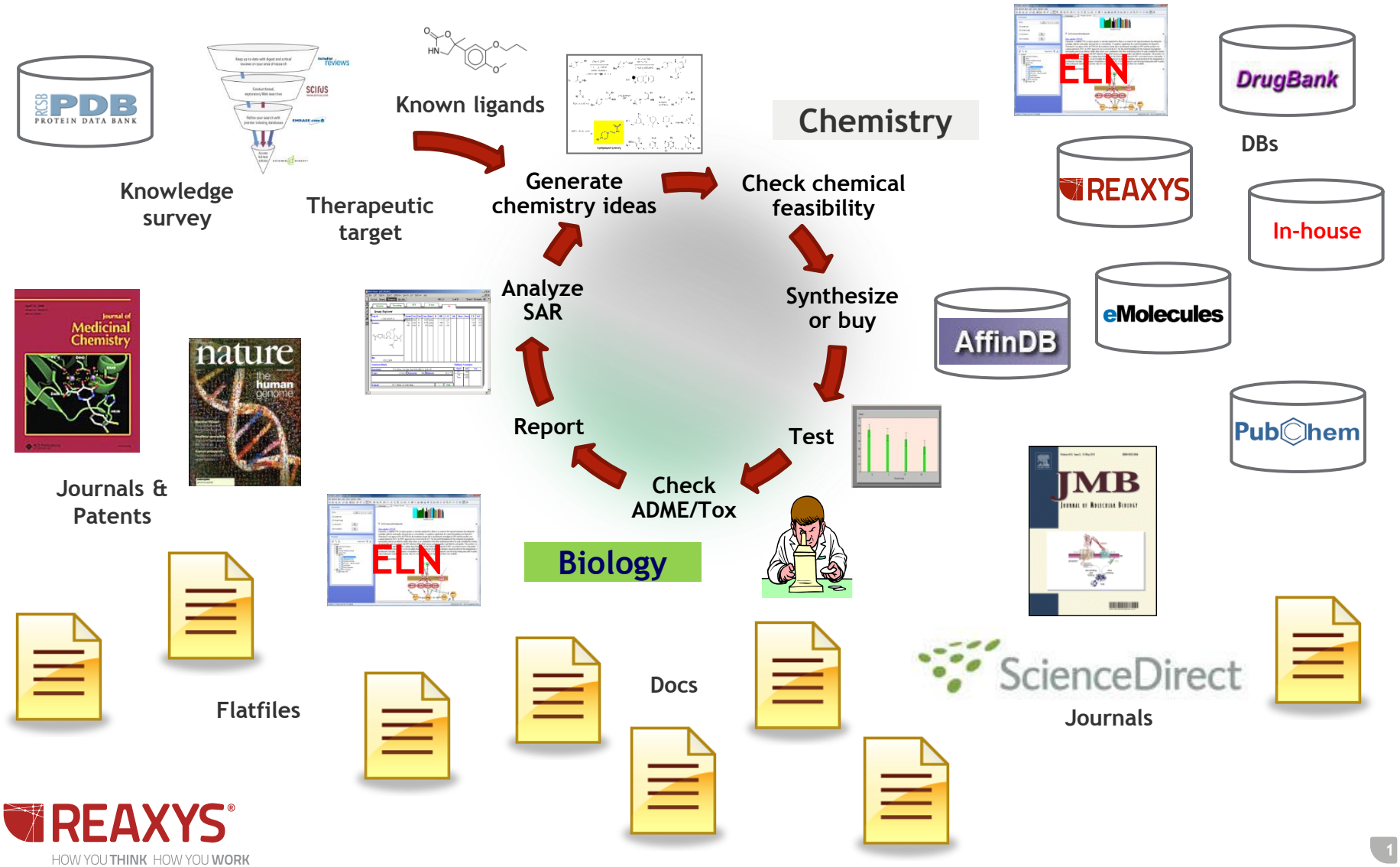
DRUG DISCOVERY TODAY



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Dr. Sebastian Radestock
Product Manager Reaxys

Elsevier Information Systems GmbH

Frankfurt am Main
Germany

MAKING HIDDEN DATA DISCOVERABLE:

HOW TO BUILD EFFECTIVE DRUG DISCOVERY ENGINES?

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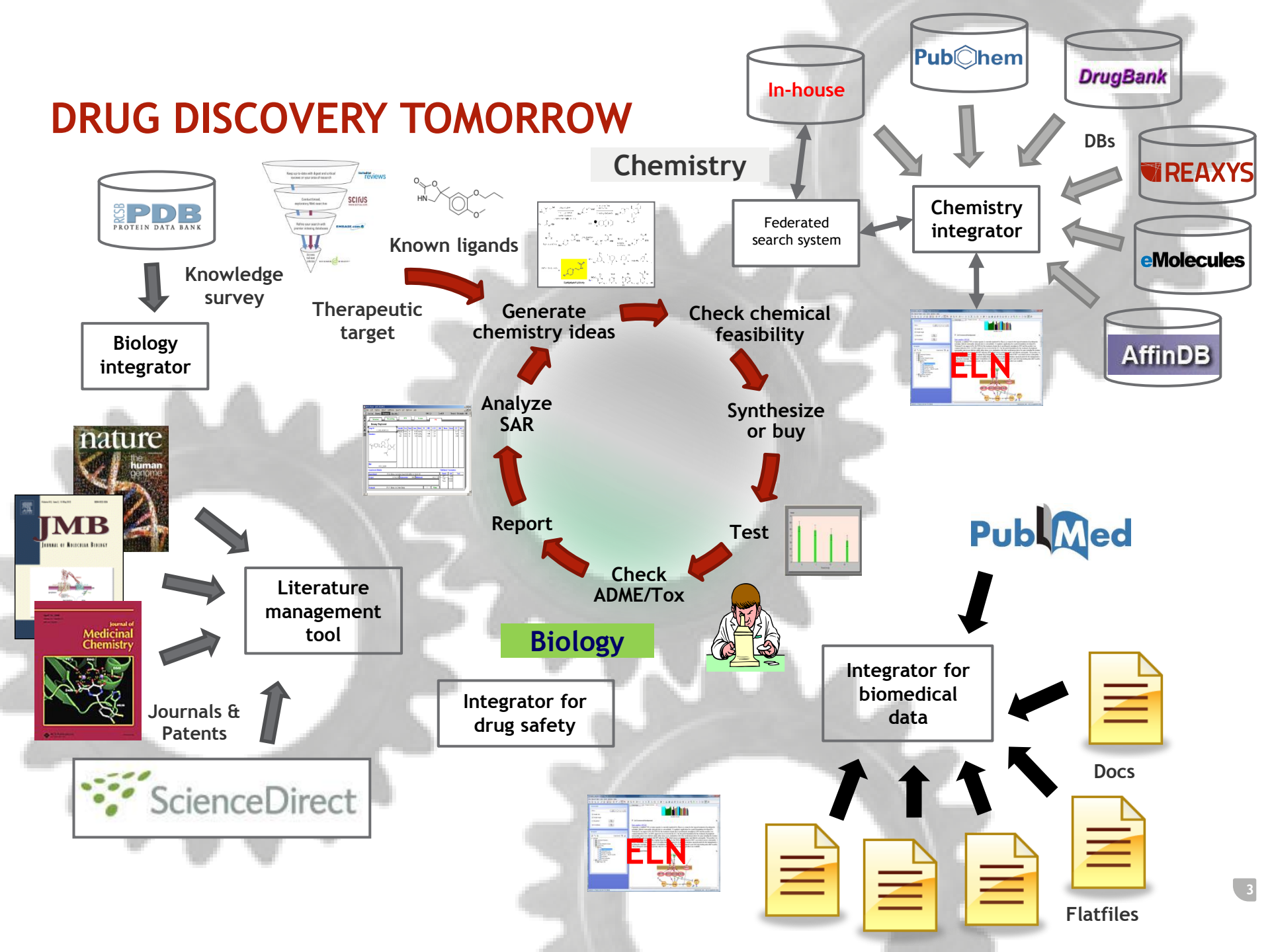
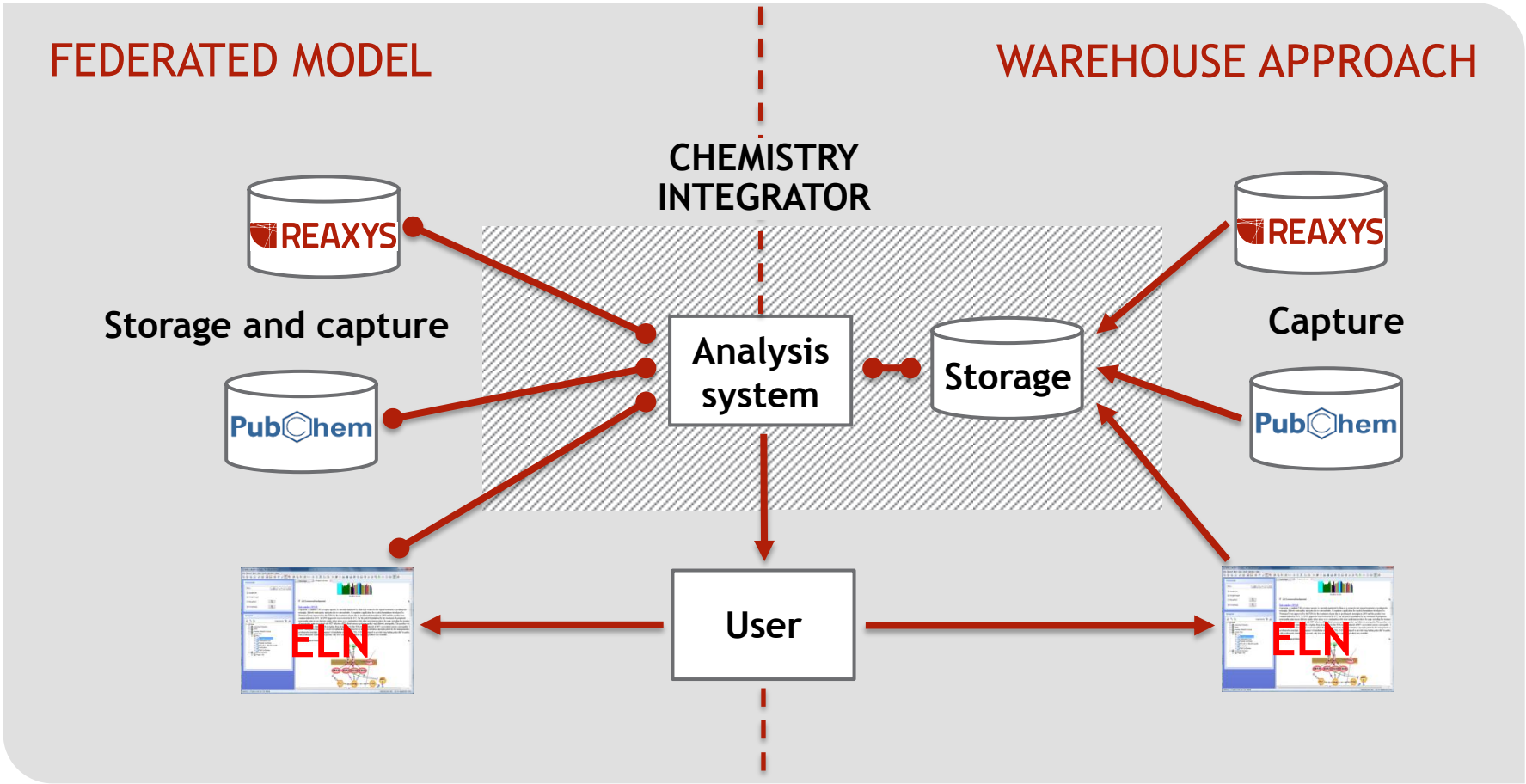
DRUG DISCOVERY TOMORROW

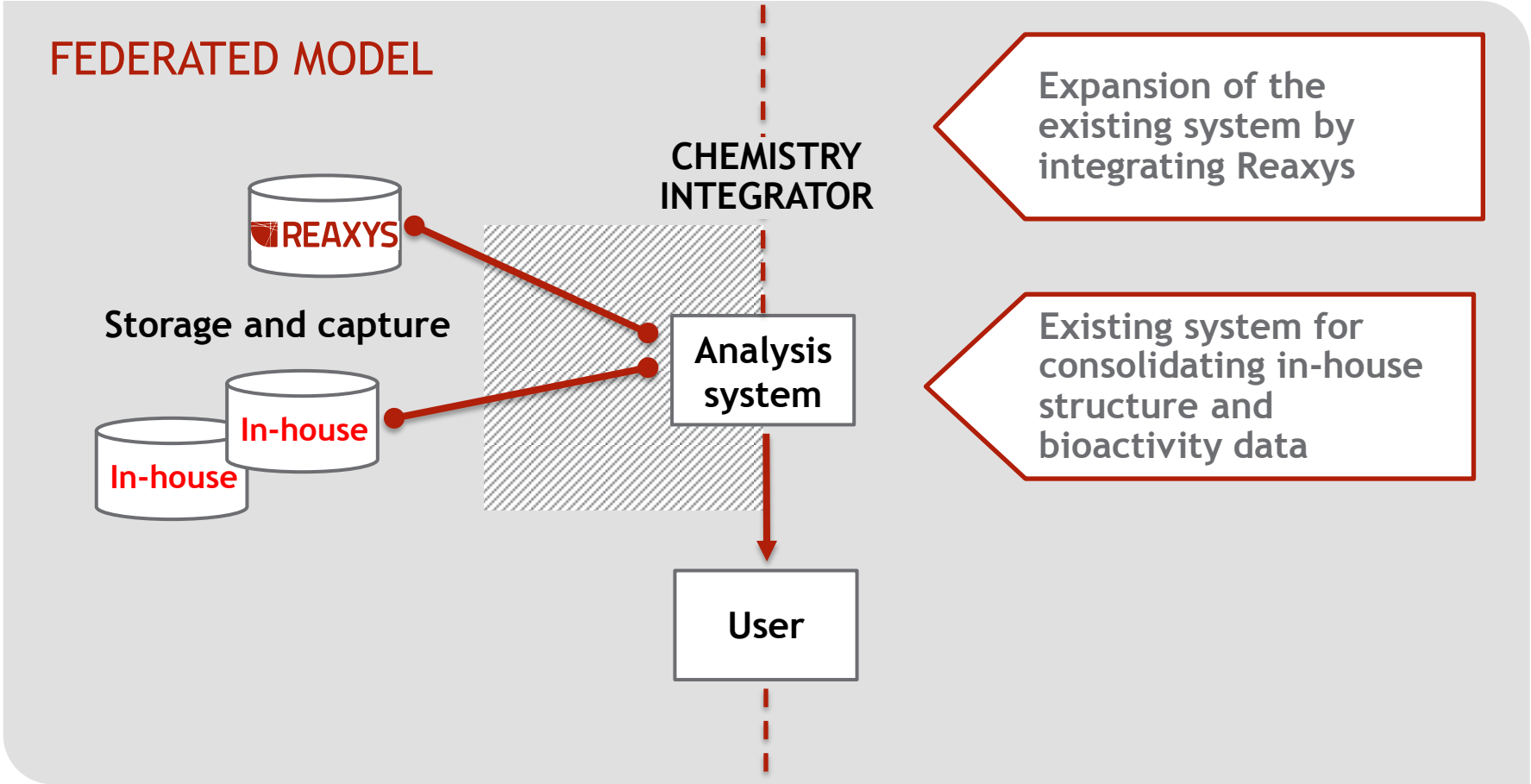


DRUG DISCOVERY TOMORROW

TWO APPROACHES TO SOLVING THE CHALLENGE OF DATA ACCESS



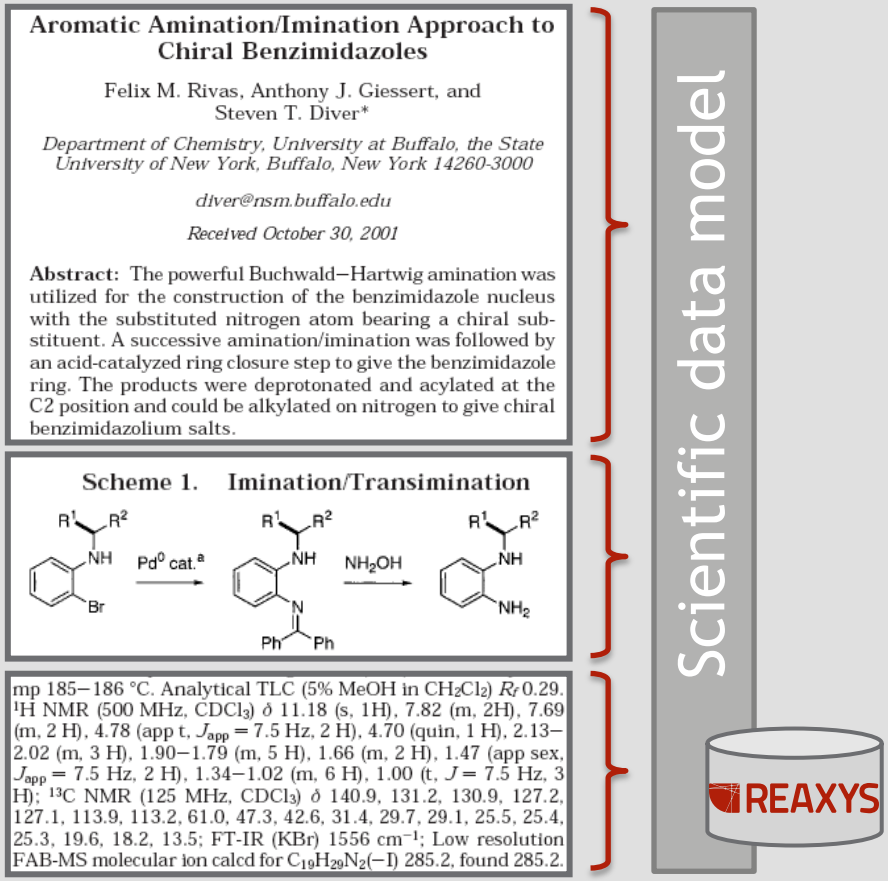
EXAMPLE IMPLEMENTATION OF THE FEDERATED MODEL



THE REAXYS DATA BASE

CONTAINS ALL PUBLISHED AND HISTORICAL CHEMISTRY DATA

- Compounds, substance property data, preparations, reactions, and bibliographic information…
  …from 400 core chemistry journals
  …from relevant chemistry patents
- Manual extraction of all the data
- Coverage of 500 property data fields, from basics like boiling point or melting point, via crystal data and magnetic properties, to spectra
- All together 750 million data points
- Historical chemistry data…
  …dating back to 1771



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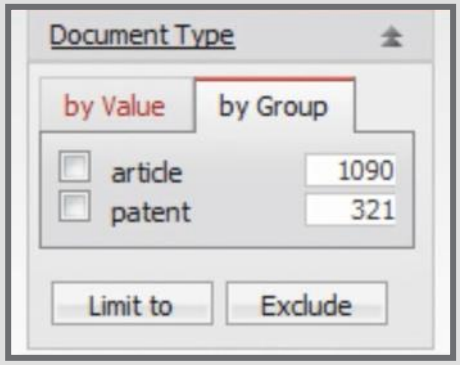
EXPANDED BIBLIOGRAPHIC CONTENT IN REAXYS

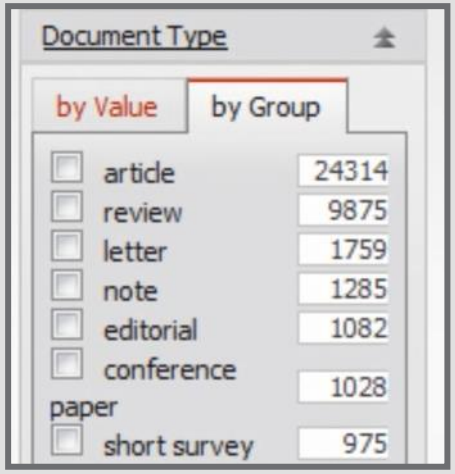
SUPPORTING MULTI-DISCIPLINARY RESEARCH

- Bibliographic data from 16.000 periodicals covering chemistry and related sciences have been loaded into Reaxys
- This goes beyond journals and patents, it includes conference proceedings, business articles, reviews etc.

old



new



AGRICULTURAL AND BIOLOGICAL SCIENCES

BIOCHEMISTRY, GENETICS AND MOLECULAR BIOLOGY

CHEMICAL ENGINEERING

DENTISTRY

EARTH AND PLANETARY SCIENCES

ENERGY

ENGINEERING

ENVIRONMENTAL SCIENCE

IMMUNOLOGY AND MICROBIOLOGY

MATERIALS SCIENCE

MEDICINE

NEUROSCIENCE

PHARMACOLOGY, TOXICOLOGY AND PHARMACEUTICS

PHYSICS AND ASTRONOMY

VETERINARY

ETC.

REAXYS-TREE AND AUTOMATIC INDEXING

THE NEXT STEP… COMING 2014

- Classes
  - ReaxysTree
    - chemical reaction
      - chemical reaction class
      - chemical reaction product
      - chemical reaction reagent
      - chemical reaction starting material
    - chemical substance
      - chemical substance by application
      - chemical substance by authority
      - chemical substance type
    - chemical substance property
      - bioactivity
      - electrical property
      - electrochemical property
      - energy parameter
      - magnetic property
      - mechanical property
      - molecular property
      - optical property
      - phase property
      - phase transition
      - safety property
      - solution behavior
      - sound property
      - structure analysis
      - substance spectroscopy
      - thermal behavior
      - thermodynamic property
      - transport phenomene
    - procedure
      - calculation method
      - crystal structure determination
      - electro-analytical method
      - separation method
      - spectroscopical analysis

Step 1

Index for chemistry terms

Step 2

Add chemistry relevant keywords and identified chemical entities

Step 3

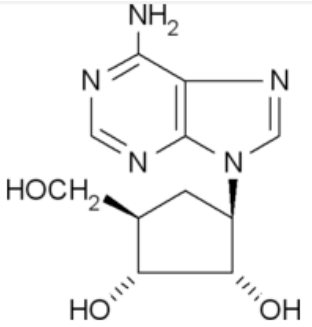
Translate chemical names into structures and make them searchable

Title/Abstract

The Biosynthesis of Aristeromycin. Conversion of Neplanocin A to Aristeromycin by a Novel Enzymatic Reduction

Partially purified cell-free extracts of the aristeromycin producer Streptomyces citricolor have been shown to catalyze the NADPH-dependent reduction of neplanocin A to aristeromycin. Stereochemical studies revealed that the reduction proceeds with anti-geometry and involves transfer of the 4 pro-R hydrogen atom of NADPH to the 6'ß position of aristeromycin.

Reaxys Keywords: Aristeromycin - biosynthesis, enzymatic reduction, Neplanocin A



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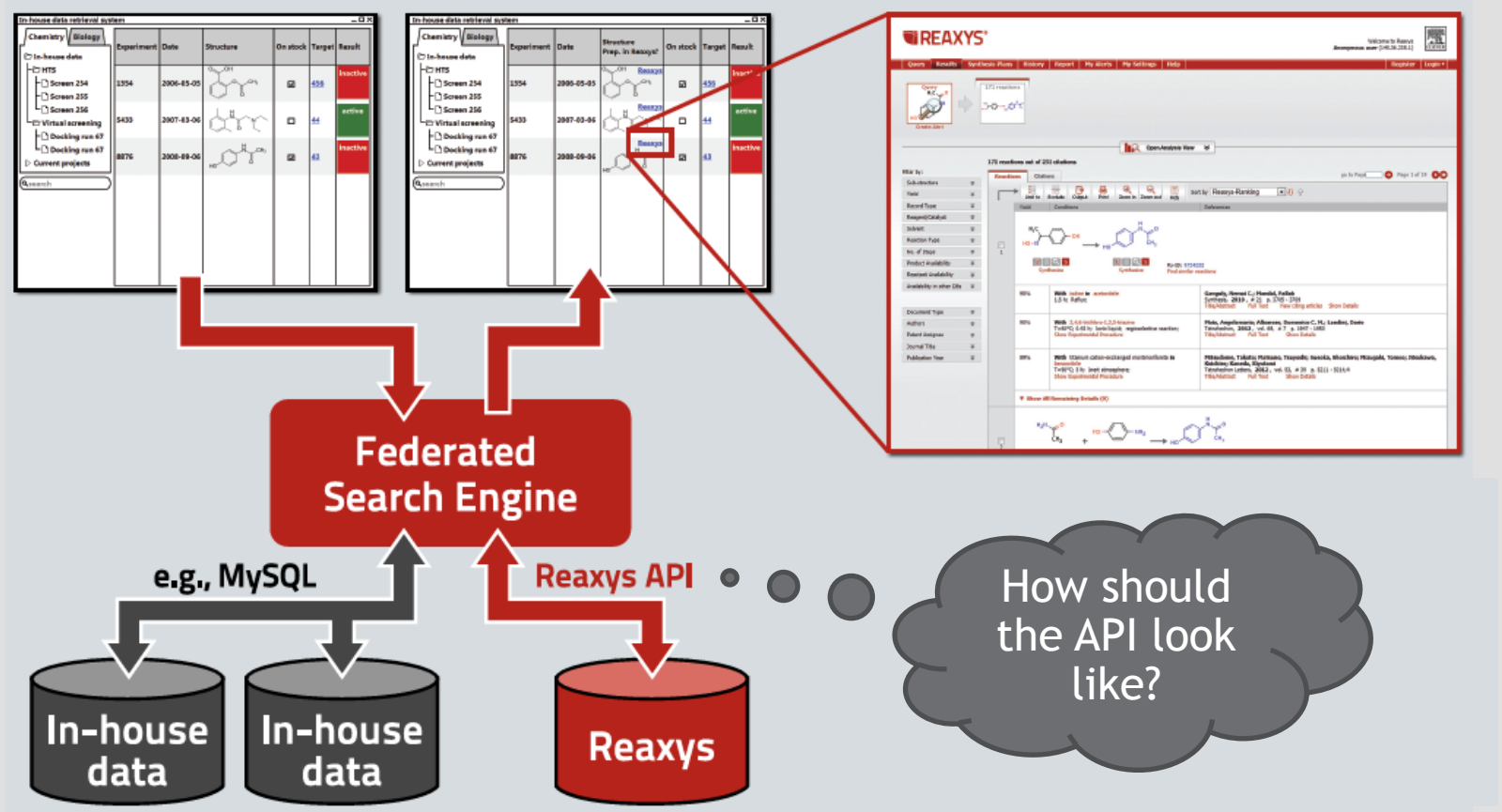
FEDERATED SEARCH SYSTEM WITH REAXYS LOOK-UP

ACCESS TO REAXYS IS VIA THE REAXYS APPLICATION PROGRAMMING INTERFACE (API)



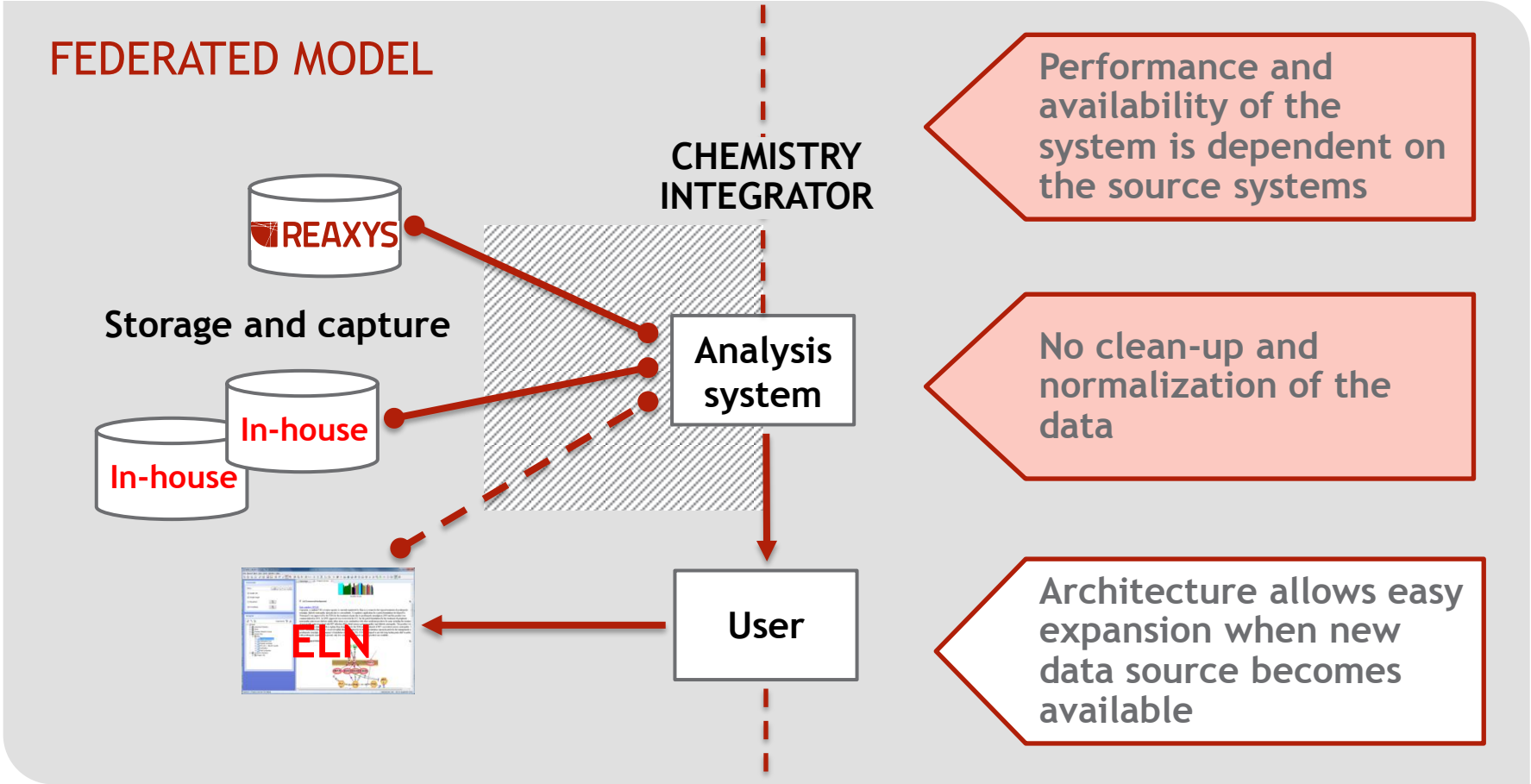
THE REAXYS APPLICATION PROGRAMMING INTERFACE (API)

LESSONS LEARNED

- Customers want to have access to all data in Reaxys
  - Substances and substance property data
  - Reactions and reaction details
  - Citations
- Customers want to have access to all functionality of Reaxys
  - Exact structure and reaction searching, similarity and substructure searching
  - Factual queries
  - Further processing of hitsets
- The Reaxys API was designed to be based on exchanging XML code between the user and the Reaxys server via HTML POST requests
- Security and usage tracking is an issue
  - Secure communication via HTTPS POST is supported
  - The Reaxys API is stateful, and login is required

LIMITATIONS OF THE FEDERATED MODEL

SOME DISADVANTAGES TO CONSIDER

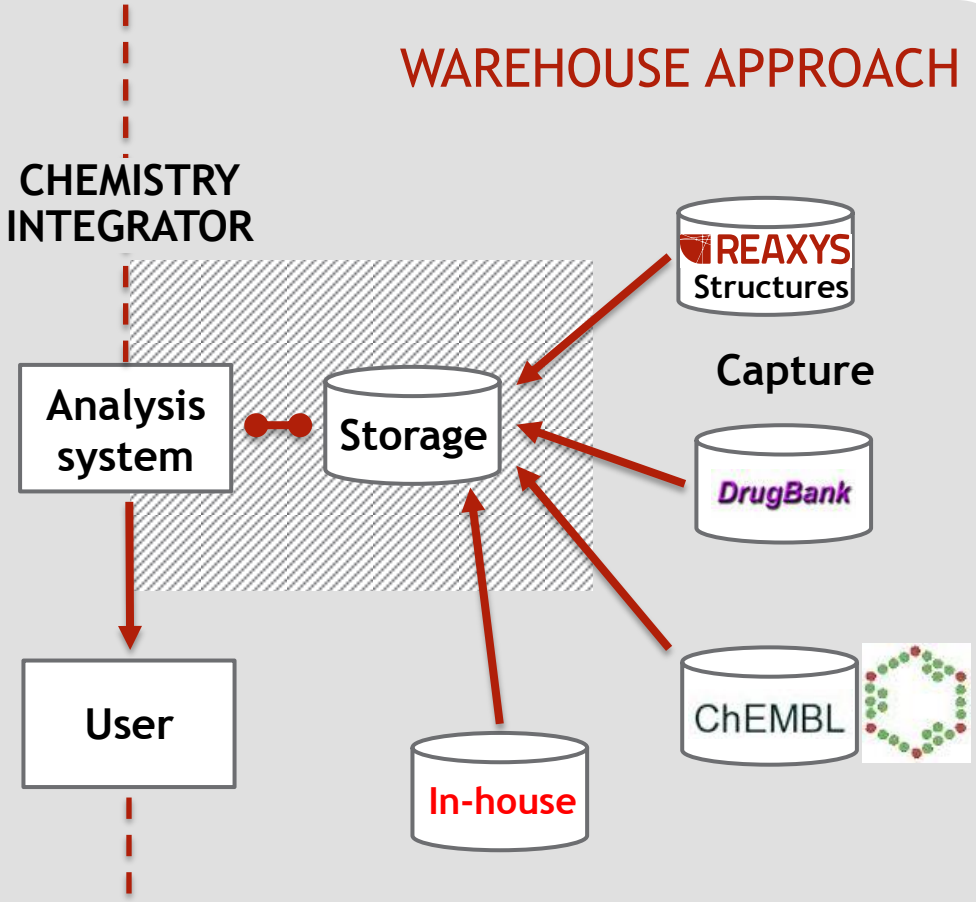


EXAMPLE IMPLEMENTATION OF THE WAREHOUSE APPROACH

Bioactivity data was normalized, and structures were de-duplicated

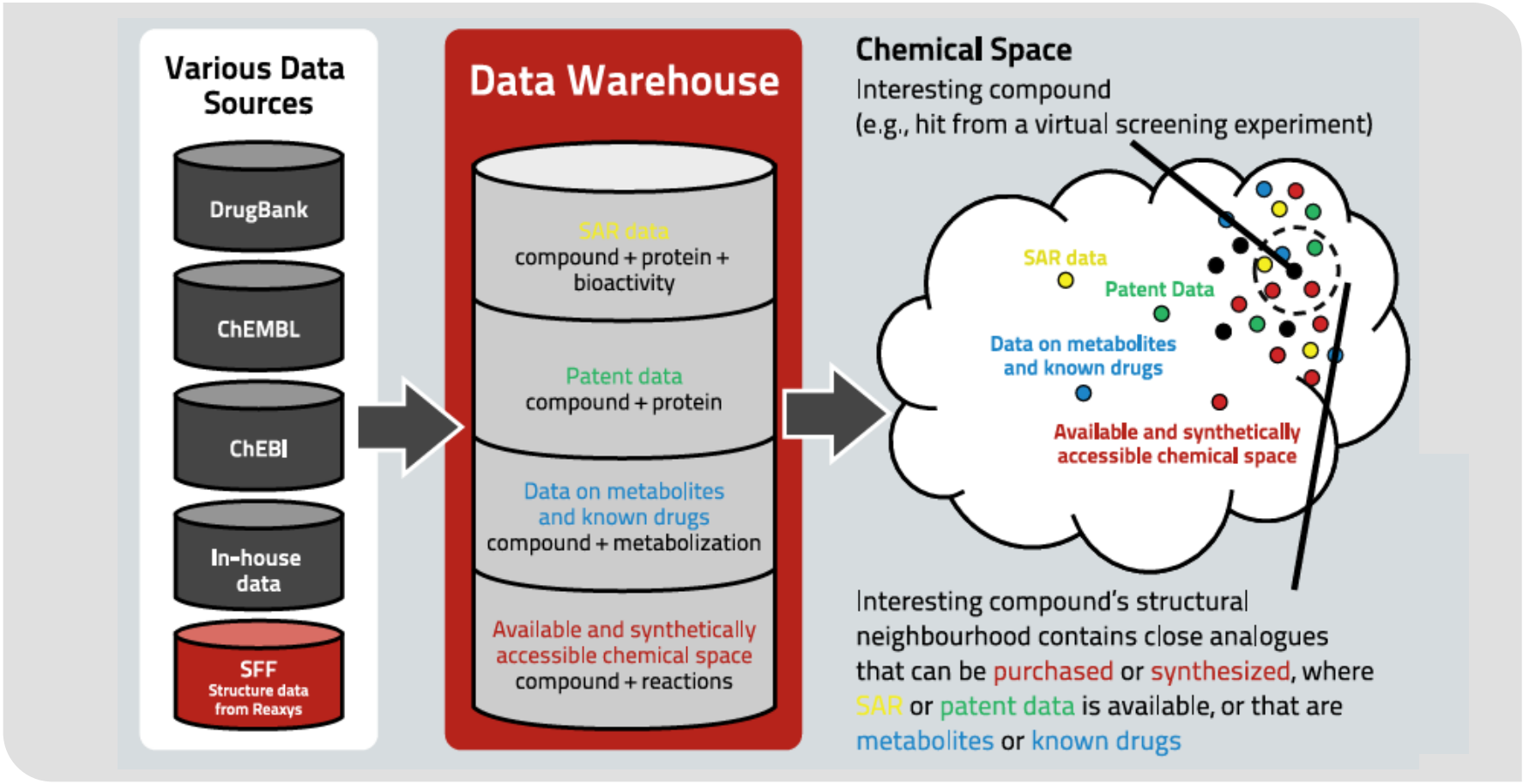
A customer set up a system that contains structure and bioactivity data, and IP information

All data was extracted, translated and loaded to fit into one unified data model (UDM)



PLATFORM FOR STRUCTURE AND BIOACTIVITY DATA

STRUCTURE DATA FROM REAXYS COMES FROM THE REAXYS STRUCTURE FLAT FILE



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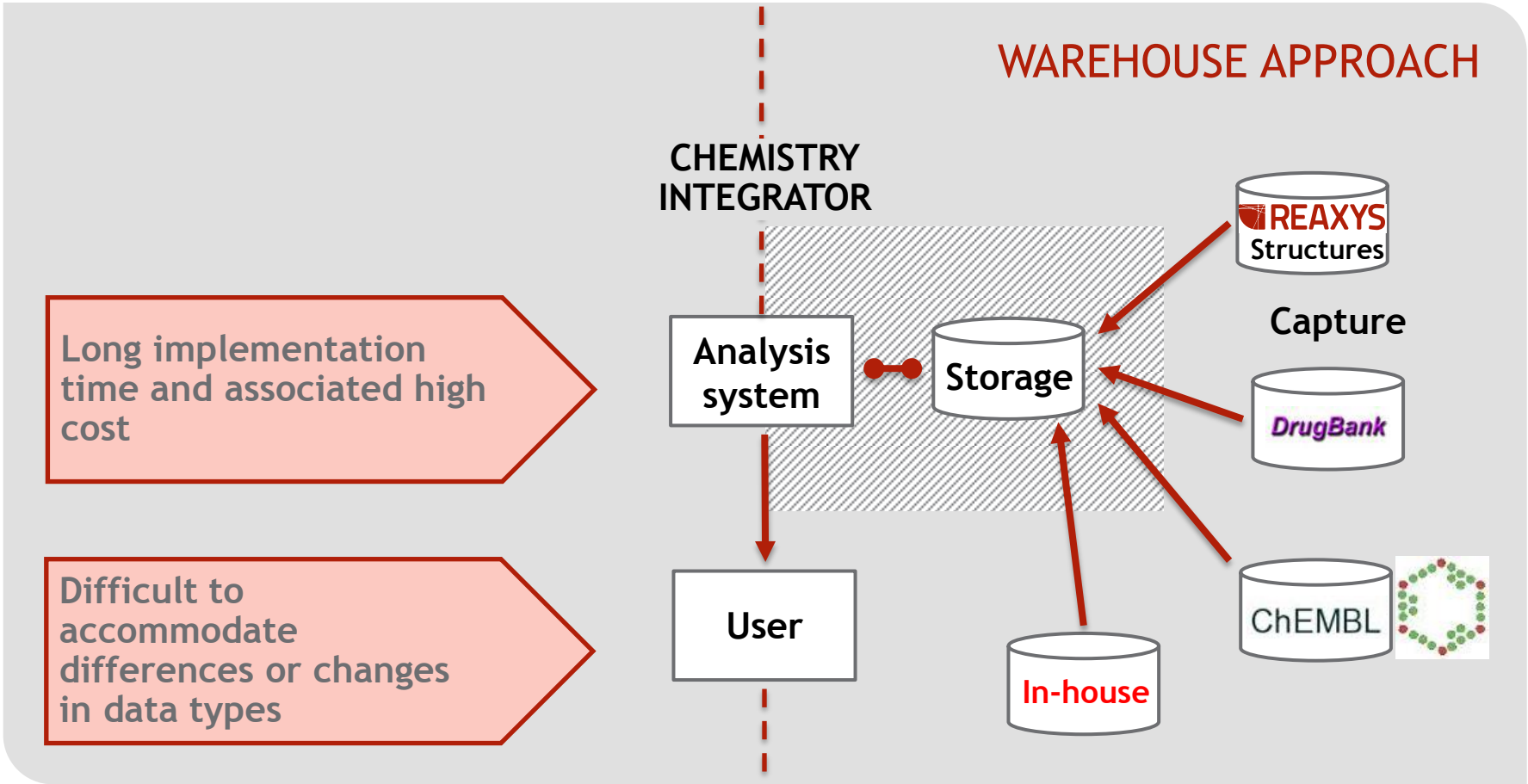
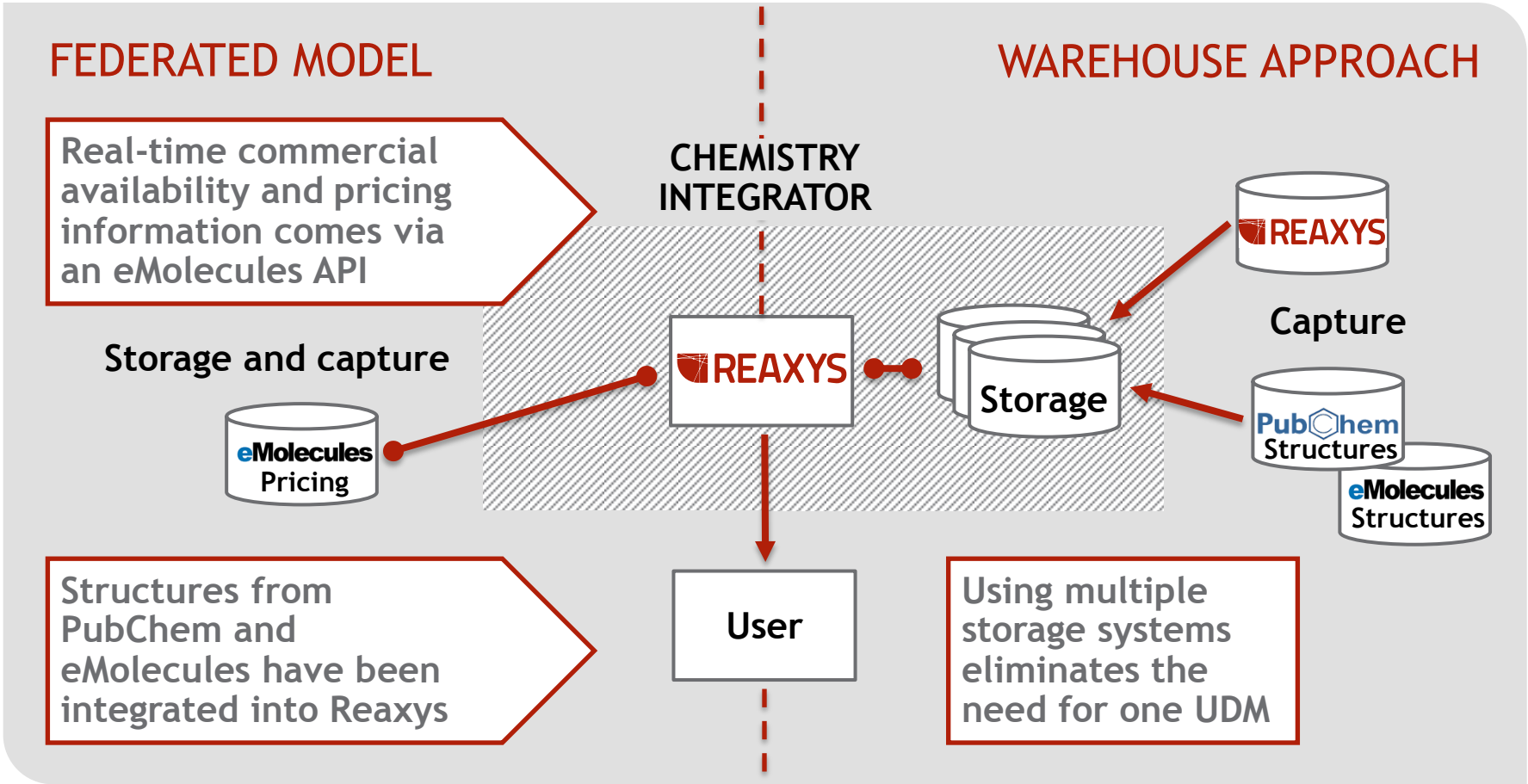
LIMITATIONS OF THE OF THE WAREHOUSE APPROACH

SOME DISADVANTAGES TO CONSIDER



EXAMPLE IMPLEMENTATION OF A FLEXIBLE APPROACH

A CONTENT INTEGRATION SOLUTION THAT IS NOW AVAILABLE TO ALL REAXYS USERS



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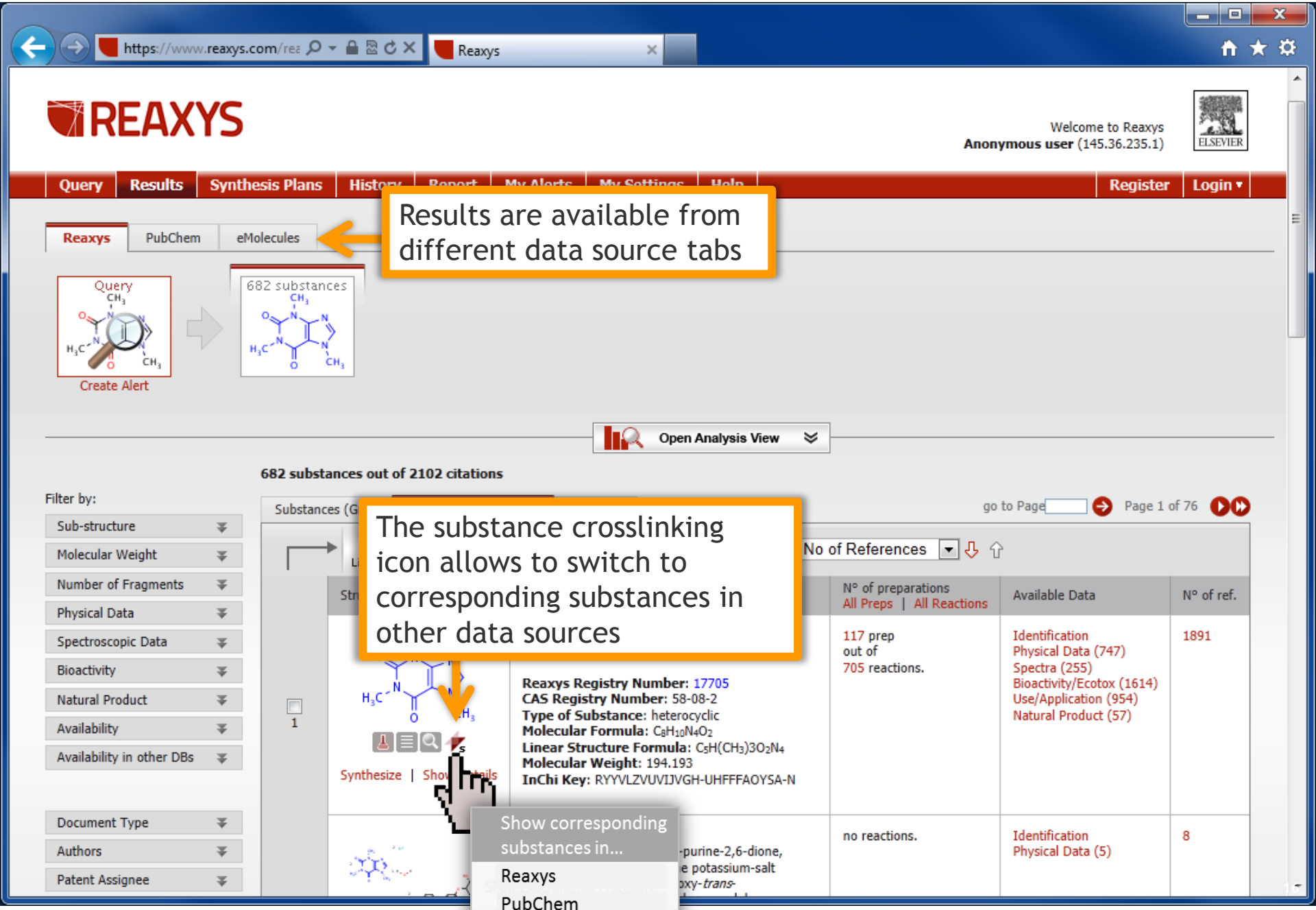
REAXYS
Welcome to Reaxys
Anonymous user (145.36.235.1)
ELSEVIER
Query
Results
Synthesis Plans
History
Report
My Alerts
My Settings
Help
Register
Login
Reaxys
PubChem
eMolecules
Results are available from different data source tabs
Query
682 substances
Create Alert
Open Analysis View
682 substances out of 2102 citations
Filter by:
Sub-structure
Molecular Weight
Number of Fragments
Physical Data
Spectroscopic Data
Bioactivity
Natural Product
Availability
Availability in other DBs
Document Type
Authors
Patent Assignee
Substances (G
go to Page
Page 1 of 76
No of References
The substance crosslinking icon allows to switch to corresponding substances in other data sources
N° of preparations
All Preps | All Reactions
Available Data
N° of ref.
117 prep
out of
705 reactions.
Identification
Physical Data (747)
Spectra (255)
Bioactivity/Ecotox (1614)
Use/Application (954)
Natural Product (57)
1891
Reaxys Registry Number: 17705
CAS Registry Number: 58-08-2
Type of Substance: heterocyclic
Molecular Formula: C8H10N4O2
Linear Structure Formula: C5H(CH3)3O2N4
Molecular Weight: 194.193
InChi Key: RYYVLZVUVIJVGH-UHFFFAOYSA-N
Synthesize
Show corresponding substances in...
Reaxys
PubChem
eMolecules
no reactions.
Identification
Physical Data (5)
8

https://www.reaxys.com/rea

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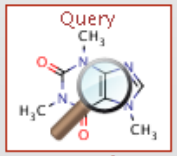
Query | Results | Synthesis Plans | History | Report | My Alerts | My Settings | Help | Register | Login

Reaxys | PubChem | eMolecules

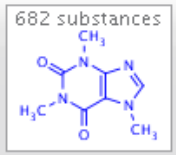
Results are available from different data source tabs

Query



Create Alert

682 substances



Open Analysis View

682 substances out of 2102 citations

Filter by:

- Sub-structure
- Molecular Weight
- Number of Fragments
- Physical Data
- Spectroscopic Data
- Bioactivity
- Natural Product
- Availability
- Availability in other DBs
- Document
- Authors
- Patent Assignee

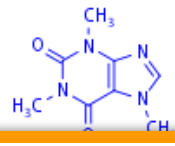
Filter for substances that are/aren't contained in other data sources

Substances (Grid) | Substances (Table) | Citations

go to Page | Page 1 of 76

Limit to | Exclude | Output | Print | Zoom in | Zoom out | Hide

Sort by: No of References

Structure	Structure/Compound Data	N° of preparations All Preps | All Reactions	Available Data	N° of ref.
	**Chemical Name:** caffeine **Reaxys Registry Number:** 17705 **CAS Registry Number:** 58-08-2 **Type of Substance:** heterocyclic $C_8H_{10}N_4O_2$ **Formula:** $C_5H(CH_3)_3O_2N_4$ 194.193 RYYVLZVUVIJVGH-UHFFFAOYSA-N	117 prep out of 705 reactions.	Identification Physical Data (747) Spectra (255) Bioactivity/Ecotox (1614) Use/Application (954) Natural Product (57)	1891
	1,3,7-trimethyl-3,7-dihydro-purine-2,6-dione, caffeine; compound with the potassium-salt of/the/ (1*S*)-3-*C*-(3,4-dihydroxy-*trans*-	no reactions.	Identification Physical Data (5)	8

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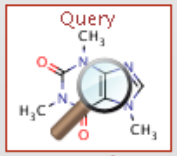
Query | Results | Synthesis Plans | History | Report | My Alerts | My Settings | Help | Register | Login

Reaxys | PubChem | eMolecules

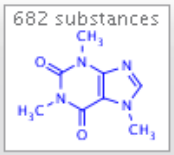
Results are available from different data source tabs

Query



Create Alert

682 substances



Open Analysis View

682 substances out of 2102 citations

Filter by:

- Sub-structure
- Molecular Weight
- Number of Fragments
- Physical Data
- Spectroscopic Data
- Bioactivity
- Natural Product
- Availability
- Availability in other DBs

by Value | by Group

PubChem	28
eMolecules	7
(no entry given)	653

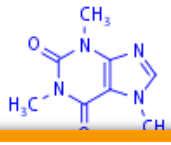
Filter for substances that are/aren't contained in other data sources

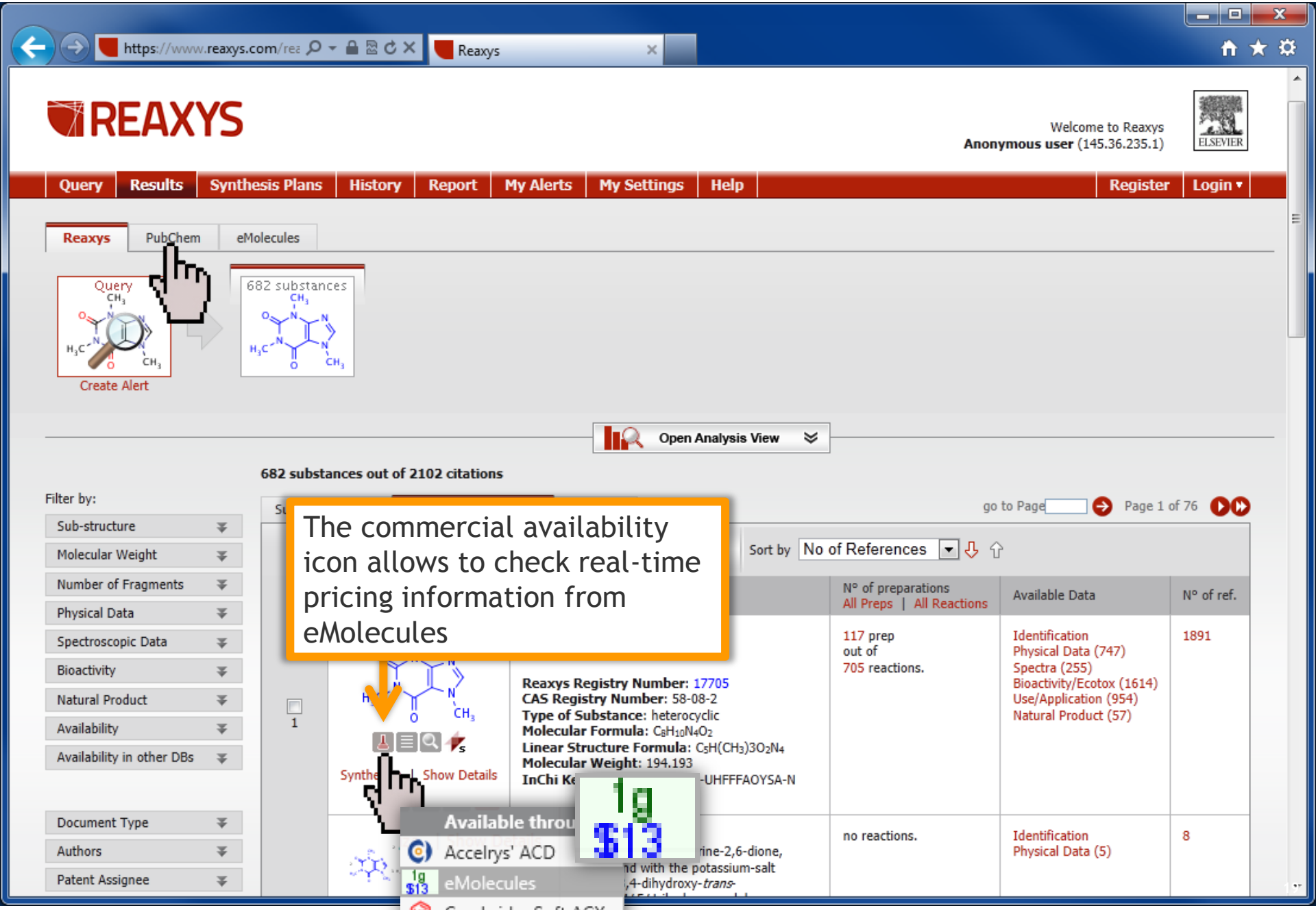
Substances (Grid) | Substances (Table) | Citations

go to Page | Page 1 of 76

Limit to | Exclude | Output | Print | Zoom in | Zoom out | Hide

Sort by: No of References

Structure	Structure/Compound Data	N° of preparations (All Preps | All Reactions)	Available Data	N° of ref.
	**Chemical Name:** caffeine **Reaxys Registry Number:** 17705 **CAS Registry Number:** 58-08-2 **Type of Substance:** heterocyclic $C_8H_{10}N_4O_2$ **Formula:** $C_5H(CH_3)_3O_2N_4$ 194.193 RYYVLZVUVIJVGH-UHFFFAOYSA-N	117 prep out of 705 reactions.	Identification Physical Data (747) Spectra (255) Bioactivity/Ecotox (1614) Use/Application (954) Natural Product (57)	1891
	1,3,7-trimethyl-3,7-dihydro-purine-2,6-dione, caffeine; compound with the potassium-salt of/the/ (1*S*)-3-*c*-(3,4-dihydroxy-*trans*-	no reactions.	Identification Physical Data (5)	8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Login
Reaxys
PubChem
eMolecules
Query
682 substances
Create Alert
Open Analysis View
682 substances out of 2102 citations
Filter by:
Sub-structure
Molecular Weight
Number of Fragments
Physical Data
Spectroscopic Data
Bioactivity
Natural Product
Availability
Availability in other DBs
Document Type
Authors
Patent Assignee
go to Page
Page 1 of 76
Sort by
No of References
The commercial availability icon allows to check real-time pricing information from eMolecules
N° of preparations
All Preps | All Reactions
Available Data
N° of ref.
117 prep
out of
705 reactions.
Identification
Physical Data (747)
Spectra (255)
Bioactivity/Ecotox (1614)
Use/Application (954)
Natural Product (57)
1891
Reaxys Registry Number: 17705
CAS Registry Number: 58-08-2
Type of Substance: heterocyclic
Molecular Formula: C8H10N4O2
Linear Structure Formula: C5H(CH3)3O2N4
Molecular Weight: 194.193
InChi Ke -UHFFFAOYSA-N
Show Details
1g
$13
Available throu
Accelrys' ACD
eMolecules
CambridgeSoft ACX
no reactions.
Identification
Physical Data (5)
8

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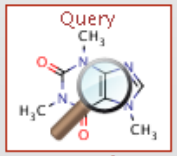
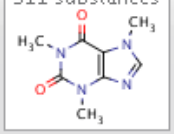
Query



Create Alert

311 substances



Open Analysis View

311 substances

Filter by:

- Sub-structure
- Molecular Weight
- Number of Fragments
- Availability in other DBs

Substances (Grid) | Substances (Table)

go to Page | Page 1 of 35

Limit to | Exclude | Output | Print | Zoom in | Zoom out | Hide | Sort by PubChem ID

Structure	Structure/Compound Data	Available Data
 Synthesize | Show Names	**Chemical Name:** 1,3,7-trimethylpurine-2,6-dione **PubChem Compound ID:** 2519 **Molecular Formula:** **Linear Structure For** **Molecular Weight:** **InChi Key:** RYYVLZVU	Identification Safety and Handling Pharmacology Exposure Standards and Regulations Monitoring and Analysis Methods Literature Biological Test Results Biomolecular Interactions and Pathways Use and Manufacturing Biomedical Effects and Toxicity Environmental Fate and Exposure Potential
	Chemical Name:	Identification

PubChem property headers with direct links to PubChem

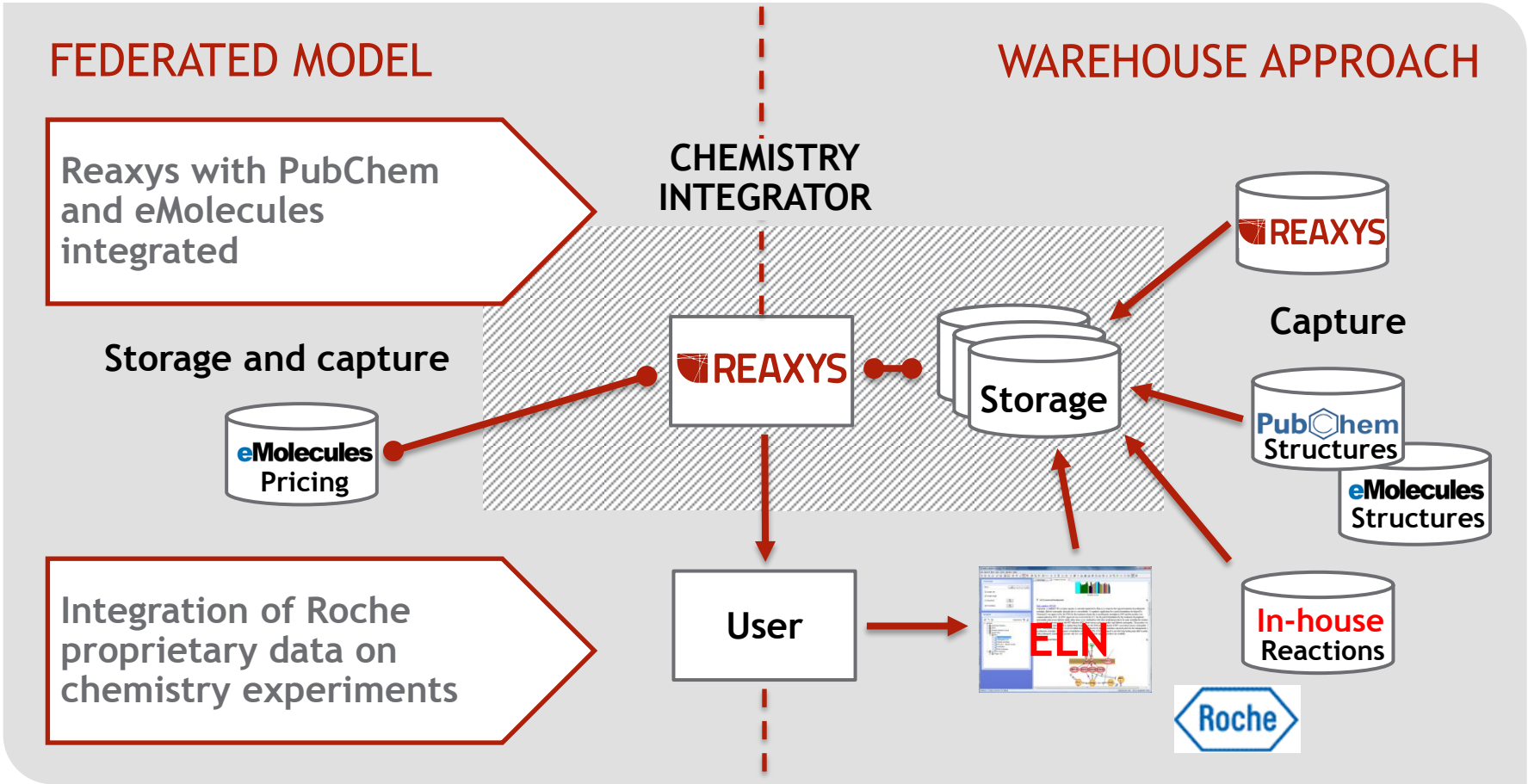
FLEXIBLE APPROACH FOR INTEGRATION

LESSONS LEARNED

- Reaxys has proven to be extremely powerful as analysis and database system
- Separation of the data from different data sources into multiple storage systems is the way to go…
  - … if a powerful crosslinking mechanism is in place
- Some pieces of information that are subject to frequent updates should be integrated using the federated model

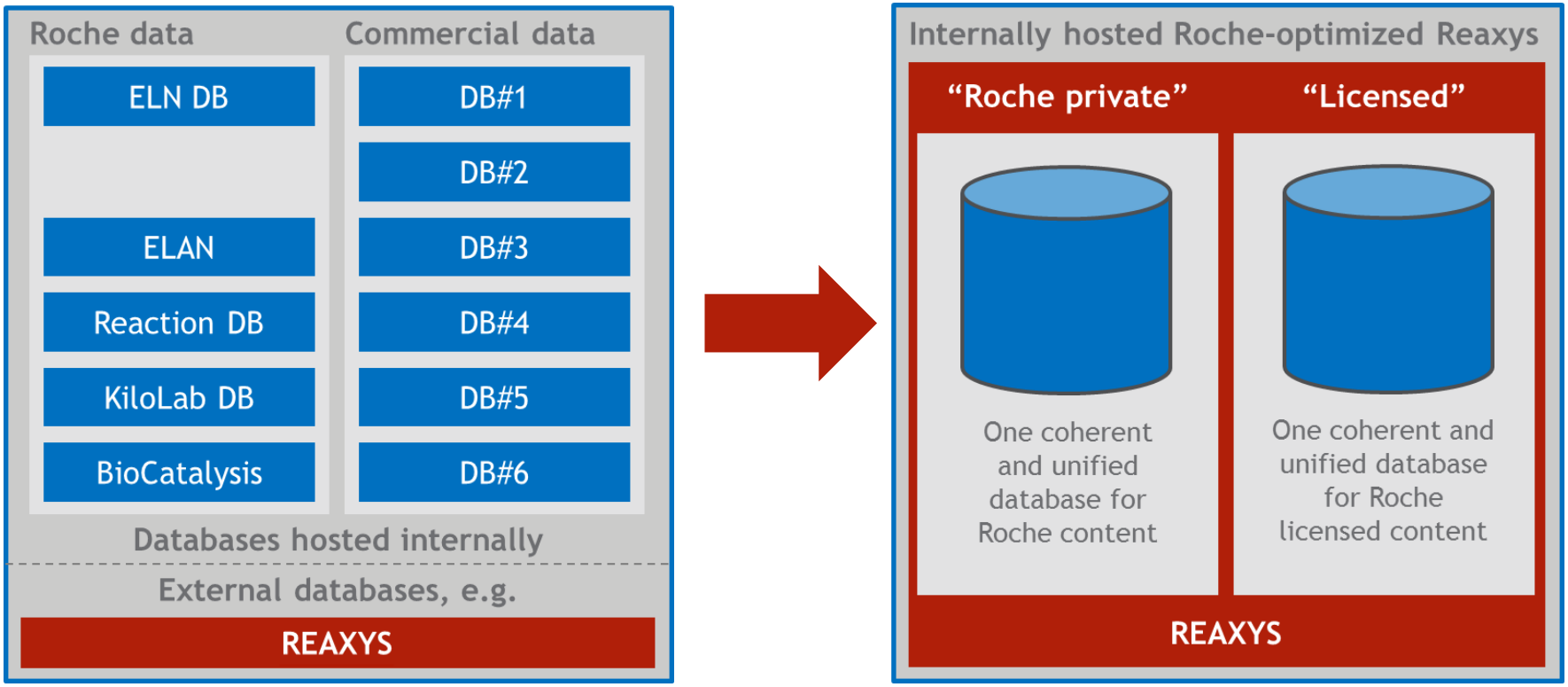
EXAMPLE IMPLEMENTATION OF A FLEXIBLE APPROACH

A CONTENT INTEGRATION SOLUTION THAT ELSEVIER BUILT FOR ROCHE



INTEGRATION OF ROCHE IN-HOUSE DATA

THE SITUATION AT ROCHE YESTERDAY… AND TODAY



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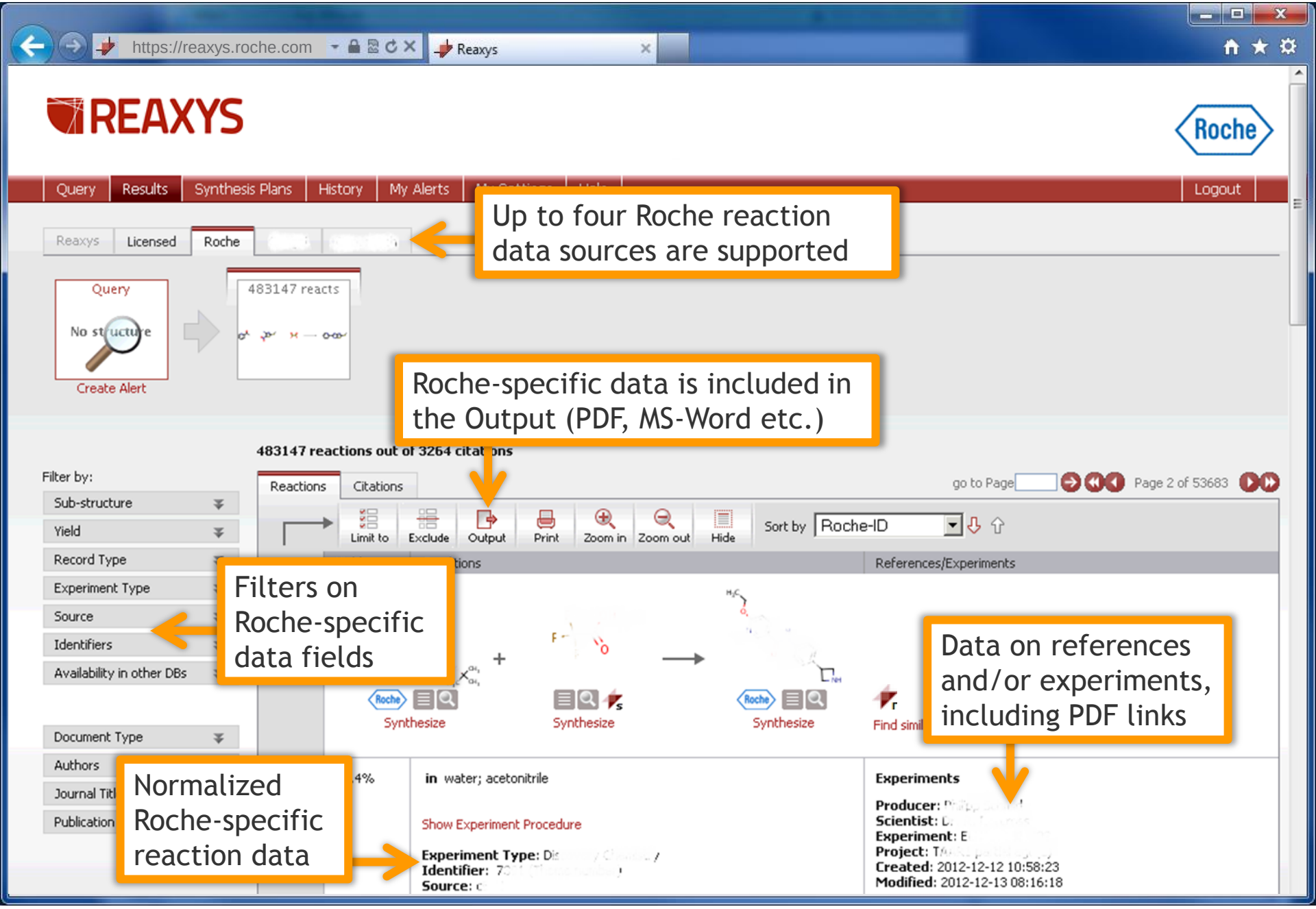
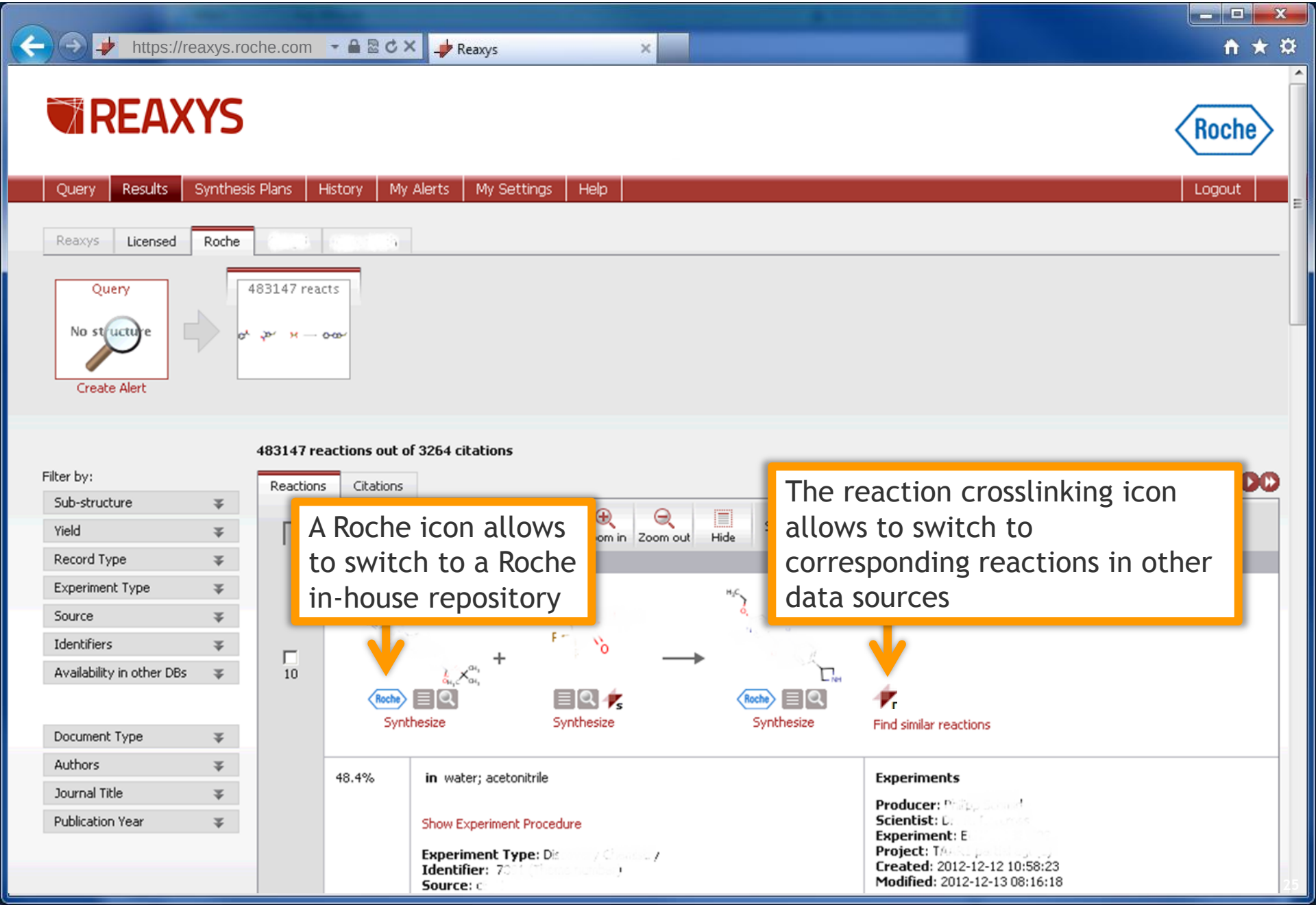
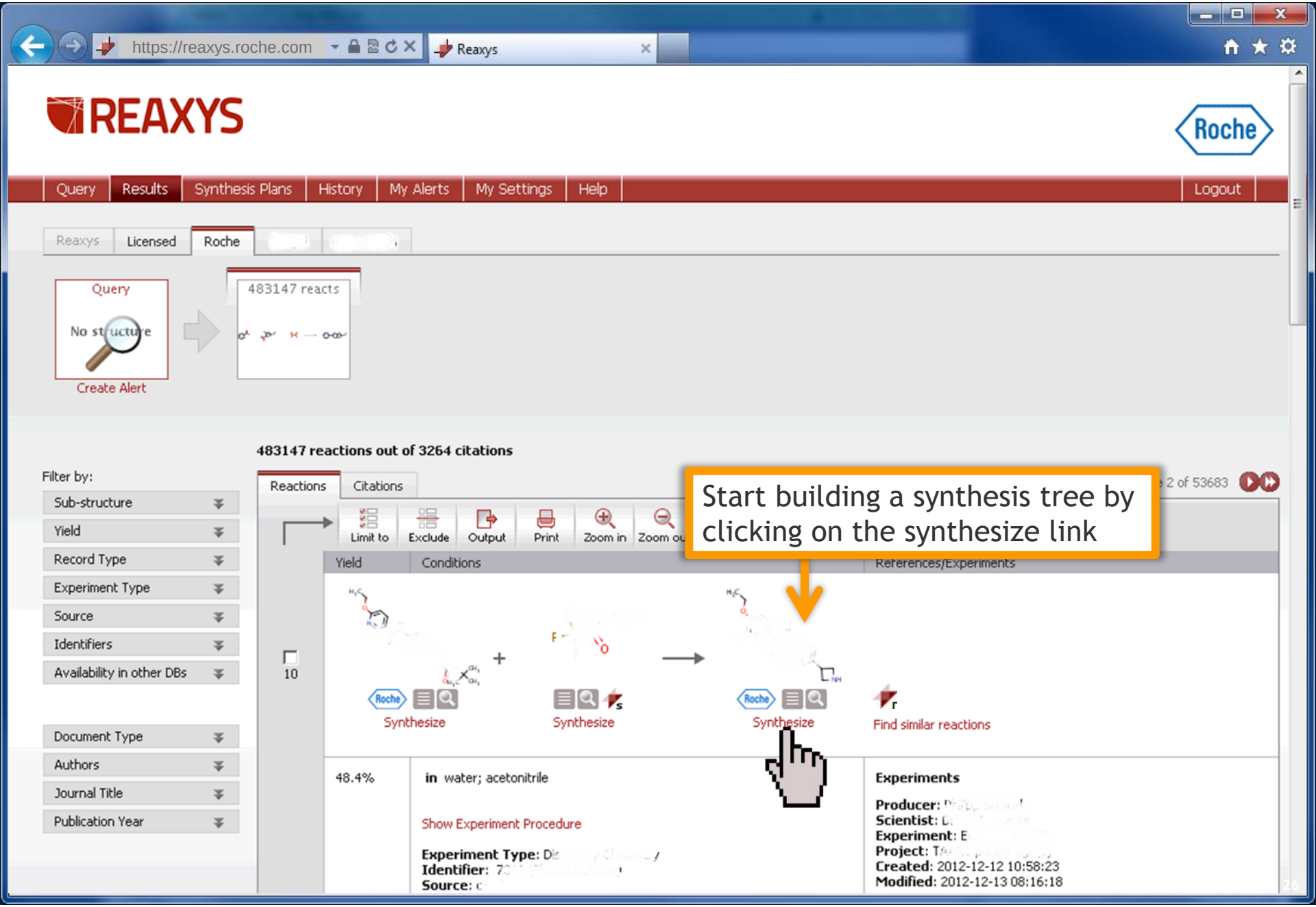
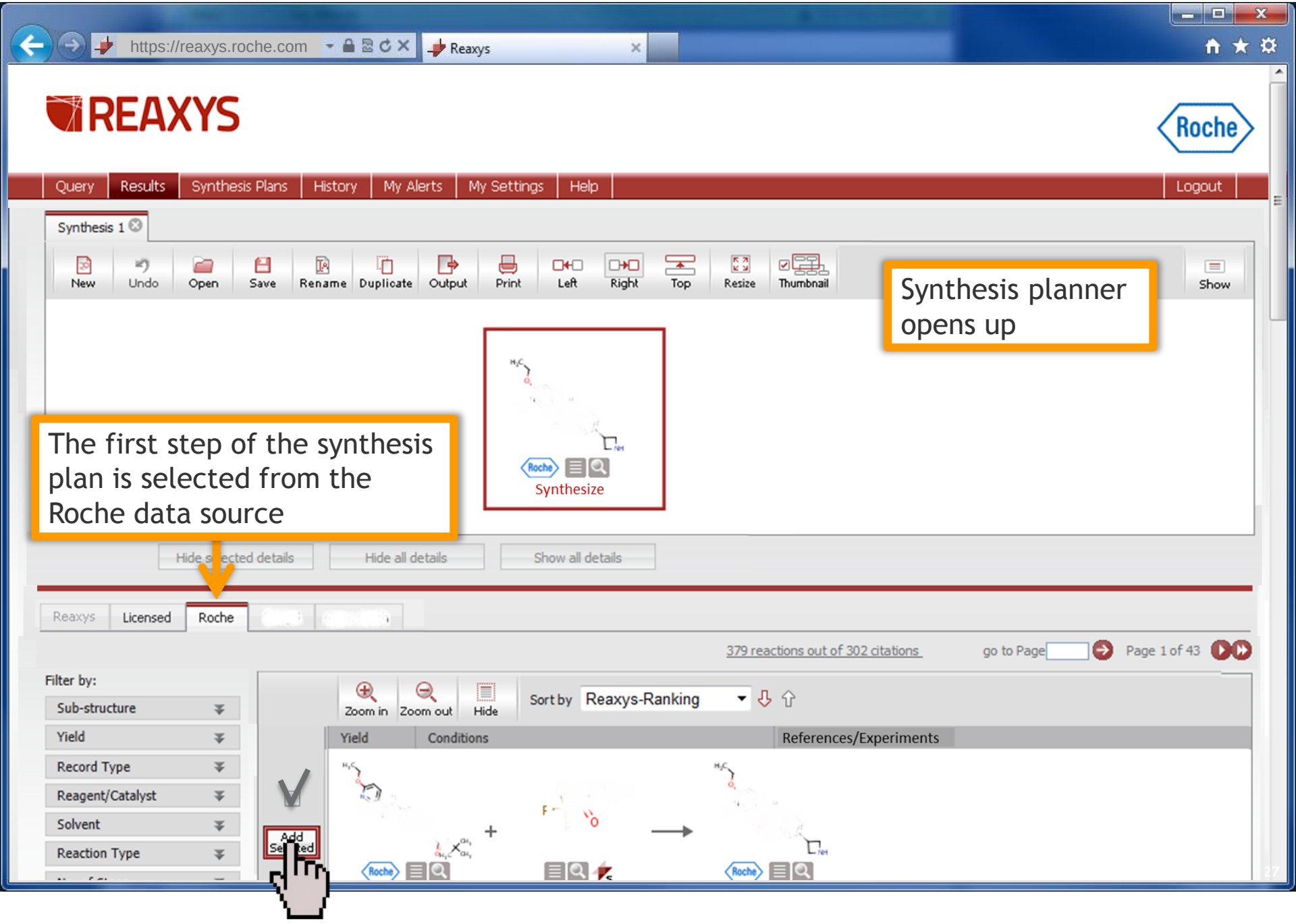

https://reaxys.roche.com
Reaxys
REAXYS
Roche
Query
Results
Synthesis Plans
History
My Alerts
Logout
Reaxys
Licensed
Roche
Up to four Roche reaction data sources are supported
Query
No structure
Create Alert
483147 reacts
Roche-specific data is included in the Output (PDF, MS-Word etc.)
483147 reactions out of 3264 citations
Filter by:
Sub-structure
Yield
Record Type
Experiment Type
Source
Identifiers
Availability in other DBs
Filters on Roche-specific data fields
Document Type
Authors
Journal Title
Publication
Reactions
Citations
go to Page
Page 2 of 53683
Limit to
Exclude
Output
Print
Zoom in
Zoom out
Hide
Sort by
Roche-ID
References/Experiments
Synthesize
Synthesize
Synthesize
Find simil
Data on references and/or experiments, including PDF links
Normalized Roche-specific reaction data
in water; acetonitrile
Show Experiment Procedure
Experiment Type:
Identifier:
Source:
Experiments
Producer:
Scientist:
Experiment:
Project:
Created: 2012-12-12 10:58:23
Modified: 2012-12-13 08:16:18


https://reaxys.roche.com
Reaxys
REAXYS
Roche
Query
Results
Synthesis Plans
History
My Alerts
My Settings
Help
Logout
Reaxys
Licensed
Roche
Query
No structure
Create Alert
483147 reacts
483147 reactions out of 3264 citations
Filter by:
Sub-structure
Yield
Record Type
Experiment Type
Source
Identifiers
Availability in other DBs
Document Type
Authors
Journal Title
Publication Year
Reactions
Citations
Zoom in
Zoom out
Hide
10
A Roche icon allows to switch to a Roche in-house repository
The reaction crosslinking icon allows to switch to corresponding reactions in other data sources
Synthesize
Synthesize
Synthesize
Find similar reactions
48.4%
in water; acetonitrile
Show Experiment Procedure
Experiment Type:
Identifier:
Source:
Experiments
Producer:
Scientist:
Experiment:
Project:
Created: 2012-12-12 10:58:23
Modified: 2012-12-13 08:16:18


https://reaxys.roche.com
Reaxys
REAXYS
Roche
Query
Results
Synthesis Plans
History
My Alerts
My Settings
Help
Logout
Reaxys
Licensed
Roche
Query
No structure
Create Alert
483147 reacts
483147 reactions out of 3264 citations
Filter by:
Sub-structure
Yield
Record Type
Experiment Type
Source
Identifiers
Availability in other DBs
Document Type
Authors
Journal Title
Publication Year
Reactions
Citations
Limit to
Exclude
Output
Print
Zoom in
Yield
Conditions
References/Experiments
10
Synthesize
Synthesize
Synthesize
Find similar reactions
48.4%
in water; acetonitrile
Show Experiment Procedure
Experiment Type:
Identifier:
Source:
Experiments
Producer:
Scientist:
Experiment:
Project:
Created: 2012-12-12 10:58:23
Modified: 2012-12-13 08:16:18
Start building a synthesis tree by clicking on the synthesize link


https://reaxys.roche.com
Reaxys
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Query
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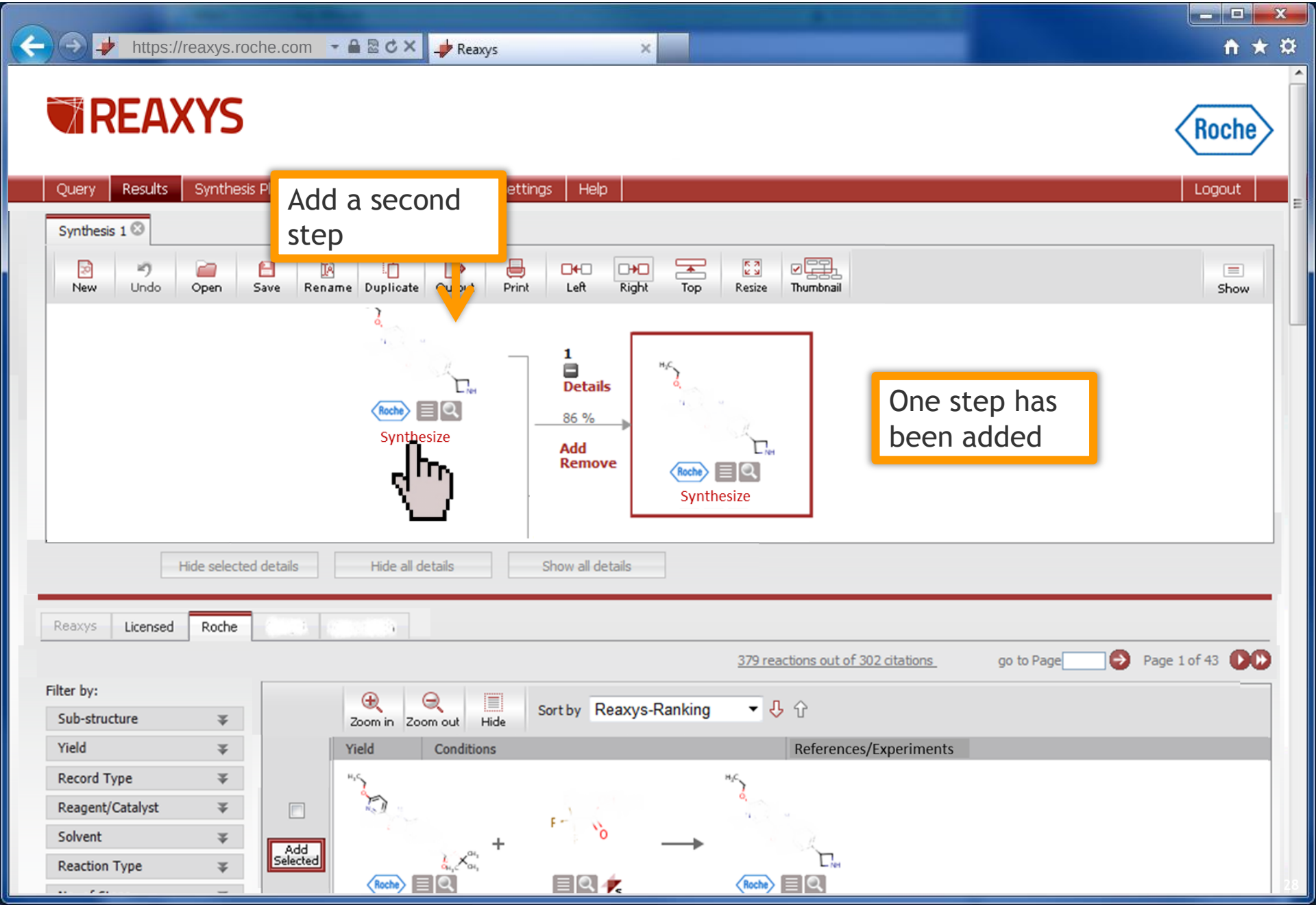
Synthesis Plans
History
My Alerts
My Settings
Help
Logout
Synthesis 1
New
Undo
Open
Save
Rename
Duplicate
Output
Print
Left
Right
Top
Resize
Thumbnail
Show
Synthesis planner opens up
Synthesize
The first step of the synthesis plan is selected from the Roche data source
Hide all details
Show all details
Reaxys
Licensed
Roche
379 reactions out of 302 citations
go to Page
Page 1 of 43
Filter by:
Sub-structure
Yield
Record Type
Reagent/Catalyst
Solvent
Reaction Type
Zoom in
Zoom out
Hide
Sort by
Reaxys-Ranking
Yield
Conditions
References/Experiments
Add


https://reaxys.roche.com
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Query
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ettings
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Logout
Add a second step
Synthesis 1
New
Undo
Open
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Duplicate
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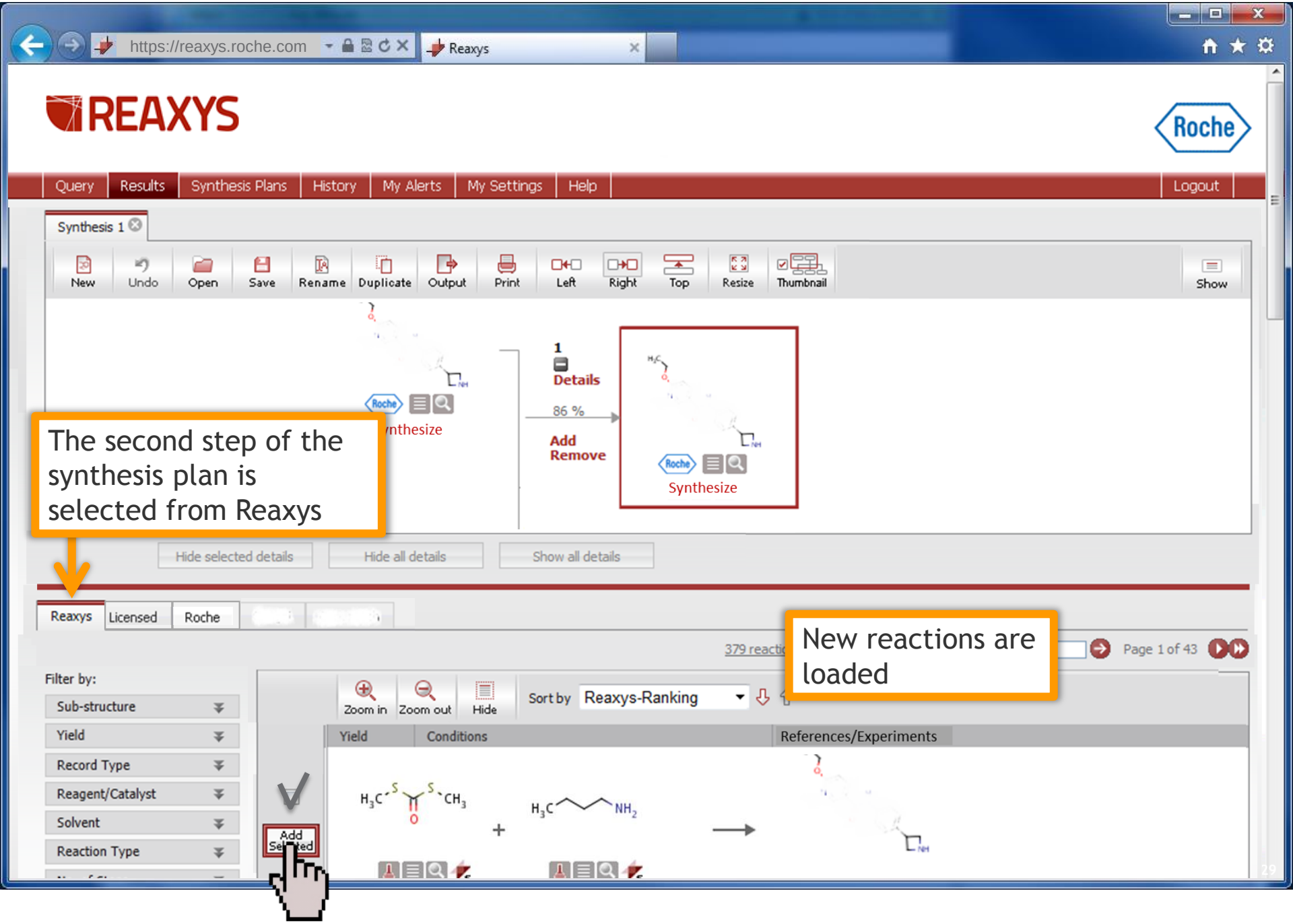
Left
Right
Top
Resize
Thumbnail
Show
Synthesize
1
Details
86 %
Add
Remove
Synthesize
One step has been added
Hide selected details
Hide all details
Show all details
Reaxys
Licensed
Roche
379 reactions out of 302 citations
go to Page
Page 1 of 43
Filter by:
Sub-structure
Yield
Record Type
Reagent/Catalyst
Solvent
Reaction Type
Zoom in
Zoom out
Hide
Sort by
Reaxys-Ranking
Yield
Conditions
References/Experiments
Add Selected


https://reaxys.roche.com
Reaxys
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Synthesis Plans
History
My Alerts
My Settings
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Synthesis 1
New
Undo
Open
Save
Rename
Duplicate
Output
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Left
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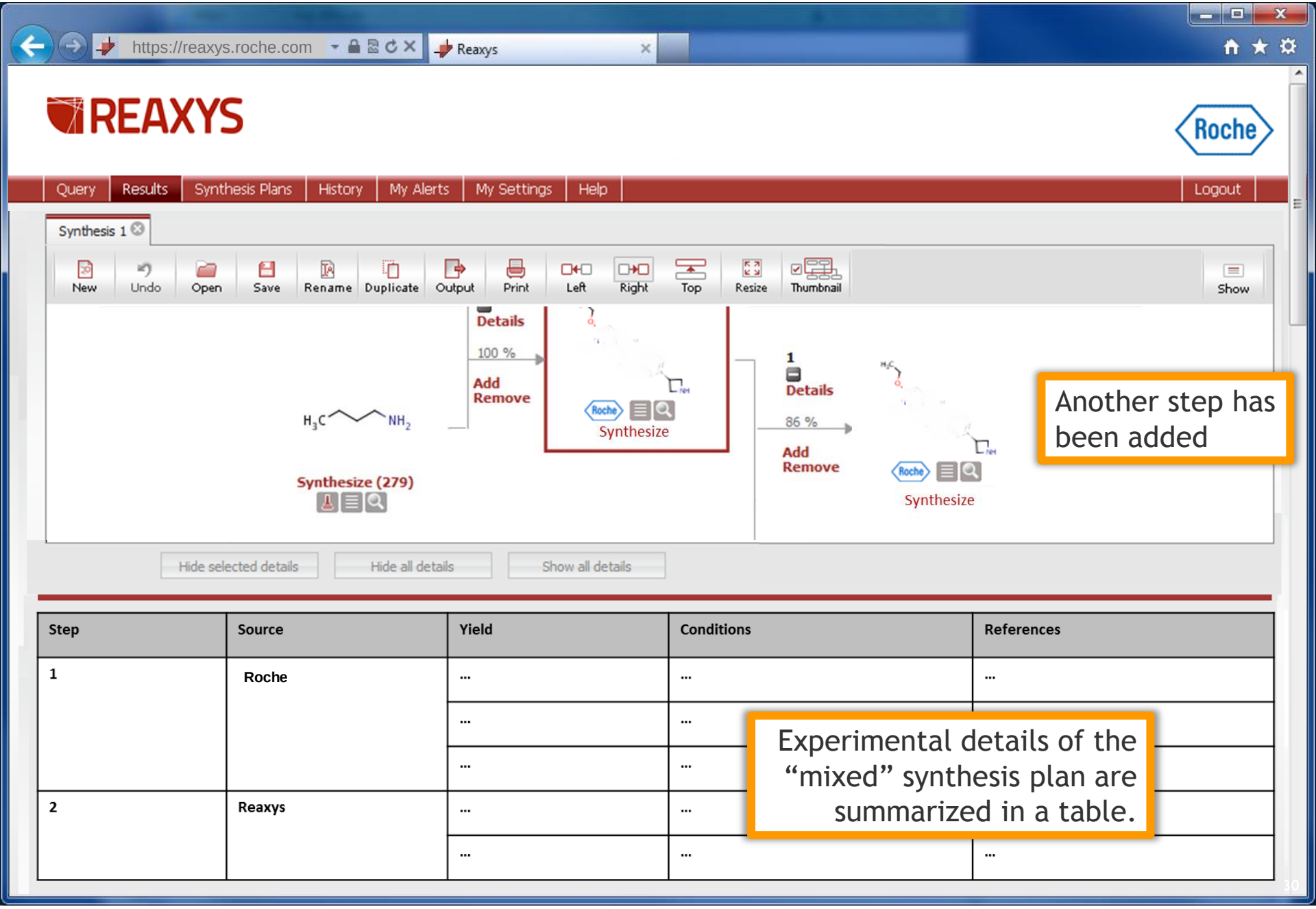
Resize
Thumbnail
Show
1
Details
86 %
Add
Remove
Synthesize
Hide selected details
Hide all details
Show all details
The second step of the synthesis plan is selected from Reaxys
Reaxys
Licensed
Roche
379 reactio
Page 1 of 43
New reactions are loaded
Filter by:
Sub-structure
Yield
Record Type
Reagent/Catalyst
Solvent
Reaction Type
Zoom in
Zoom out
Hide
Sort by
Reaxys-Ranking
Yield
Conditions
References/Experiments
Add Selected



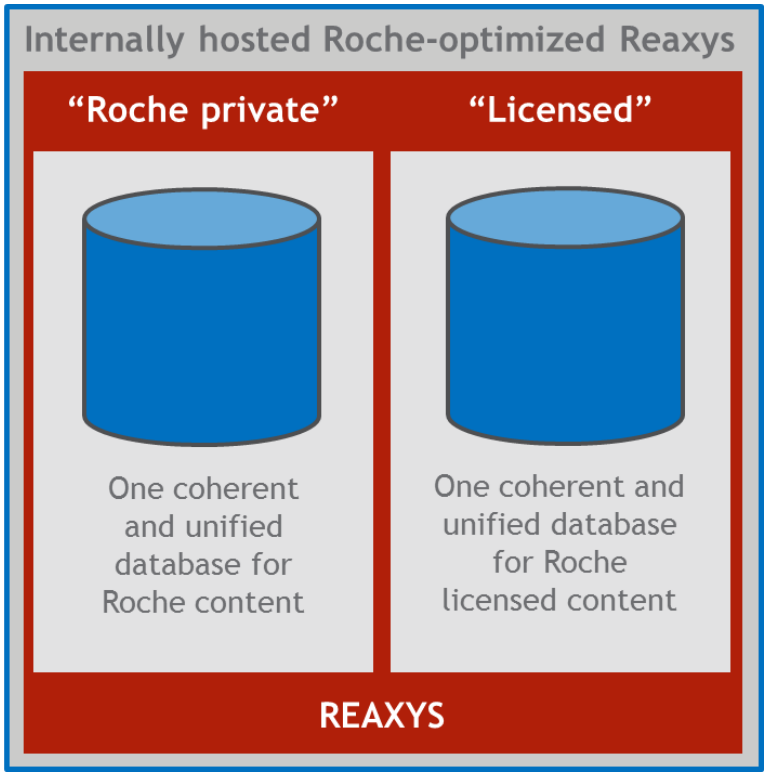
Step	Source	Yield	Conditions	References
1	Roche	…	…	…
		…	…	
		…	…	
2	Reaxys	…	…	
		…	…	…

Experimental details of the "mixed" synthesis plan are summarized in a table.

INTEGRATION OF ROCHE IN-HOUSE DATA

CUSTOMER FEEDBACK

- Usability and acceptance tests by Roche showed:
  - Increased productivity of researchers at Roche
  - Increased discoverability of the Roche reaction content
- Reduced maintenance effort for Roche:
  - Legacy systems were decommissioned
  - Roche gets on-going maintenance and functionality improvements by Elsevier
- Not compromise in security
- Flexible approach:
  - Additional data sources have been added



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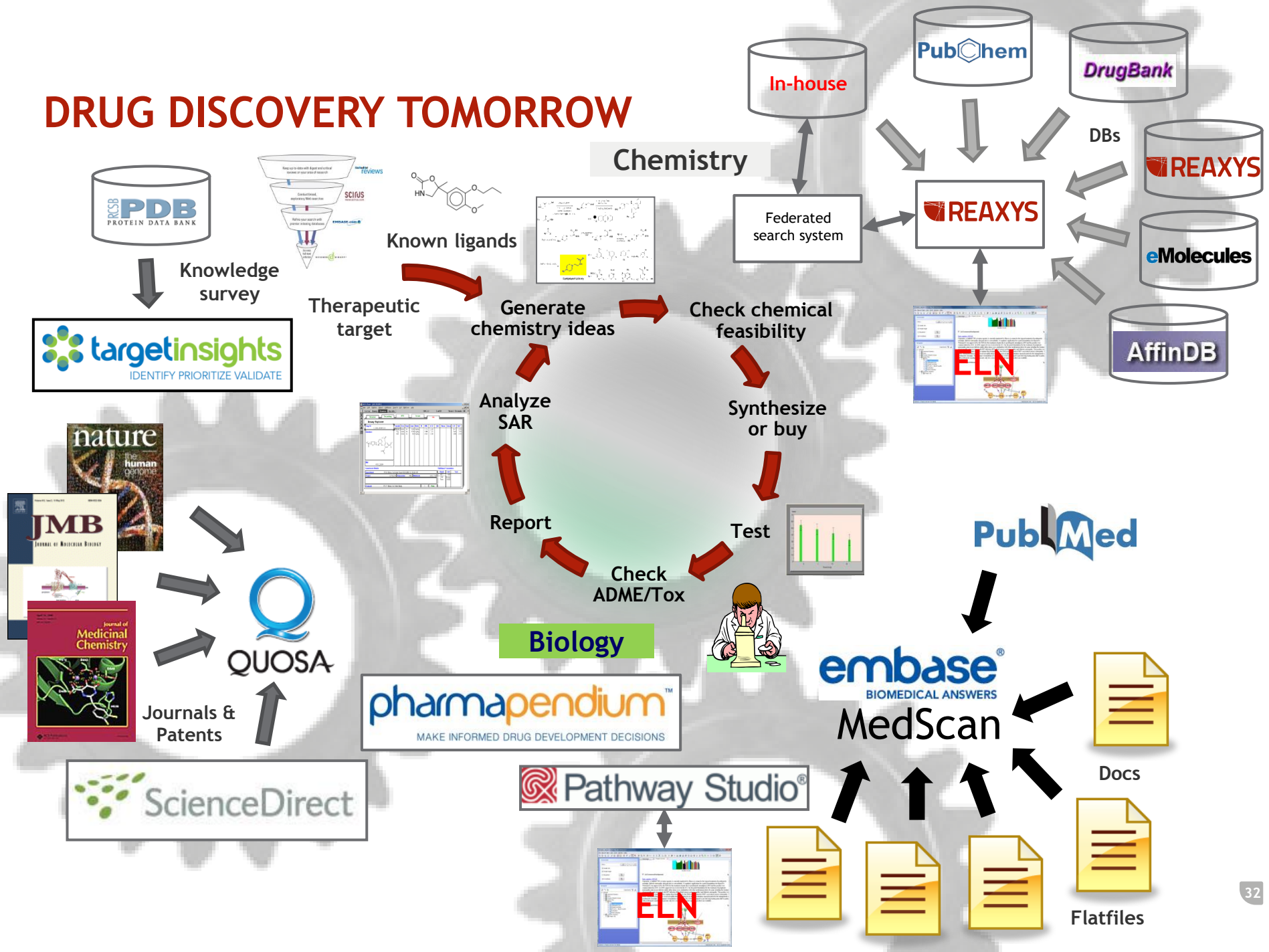
HOW YOU THINK HOW YOU WORK

DRUG DISCOVERY TOMORROW



THANK YOU – QUESTIONS?

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