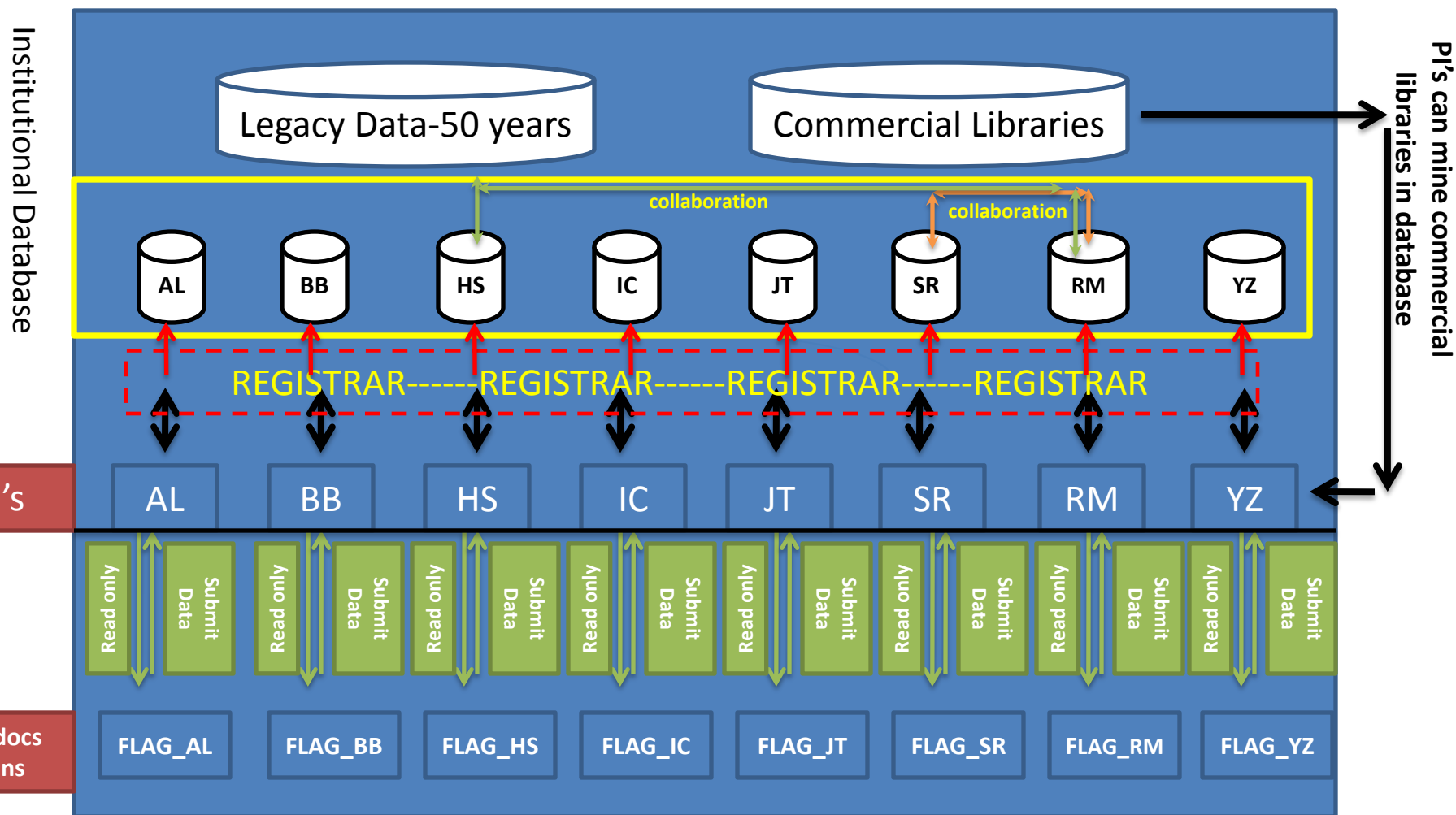


TYPE II

Collaborators PI and co-investigator

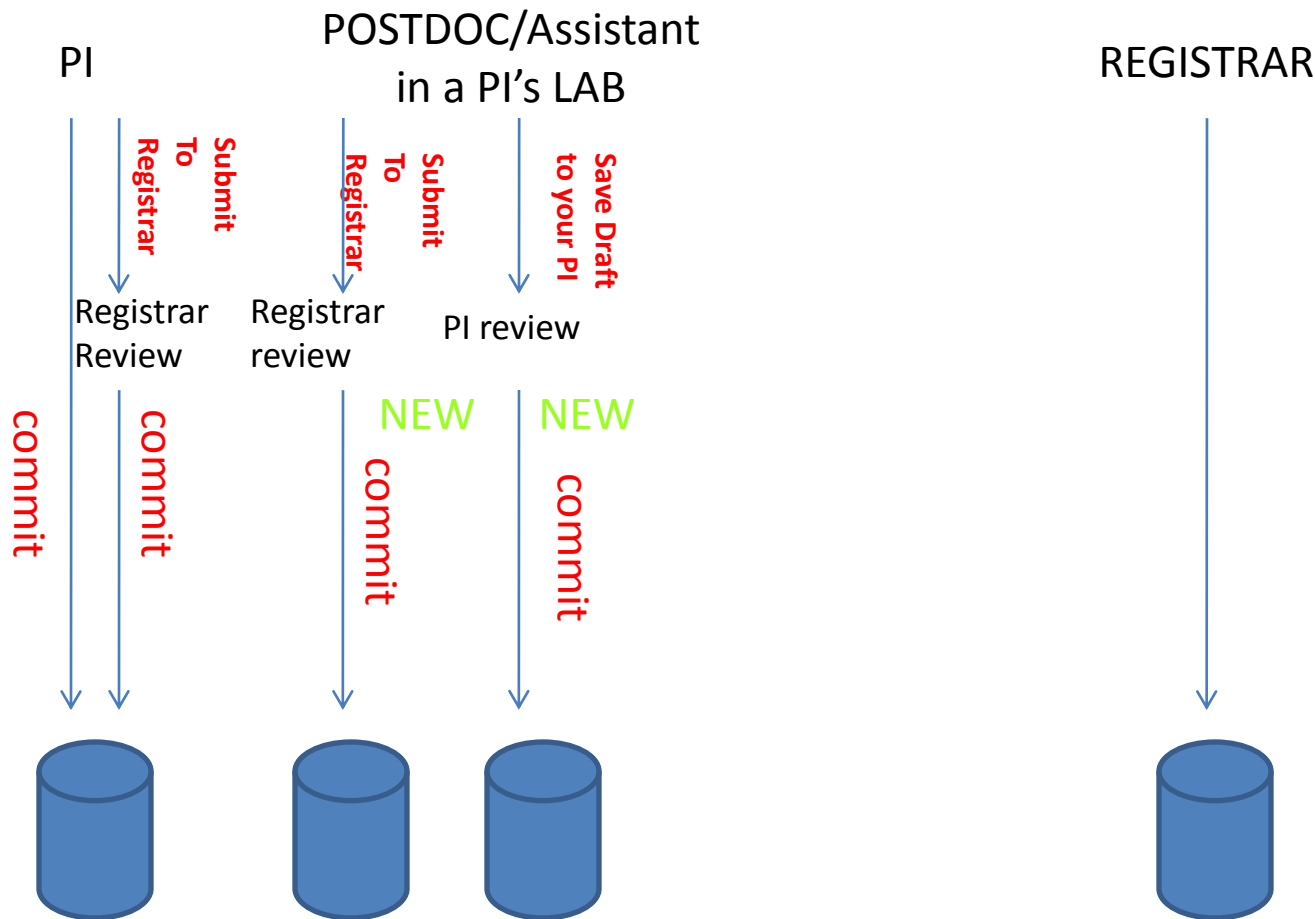


Or the PI or PostDoc/Admin will submit to a Registrar who determines whether minimum criteria for registration have been met and then commits the compound data to the PI's datavault



Current (revised-ChemCart) paths to compound registration.

SUBMITTER
ROLE:



POST-REGISTRATION CORRECTIONS

POST-REGISTRATION CORRECTIONS

ChemAxon Properties

- Marvin Applets
- Marvin Beans
- JChemBase
- JChemCartridge
- Standardizer
- Structure Search
- Partitioning Plugin Group(log P/logD)
- Refractivity Plugin
- HBDA Plugin(Donor/Acceptor)
- Structure to Name Plugin
- Protonation(pKa/Microspecies)
- Geometry
- Name to Structure

Within Marvin.... You can evaluate many other details from within ChemCart

The screenshot displays the ChemCart software interface within a Windows Internet Explorer browser. The main window shows a 'logD Options' dialog box on the left, a 'Sketcher' window in the center, and a 'logD' data window on the right. The 'logD Options' dialog includes sections for 'General Options', 'Method weights', 'Electrolyte concentration', and 'pKa correction library'. The 'Sketcher' window shows the chemical structure of pyridin-2-ylideneacetic acid. The 'logD' window displays a table of pH vs logD values and a corresponding plot.

logD Options Dialog:

- logP method: VG, KLOP, PHYS, User defined, Weighted
- logP training ID: [dropdown]
- Method weights: VG: 1, KLOP: 1, PHYS: 1, User defined: 0
- Electrolyte concentration: Cl⁻ concentration (mol/dm³): 0.1, Na⁺ K⁺ concentration (mol/dm³): 0.1
- pKa correction library: Use pKa correction library, pKa correction library: [dropdown]
- Consider tautomerization

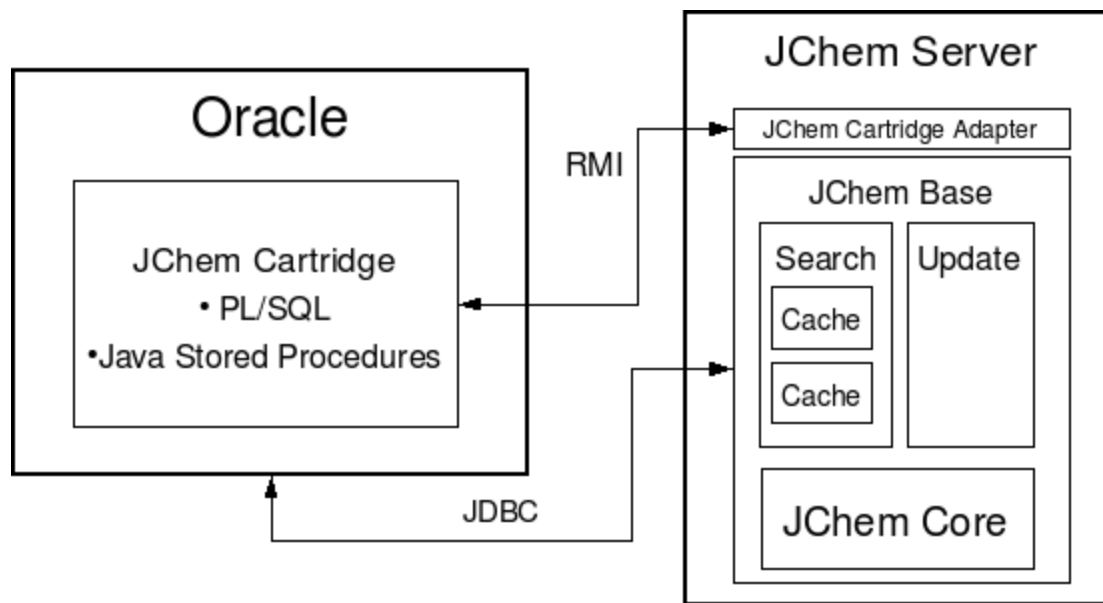
logD Data Table:

pH	logD
0.00	0.71
0.50	0.71
1.00	0.71
1.50	0.71
2.00	0.70
2.50	0.68
3.00	0.61
3.50	0.44
4.00	0.15
4.50	-0.26
5.00	-0.73
5.50	-1.21
6.00	-1.68
6.50	-2.12
7.00	-2.46
7.50	-2.67
8.00	-2.77
8.50	-2.80
9.00	-2.81
9.50	-2.82
10.00	-2.82

logD vs pH Plot:

The plot shows logD on the y-axis (ranging from -2.82 to 0.71) versus pH on the x-axis (ranging from 0.0 to 11.0). The curve starts at a logD of approximately 0.71 at pH 0 and remains relatively constant until pH 4, then drops sharply to a logD of approximately -2.82 at pH 10.

Rapid Retrieval of ChemAxon Informatic Properties via SQL Calls.



<http://www.chemaxon.com/jchem/doc/dev/cartridge/>

Adding Chemical Knowledge to Products Based on the Oracle Platform.

- “JChem Cartridge” adds chemical information to the database. You can search data by structure, substructure and similarity through extensions to Oracle's native SQL language. Chemical data can be easily inserted and modified using SQL procedures of the JChem Cartridge. “

Simple Calls within the API Retrieve Licensed Properties.

```
• FUNCTION GET_SMILES(orig Blob) return Varchar2 is vName Varchar2(4000);  
• tmpBlob Blob;  
• emptyBlob Blob;  
• Begin  
•  
• tmpBlob:=jcf.molconvertb(orig,'SMILES',emptyBlob);  
• vName:=utl_raw.CAST_TO_VARCHAR2(tmpBlob);  
• return (vName);  
• EXCEPTION  
• WHEN OTHERS THEN  
• vName:=null;  
• RETURN(vName);  
• End;  
• FUNCTION GET_INCHI(orig Blob) return Varchar2 is vName Varchar2(4000);  
• tmpBlob Blob;  
• emptyBlob Blob;  
• Begin  
•  
• tmpBlob:=jcf.molconvertb(orig,'INCHI:AuxNone',emptyBlob); -- without AuxInfo  
• -- tmpBlob:=jcf.molconvertb(orig,'INCHI',emptyBlob); with AuxInfo  
• vName:=utl_raw.CAST_TO_VARCHAR2(tmpBlob);  
• return (vName);  
• EXCEPTION  
• WHEN OTHERS THEN  
• vName:=null;  
• RETURN(vName);  
• End;  
• FUNCTION GET_INCHIKEY(orig Blob) return Varchar2 is vName Varchar2(4000);  
• tmpBlob Blob;  
• emptyBlob Blob;  
• Begin  
•  
• tmpBlob:=jcf.molconvertb(orig,'INCHIKEY',emptyBlob);  
• vName:=utl_raw.CAST_TO_VARCHAR2(tmpBlob);  
• return (vName);  
• EXCEPTION  
• WHEN OTHERS THEN  
• vName:=null;  
• RETURN(vName);  
• End;
```

Cartridge API

[jc_evaluate](#) (logp, logd, psa, acceptorCount, donorCount, charge, etc.)

Upon Registration(properties)

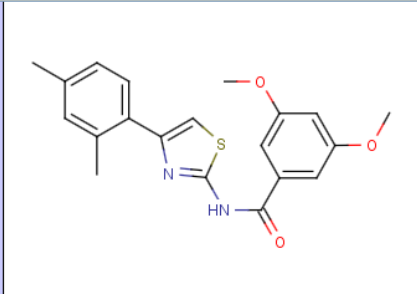
ChemCart - COMPOUND_REGISTRATION_PI - Windows Internet Explorer

http://10.172.10.48:8080/chemcart/chemcart.jsp?app=COMPOUND_REGISTRATION_PI&datasource=default

File Edit Form List Search Sort Pivot Update Tools Options Help


Hit List: 2 of 5974 (CHEMREG_COMPOUND_V)
Selected: 2 of 5974 (CHEMREG_COMPOUND_V)
Searching: All

Chemreg



New Compound **New Batch**

Open Draft Manager to Submit to DRAFT_XX



Compound Registration

SORT

Accession #		Therapeutic Target	DLH-Libraries
Corp ID	RTI-1000424	Project	DH-IN-DEV-001
Reg. No.	1000424	Solvate	
Batch ID	RTI-1000424-0-1	Solubility	
Mol Formula	C ₂₀ H ₂₀ N ₂ O ₃ S	Purity	
Batch Formula	C ₂₀ H ₂₀ N ₂ O ₃ S	Purification Method	
Mol Weight	368.45	Melting Point (°C)	
MW w Salt/Solvate	368.45	Boiling Point (°C)	
Exact Mass	368.12	Library	LIFECHGPCR
Reg Date	17-Aug-2011	External Source	
Reg By	DANNIHARRIS	External Reg. #	F0007-0756

Salt Form	No Salt	#	
Solvate Form	No Solvate	#	
Notebook Ref	NA		
Amount Submitted		Units	
Submitter	DANNI HARRIS		
Stereochemistry			
Appearance			

Reference	
Chemical Name	
Comments	

ChemSpider ID		# Donors (pH=7.4)	1	TPSA	60.45	ClarkBBModel	
PubChem ID		# Acceptors	4	InChI Key	DXYJFCKJAAA00-UHFFFAOYSA-N		9.25
CAS (Structure)		LogP	5.15				
CAS (Salt)		Log D (pH=7.4)	5.15				

InChI	1S/C20H20N2O3S/c1-12-5-6-17(13(2)7-12)18-11-26-20(21-18)22-19(23)14-8-15(24-3)10-16(9-14)25-4/h5-11H,1-4H3,(H,21,22,23)
SMILES	COC1=CC(=CC(OC)=C1)C(=O)NC1=NC(=CS1)C1=CC=C(C)C=C1C
IUPAC Name	N-[4-(2,4-dimethylphenyl)-1,3-thiazol-2-yl]-3,5-dimethoxybenzamide
IUPAC (Trad)	N-[4-(2,4-dimethylphenyl)-1,3-thiazol-2-yl]-3,5-dimethoxybenzamide

Compound Batch Sample Images Documents

Done

'Program' other metrics based on ChemAxon Properties: e.g. Clark BB Model.

The screenshot shows a web browser window titled 'ChemCart - COMPOUND_REGISTRATION_PI' with a URL of `http://10.172.10.48:8080/chemcart/chemcart.jsp?app=COMPOUND_REGISTRATION_PI&datasource=default`. The browser's address bar and menu bar are visible. Below the browser, a table titled 'Chemreg' is displayed. The table has columns for various chemical and registration properties. A dialog box titled 'Edit Box Properties' is open over the table, showing a list of fields and their corresponding dynamic field expressions. The 'ClarkBBModel' field is selected, and its properties are shown in the right pane of the dialog.

Dynamic Field Expression	Display Name
<input checked="" type="checkbox"/> $=(0.152 * \text{Tpsa}) - (0.0148 * \text{Logp}) + 0.139$	ClarkBBModel
<input type="checkbox"/>	

The 'Edit Box Properties' dialog box shows the following properties for the selected field:

Label	
Content	ClarkBBModel
Font	Arial, bold, 12
Foreground	Blue
Background	White
Alignment	TOP_LEFT
Tooltip	

Data	
Font	Arial, plain, 12
Foreground	Black
Background	White
Conditional Format	No rules defined
Alignment	BOTTOM
Line Format	Display on single line
Is Data HTML	False
Scrolling	If Needed
Precision	2
Helper Program	<none>

Element	
Border Width	1
Border Color	Black
Tab Order	10000
Tag	

Case Studies GPCR Targets (cross correlations from recently deorphanized receptors)

Institute-wide(50 year depth)

chemcart_user_guide.pdf - Adobe Reader

File Edit View Document Tools Window Help

151 / 253 173%

Find

PIVOTING

Pivot Result Window

Pivot Result

CORPID	LNS CELL First	LNS NLOGLC50 Ave	COL CELL First	COL NLOGLC50 Ave	OVA CELL First	OVA NLOGLC50 Ave	LEU CELL First	LEU NLOGLC50 Ave	REN CELL First	REN NLOGLC50 Ave	MEL CELL First	MEL NLOGLC50 Ave
DS-001145	NCI-H23	6.95	HT29	6.80	OVCAR-3	6.39	P388	5.81	UO-31	6.70	LOXIMVI	7.18
DS-000907	NCI-H23	5.14	HT29	5.16	OVCAR-3	5.23	CCRF-CEM	4.06	UO-31	5.21	LOXIMVI	5.14
DS-000932	NCI-H23	5.11	HT29	5.14	OVCAR-3	5.05	CCRF-CEM	4.02	UO-31	5.08	LOXIMVI	5.20
DS-000131	NCI-H23	5.09	HT29	5.04	OVCAR-3	5.10	CCRF-CEM	5.00	UO-31	5.22	MALME-3M	5.31
DS-000450	NCI-H23	5.08	HT29	5.04	OVCAR-3	5.15	CCRF-CEM	4.44	UO-31	5.21	LOXIMVI	4.88
DS-000850	NCI-H23	5.00	HT29	5.00	OVCAR-3	5.00	CCRF-CEM	5.00	UO-31	5.00	LOXIMVI	5.00
DS-001146	NCI-H23	4.91	HT29	5.03	OVCAR-3	4.67	P388	4.28	UO-31	4.87	LOXIMVI	5.15
DS-000466	NCI-H23	4.89	HT29	4.84	OVCAR-3	4.55	CCRF-CEM	4.10	UO-31	4.69	LOXIMVI	5.22
DS-000315	NCI-H23	4.79	HCT-15	5.00	OVCAR-3	4.75	CCRF-CEM	4.05	UO-31	4.57	LOXIMVI	4.65
DS-000424	EKVX	4.79	HCC-2998	5.42	OVCAR-3	5.23	K-562	4.28	UO-31	5.18	MALME-3M	5.06
DS-000417	NCI-H23	4.74	HT29	4.99	OVCAR-3	4.55	CCRF-CEM	5.14	UO-31	4.98	LOXIMVI	5.02
DS-000121	NCI-H23	4.59	HT29	4.64	SK-OV-3	4.30	CCRF-CEM	4.06	UO-31	4.42	LOXIMVI	4.70
DS-000406	NCI-H23	4.55	HT29	4.50	OVCAR-3	4.50	CCRF-CEM	4.50	UO-31	4.72	SK-MEL-28	4.48
DS-000202	NCI-H23	4.39	HT29	4.51	OVCAR-3	4.10	CCRF-CEM	4.05	UO-31	4.44	LOXIMVI	5.07
DS-000902	NCI-H23	4.32	HT29	4.50	OVCAR-3	4.31	CCRF-CEM	4.94	UO-31	4.36	LOXIMVI	4.45
DS-000676	A549(ATCC)	4.28	HT29	4.55	OVCAR-3	4.26	CCRF-CEM	4.52	UO-31	4.38	LOXIMVI	4.56
DS-000130	NCI-H23	4.28	HT29	4.27	OVCAR-3	4.27	CCRF-CEM	4.00	UO-31	4.32	LOXIMVI	4.46
DS-000425	NCI-H23	4.25	HT29	4.59	OVCAR-3	4.18	CCRF-CEM	4.15	A498	4.21	MALME-3M	4.34
DS-000505	NCI-H23	4.25	HT29	4.27	OVCAR-3	4.27	CCRF-CEM	4.05	SN12C	4.18	LOXIMVI	4.25
DS-000506	NCI-H23	4.24	HT29	4.24	OVCAR-3	4.21	CCRF-CEM	4.01	UO-31	4.25	LOXIMVI	4.22
DS-000408	NCI-H23	4.23	HT29	4.35	OVCAR-3	4.07	CCRF-CEM	4.26	UO-31	4.30	LOXIMVI	4.87
DS-000531	NCI-H23	4.22	HT29	4.00	OVCAR-3	4.33	CCRF-CEM	4.00	UO-31	4.45	MALME-3M	4.00
DS-000139	NCI-H23	4.21	HCC-2998	4.26	OVCAR-3	4.20	CCRF-CEM	4.21	UO-31	4.13	MALME-3M	4.35
DS-000864	NCI-H23	4.20	HT29	4.28	OVCAR-3	4.38	CCRF-CEM	4.00	UO-31	4.19	MALME-3M	4.31
DS-000140	NCI-H23	4.18	HT29	4.41	OVCAR-3	4.16	CCRF-CEM	4.00	UO-31	4.08	LOXIMVI	4.42
DS-000432	NCI-H23	4.17	HT29	4.16	OVCAR-3	4.07	CCRF-CEM	4.03	UO-31	4.13	LOXIMVI	4.24
DS-001144	NCI-H522	4.16	HCC-2998	4.15	OVCAR-3	4.14	CCRF-CEM	4.00	UO-31	4.17	LOXIMVI	4.49
DS-000415	NCI-H23	4.15	HT29	4.20	OVCAR-3	4.12	CCRF-CEM	4.16	SN12C	4.12	LOXIMVI	4.23

Print Edit This Pivot Close

Summary

- ChemCart has now been revised to:
 - Give Lab-Privacy over their data-vaults.
 - Access permission to lab data based on PI-group membership or 'stated' collaborations.
 - Collaborations can be many flavors(co-equal edit or one or more 'read-only').
 - PostDoc/Admin role's have been generated and their permissions limited to read-only and submit data to PI or Registrar.
 - ChemAxon properties are now available in ChemCart-some are autopopulated upon compound registration-more may be added to PI customized forms.
 - Fast Import Option of IJC SDF files.
- Facile Cross Target Searches Across Lab/Target/Chemical Space.

