ChemAxon’s technology in Reaxys

ChemAxon’s technology supporting Reaxys and Reaxys Medicinal Chemistry (RMC) production, searching and visualization workflows

Derrick Umali at ChemAxon UGM 2019 San Diego

supported by Ralph Hössel Elena Herzog, Stefan Roller, Olivier Barberan, Rosalind Sankey, Jürgen Swienty-Busch, Christian Böhm, and Pieder Caduff

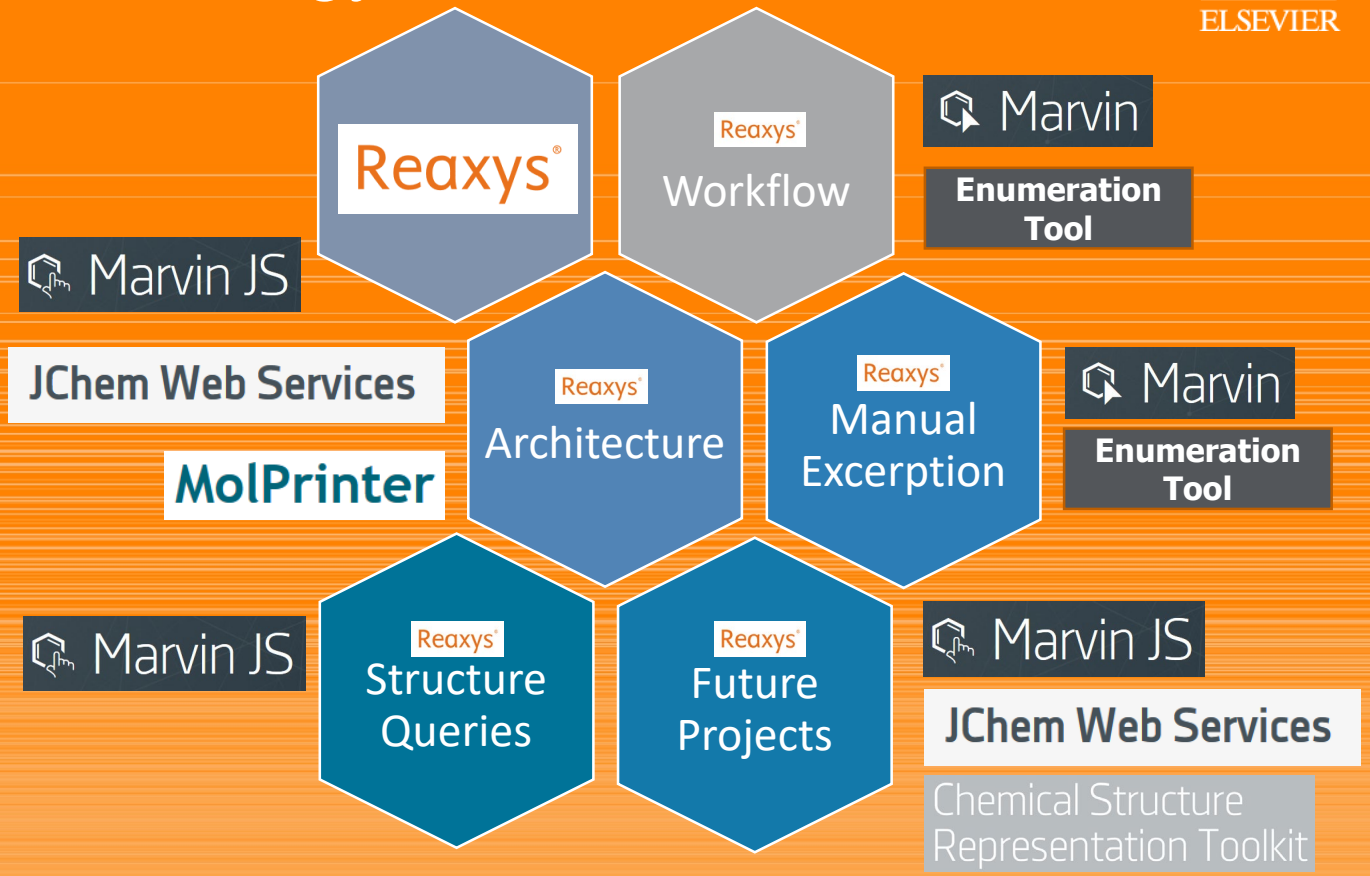
March 2019

My role at Elsevier

Life Science Solutions

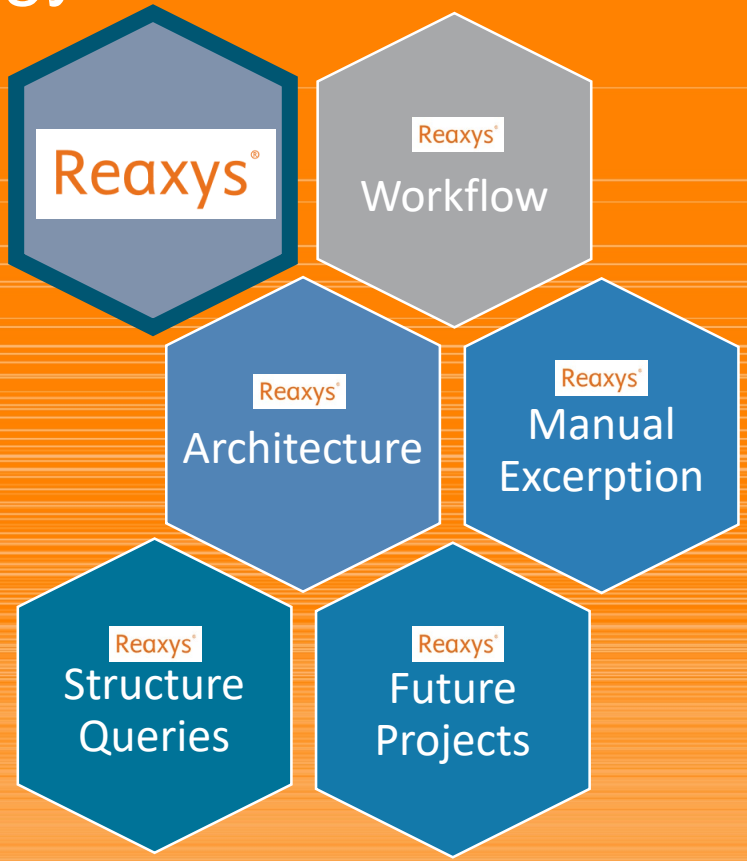
- ~ 20 years at Elsevier
  - MDL Elsevier answering phone calls on ISIS Draw / ISIS Base
  - Cheminformatics / Bioinformatics Consultant
  - Life Science Trainer
  - Life Science Sales
- Worked with Crossfire Beilstein, migration to Reaxys , Reaxys 2.0

ChemAxon's technology in Reaxys



ChemAxon

ChemAxon's technology in Reaxys



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In essence chemistry deals with two core questions across the three segments

1. "Which compound will have the desired property?" **Properties**
2. "How can a compound be made?" **Synthesis – Production**

Pharma

Pharma Research
Identify, optimize and make lead compounds with high probability of success in clinical trials

Process Chemistry
Scale-up from lab synthesis to bulk production

Chemicals

Chemicals Research
Design, optimize and make chemicals suited for a specific commercial application

A&G

Basic Research
Develop and publish novel chemistry

Teaching
Lecture and learn about chemistry

Due to their common foundation – segments share similar chemistry information needs and challenges

We have a long history in providing chemistry information and driving new developments

1817: First edition of Gmelin Handbook

1881: First edition of Beilstein Handbook

1989: Beilstein and Gmelin database go online

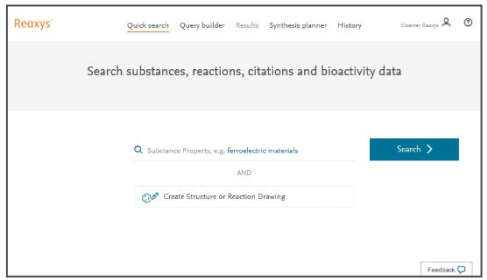
1992: CrossFire launched

2009: Reaxys launched

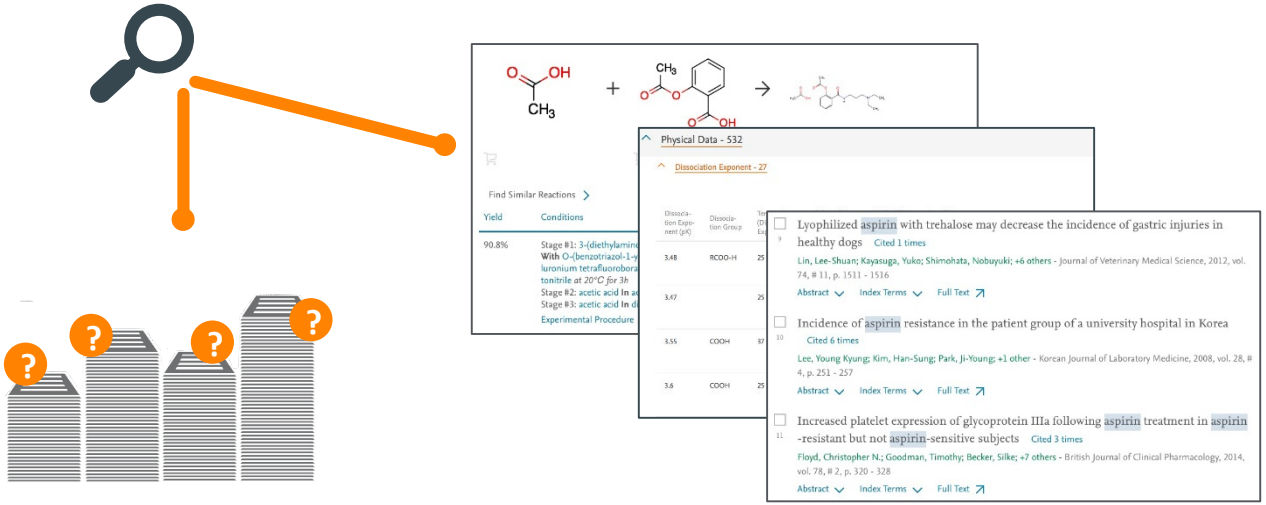
2013: Complete overhaul of Reaxys and content expansion

2016: New Reaxys launched

2017: New Reaxys Medicinal Chemistry (RMC) module



The core of our philosophy: Reaxys aims to deliver immediate access to information



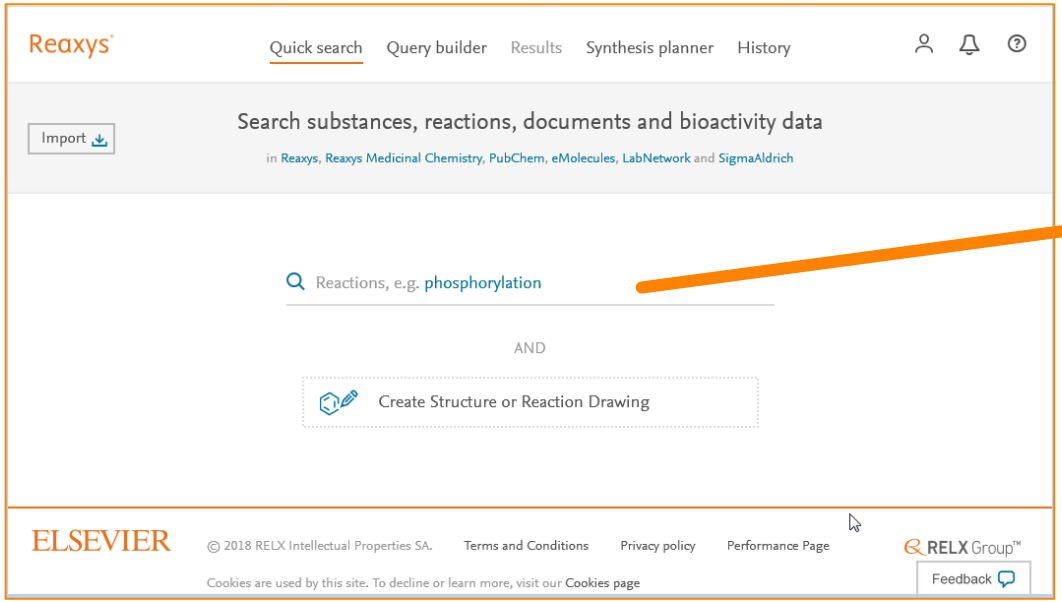
Instead of **delivering lists of references** that may be relevant to a query…

… Reaxys strives to **deliver relevant answers on the spot:**

- References ranked by relevance
- Reactions with experimental details
- Substances with extensive properties

Focus on **using** information, not searching for information

Using a clean and streamlined user interface

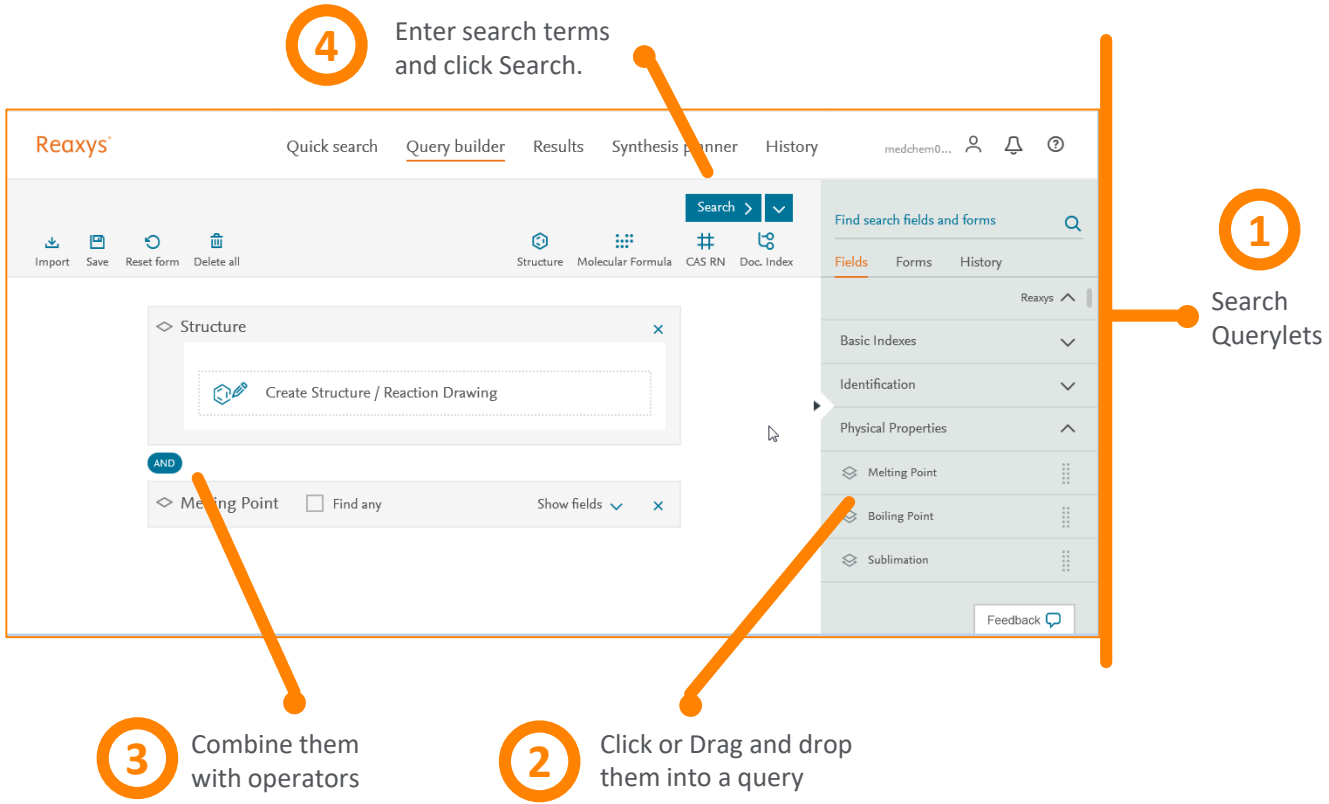


Applying user centered design, extensive user testing and Agile development methodologies helped to create a new user interface:

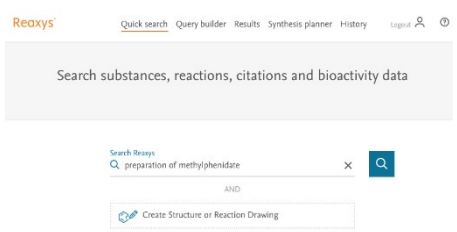
New Reaxys places powerful text and structure searches front and center on a single, easy-to-use interface.

Everyone can leverage the full capabilities of Reaxys, from first-year students to expert users

Alternatively, use Query Builder to create your own targeted queries without being an expert



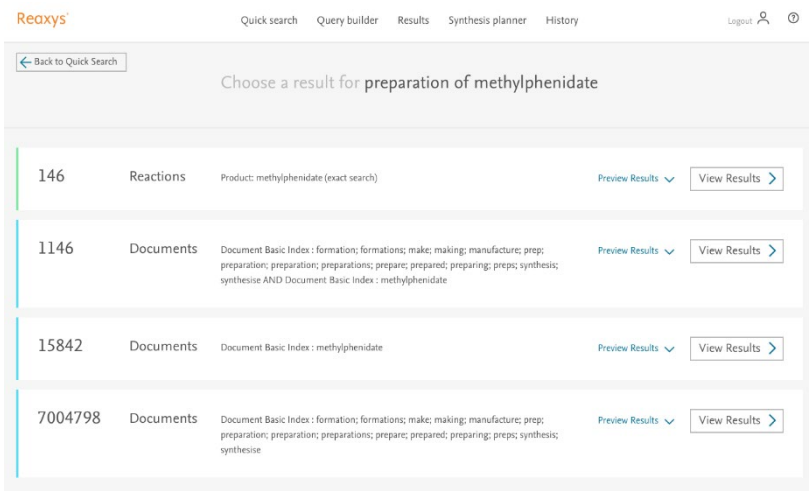
Retrieving relevant answers and anticipating needs – providing options



1 Reaxys interprets either natural language, or truncation and operators

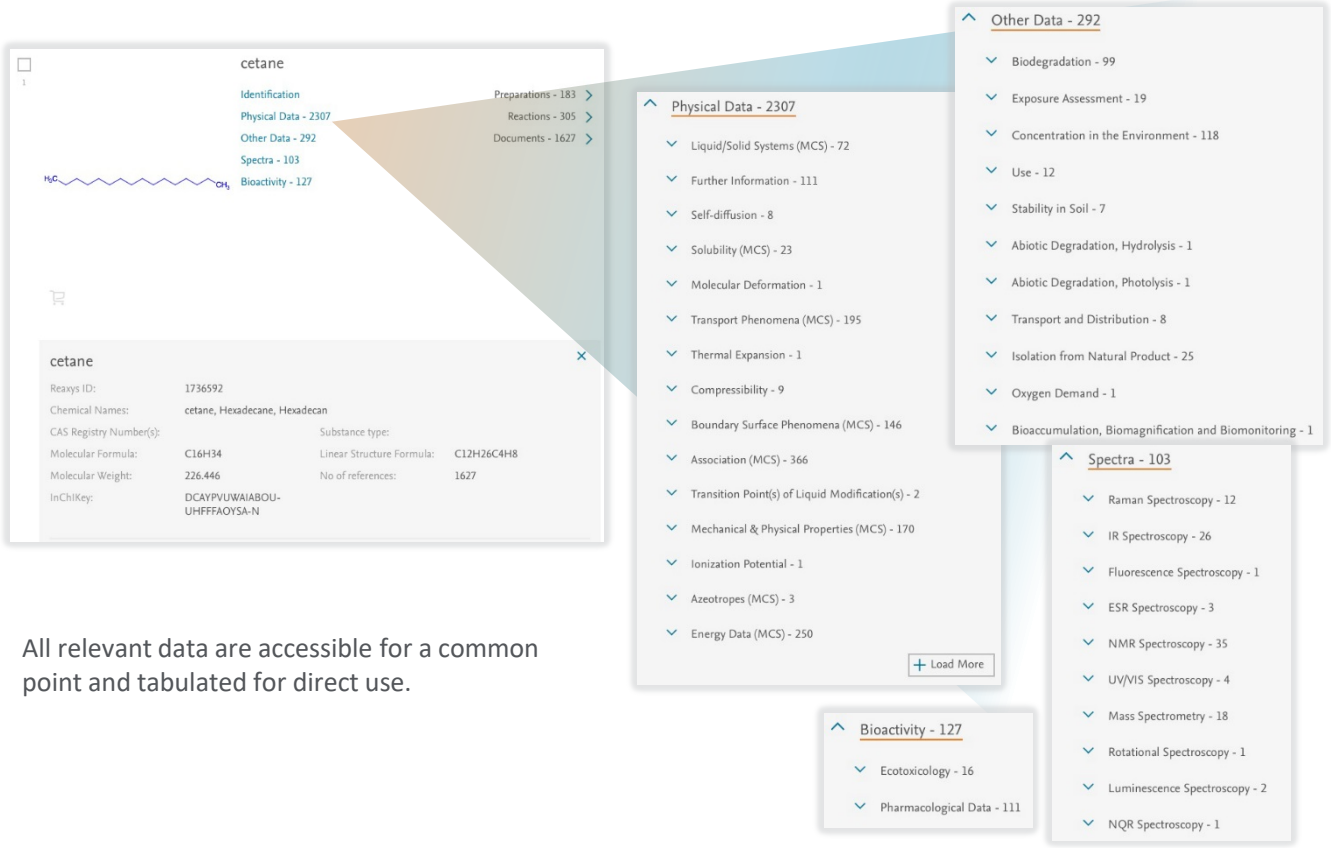
2 Recognizes search intention (reactions)

3 Delivers a ranked list of alternative results suggestions



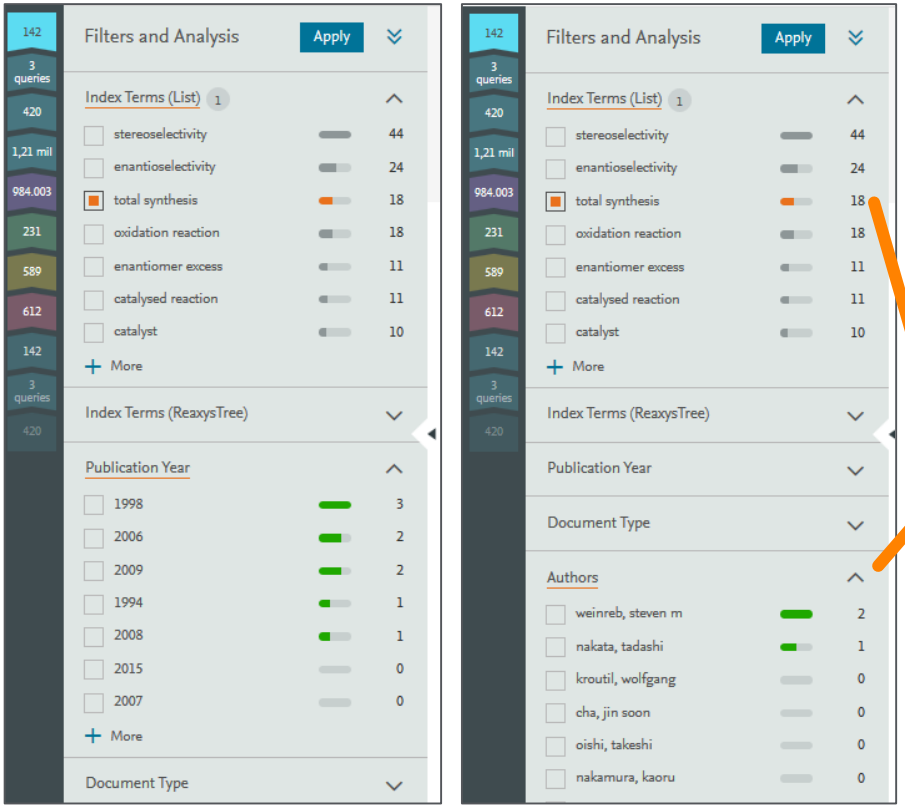
Get intended answers directly, plus relevant results you may not have considered

Presenting standardized, normalized and collated data in one record for quick and easy access



All relevant data are accessible for a common point and tabulated for direct use.

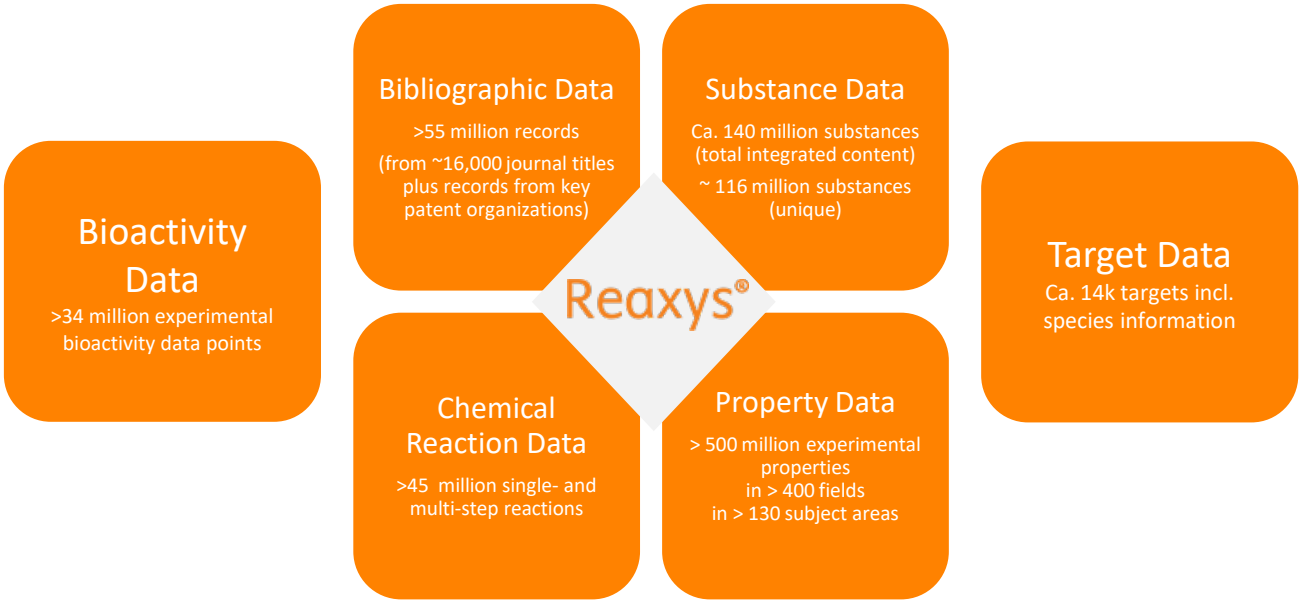
Allowing further refinement of results - Filters and Analysis are interactive for fast filtering and evaluation of results



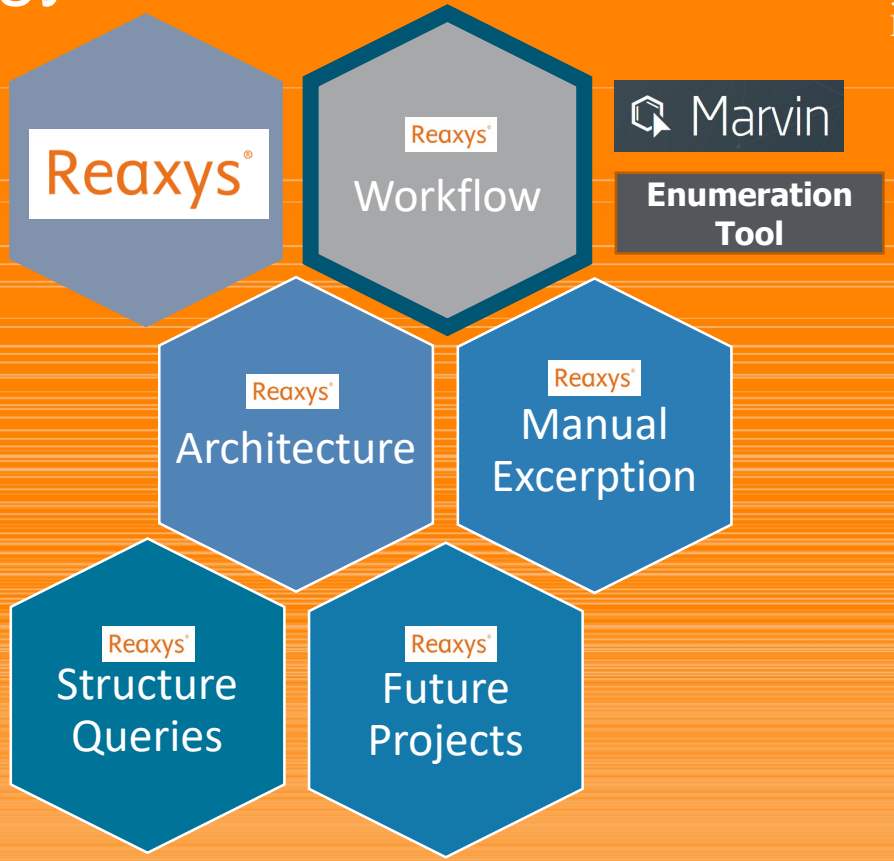
Selected index term highlights corresponding records in other filters

What does Reaxys offer to support chemistry researchers?

Reaxys and Reaxys Medicinal Chemistry provide access to 6 key chemistry subject areas



ChemAxon's technology in Reaxys



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ChemAxon

Reaxys Workflow (simplified)

SOURCE

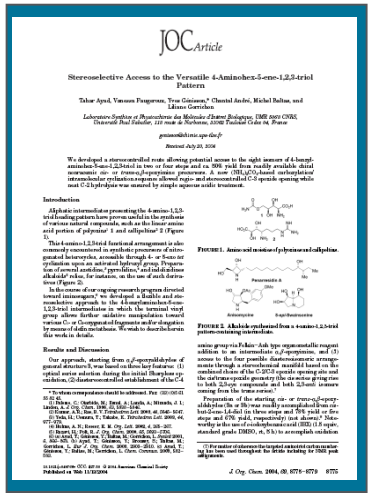
Automatic extraction of data

Excerption program

Database production

Reaxys DATABASE

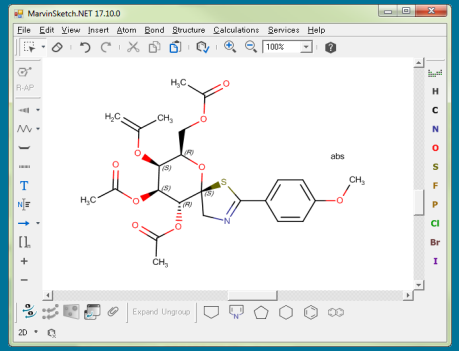
Paper or electronic file


JOC Article

Stereoselective Access to the Versatile 4-Aminohex-5-ene-1,2,3-triol Pattern

Manual excerption

Structures, Markush, chemical names, NMR, IR, MP, USE, …
Reactions, temp., solvent,…
Targets, MedChem data

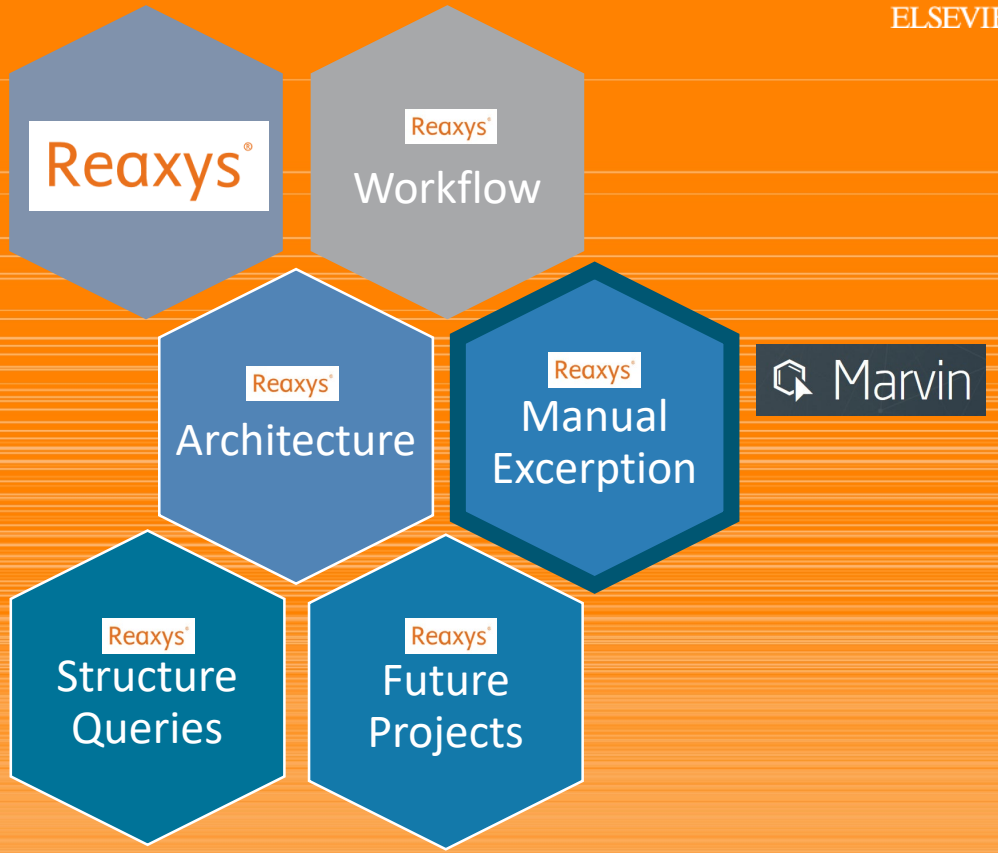


Marvin

iEI (intuitive Excerption Interface)

Reaxys®

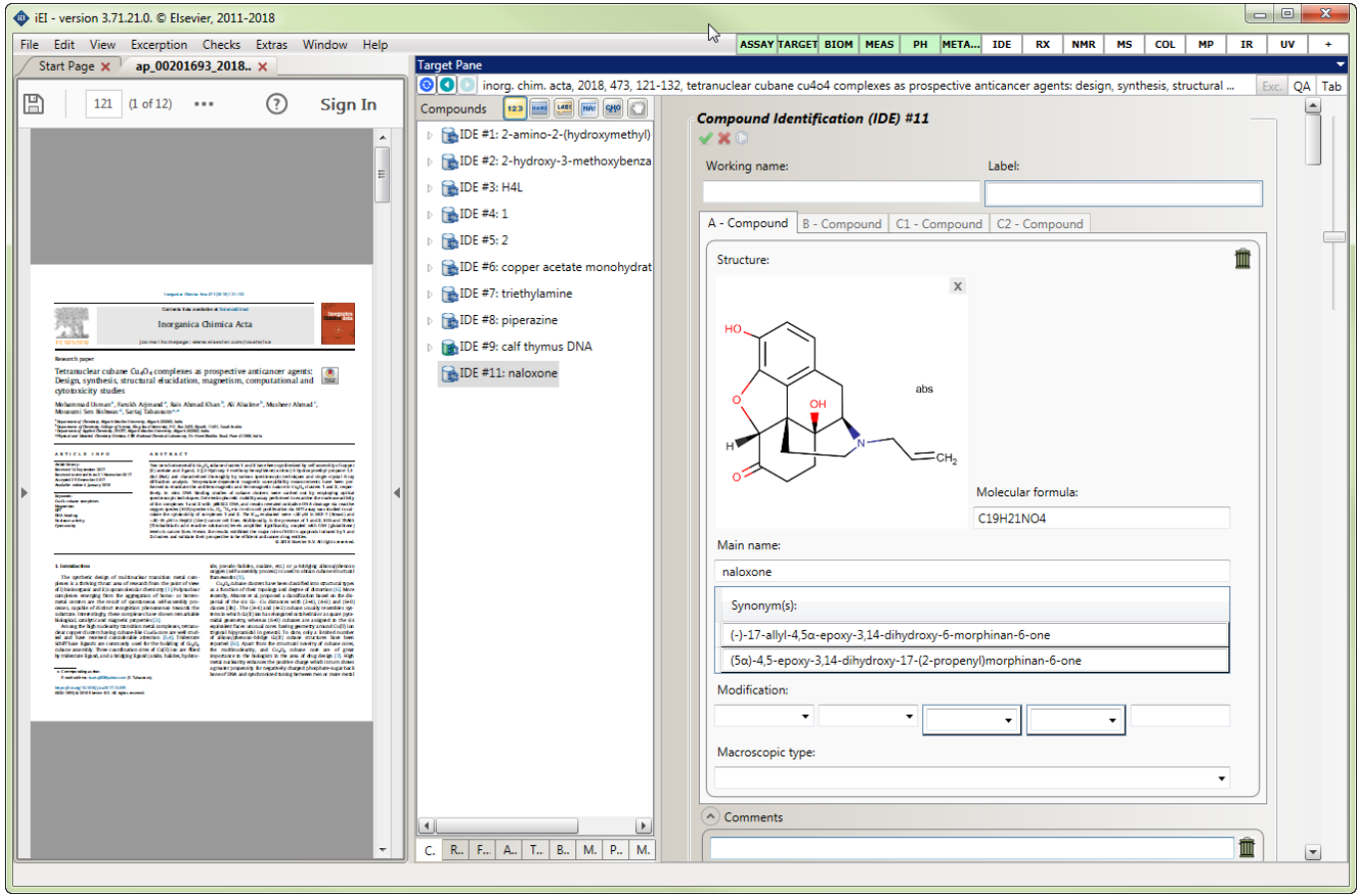
ChemAxon's technology in Reaxys



ChemAxon

ChemAxon Marvin Sketch in Reaxys excerption

Marvin



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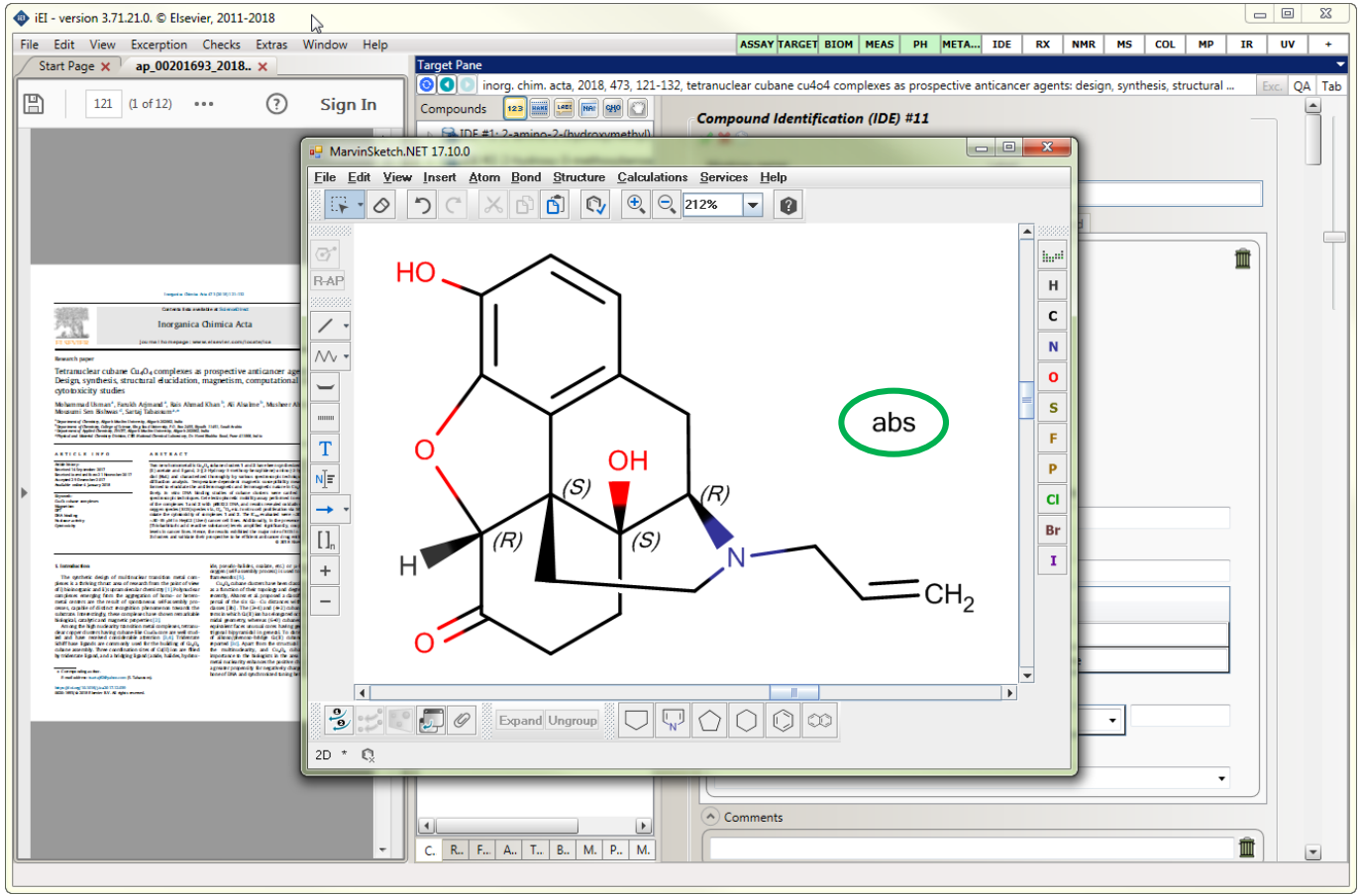

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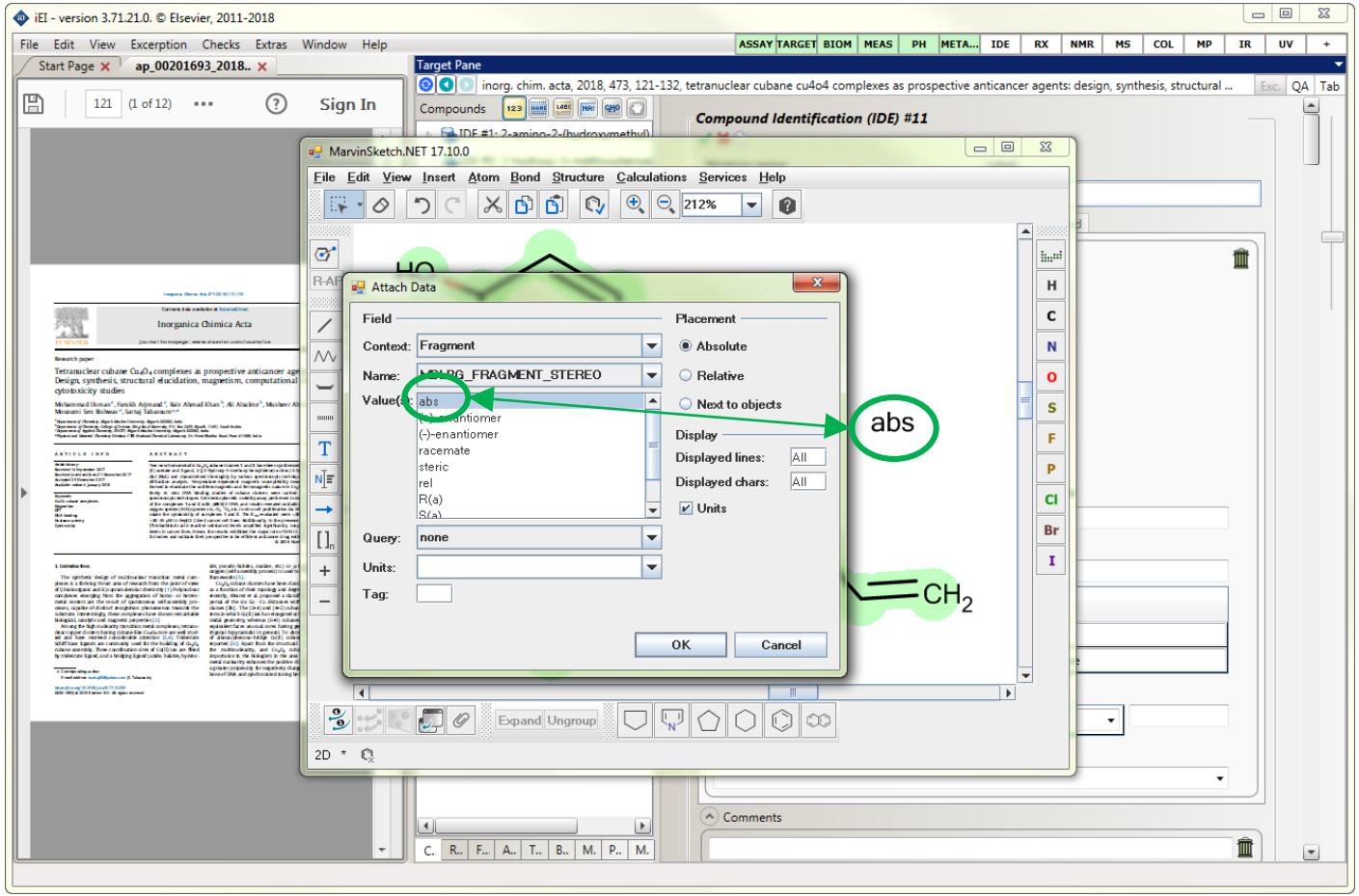
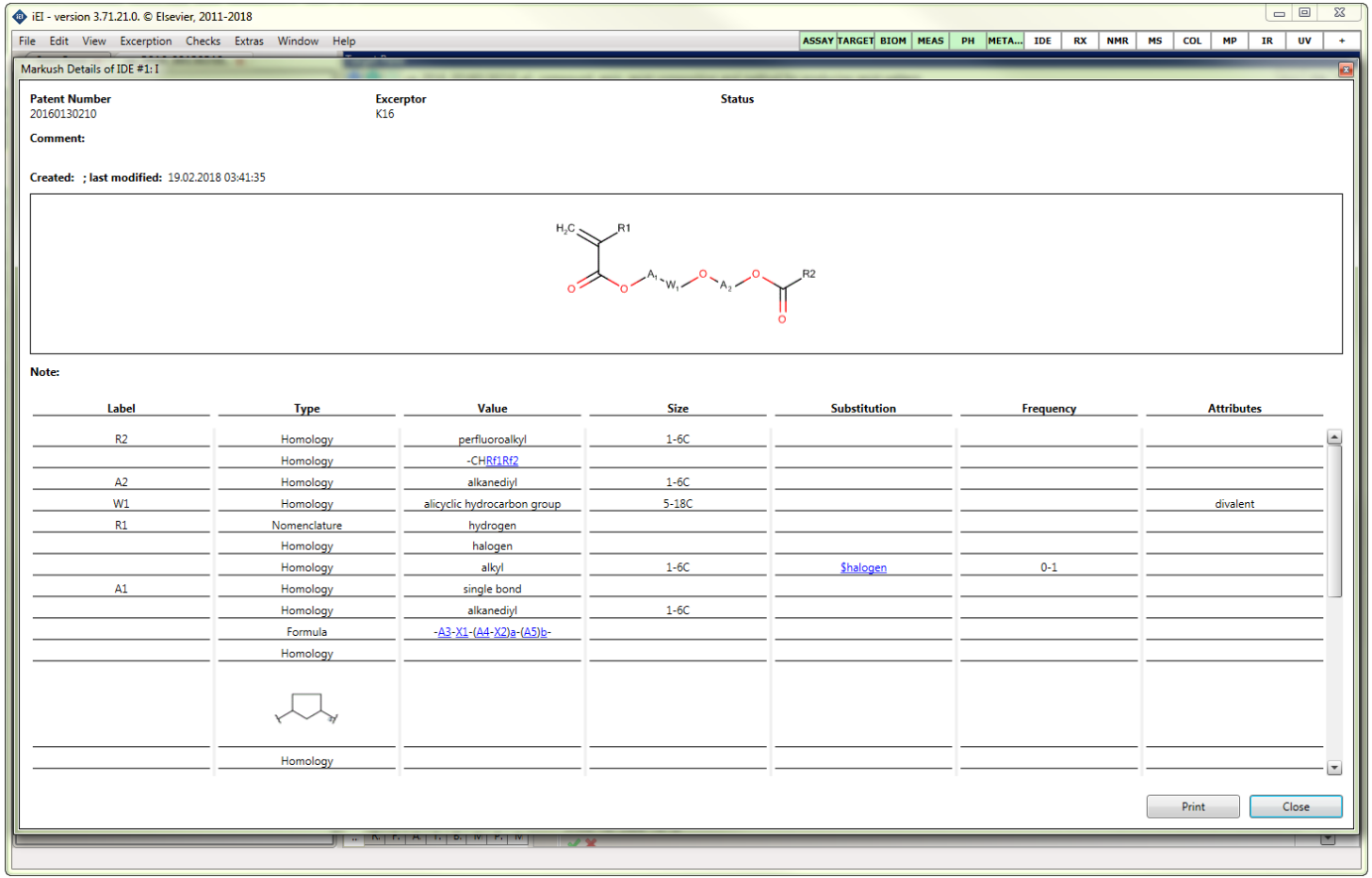


ChemAxon Marvin Sketch in Reaxys excerption - Markush structures



ChemAxon Marvin Sketch in iEI - Markush structures

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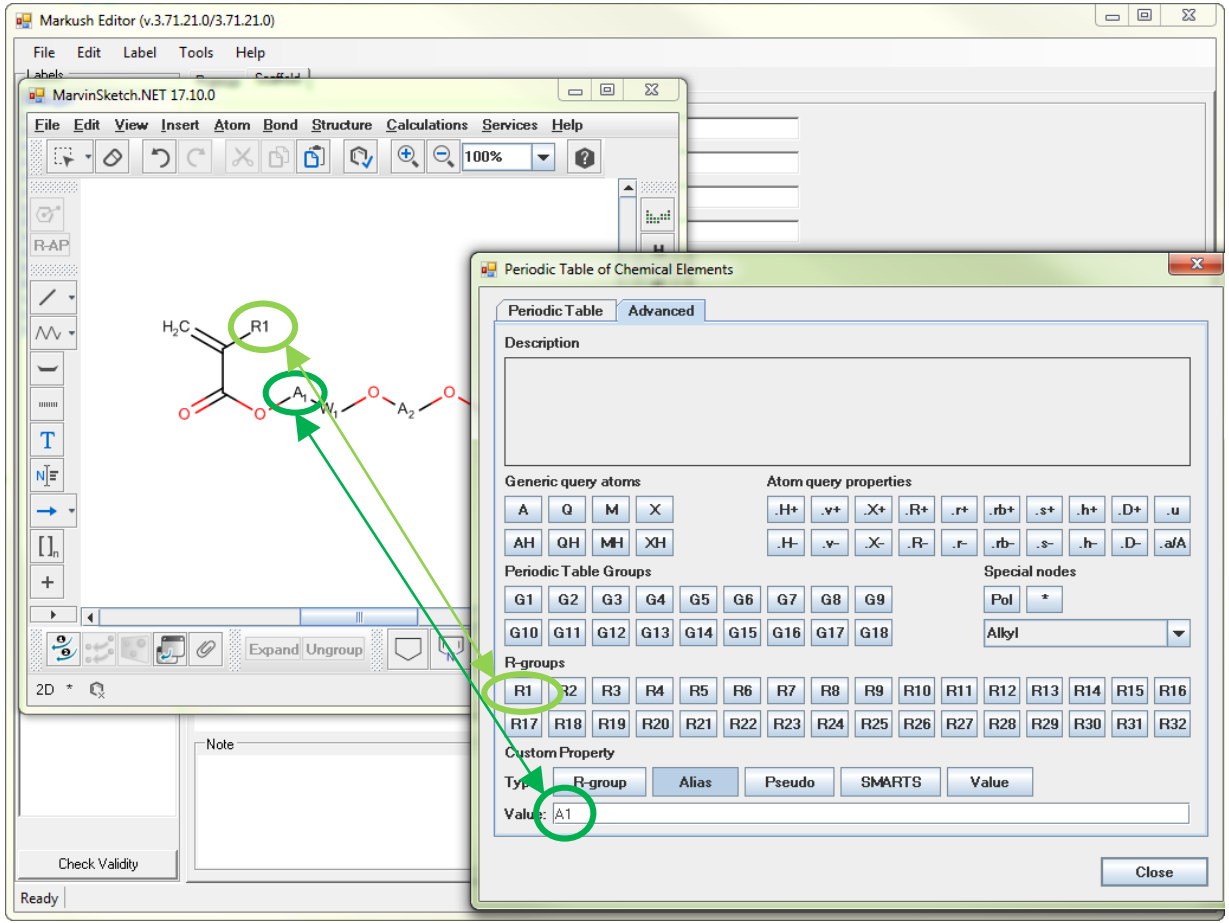
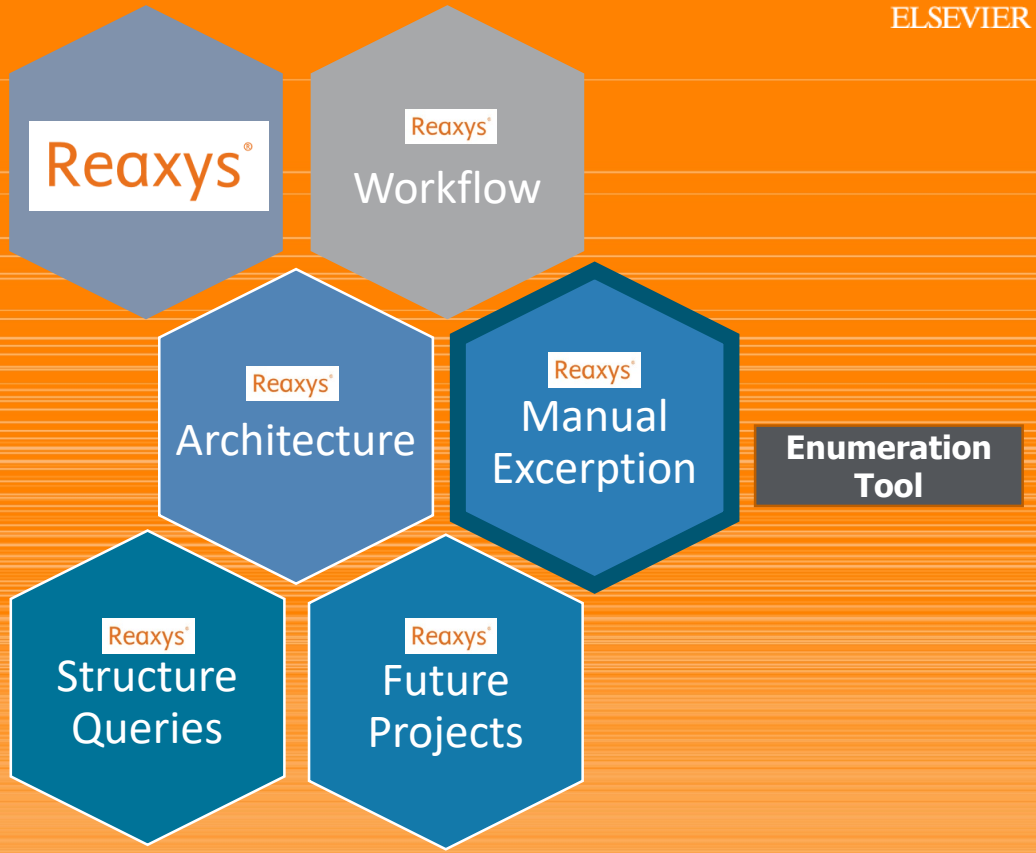


ChemAxon's technology in Reaxys



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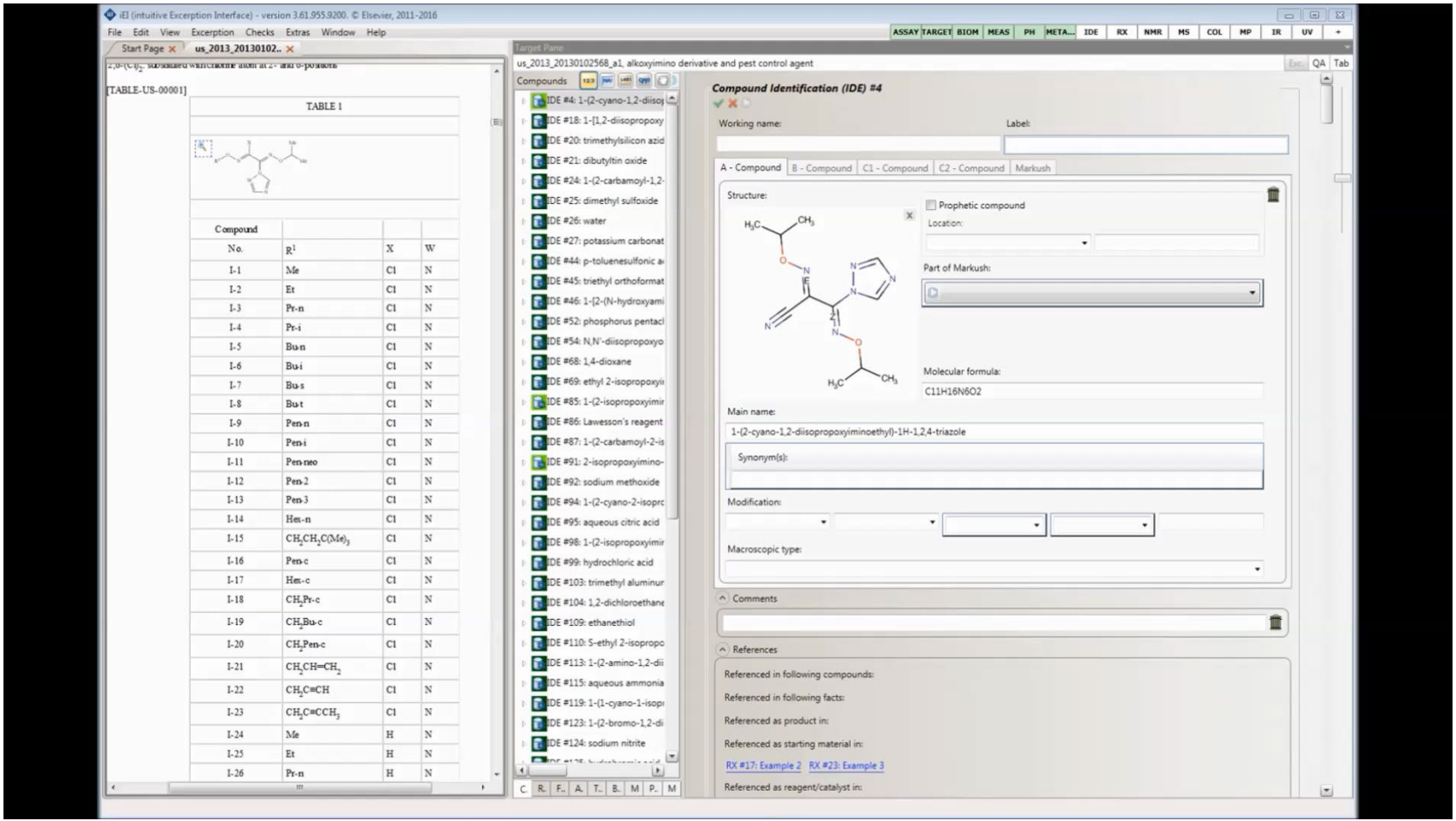
ChemAxon

ChemAxon Enumeration Tool in iEI

Enumeration Tool

Marvin



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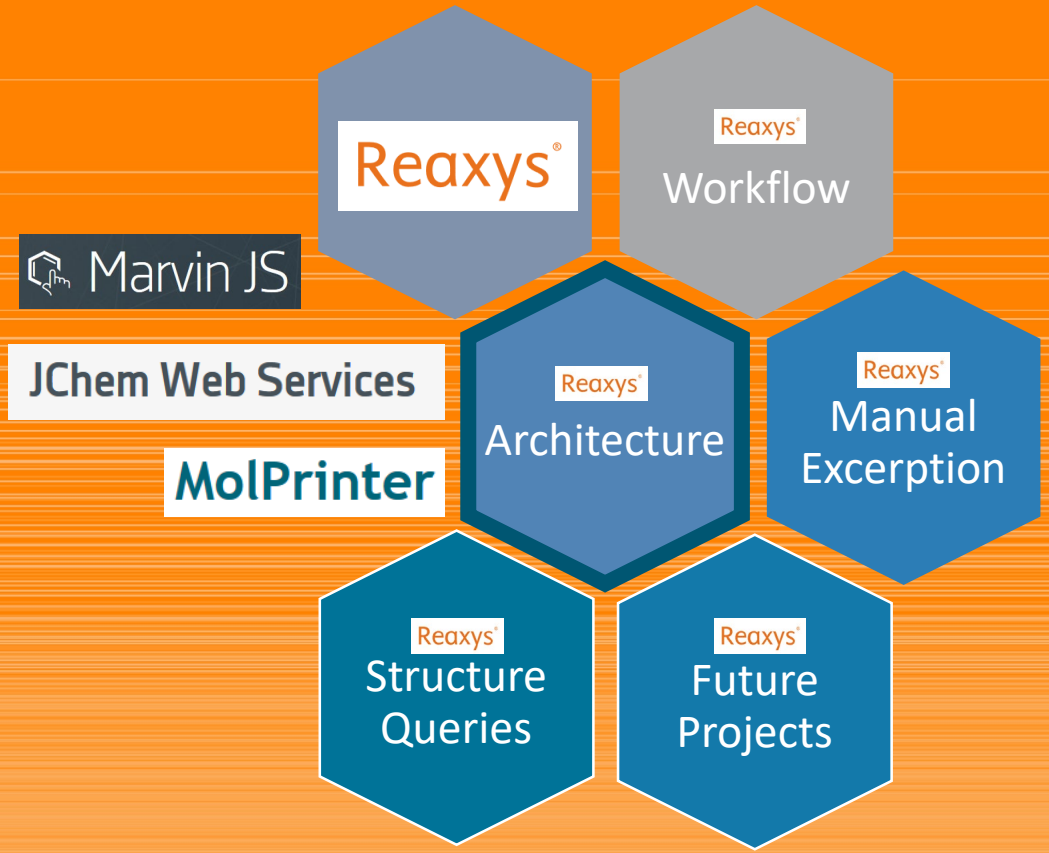

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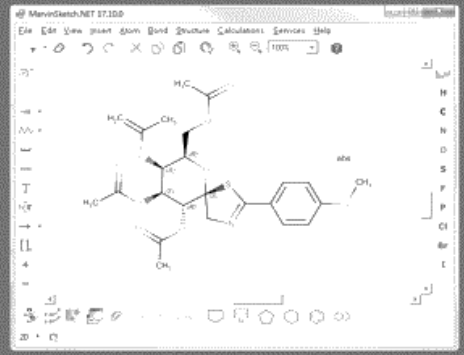
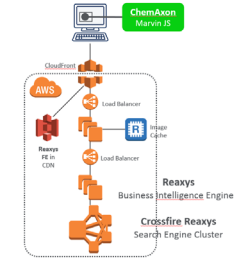
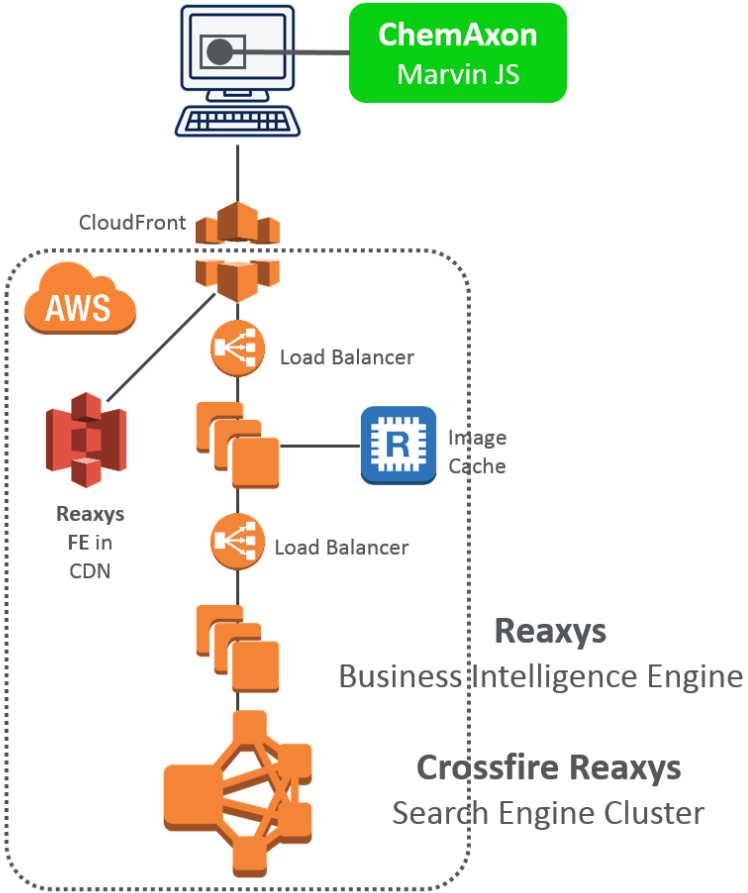


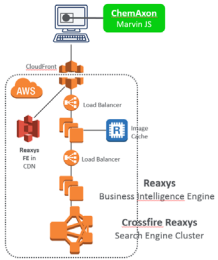
iEI (intuitive Excerption Interface)



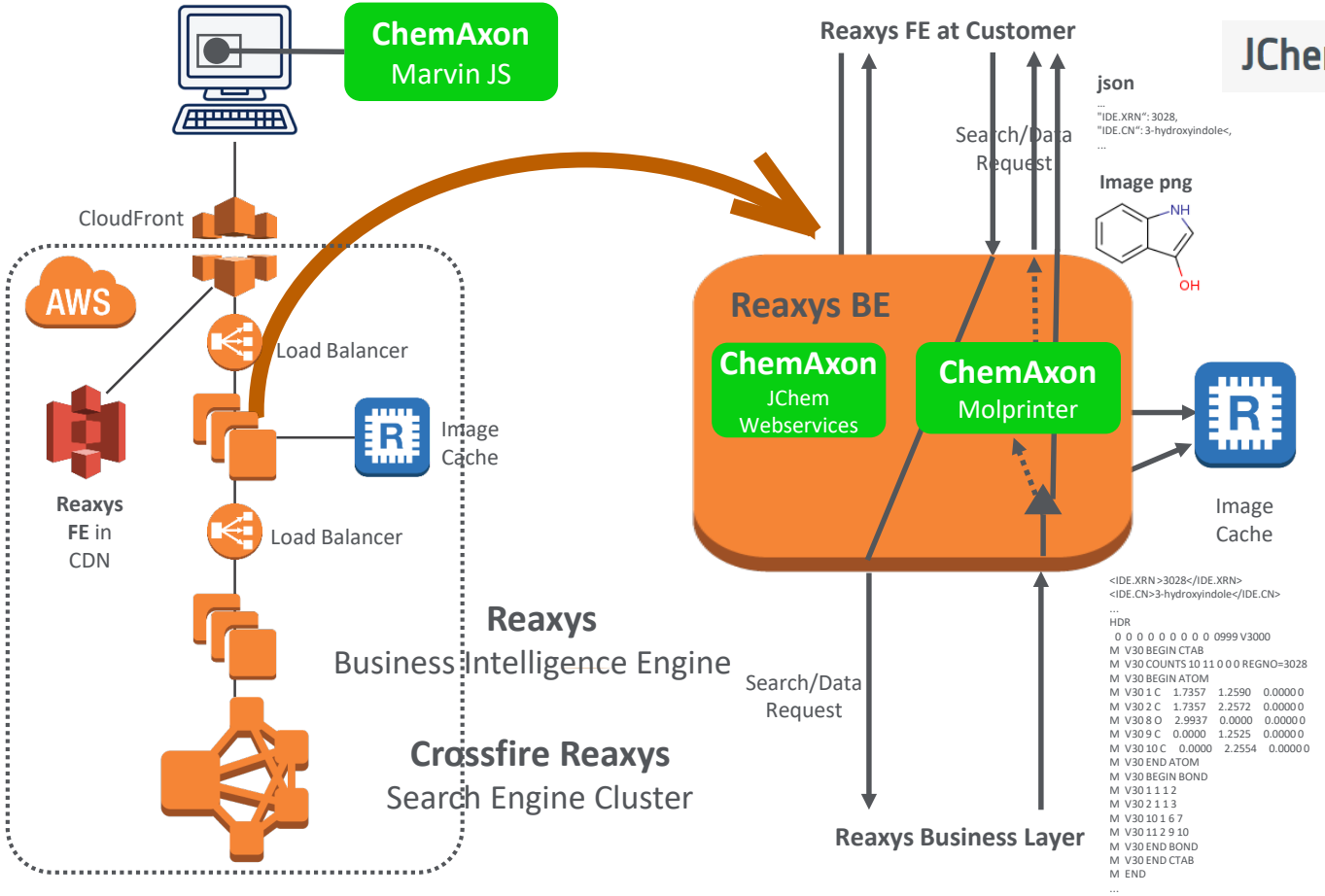
Reaxys Architecture Diagram (simplified)

Marvin JS





Reaxys Architecture Diagram (simplified)

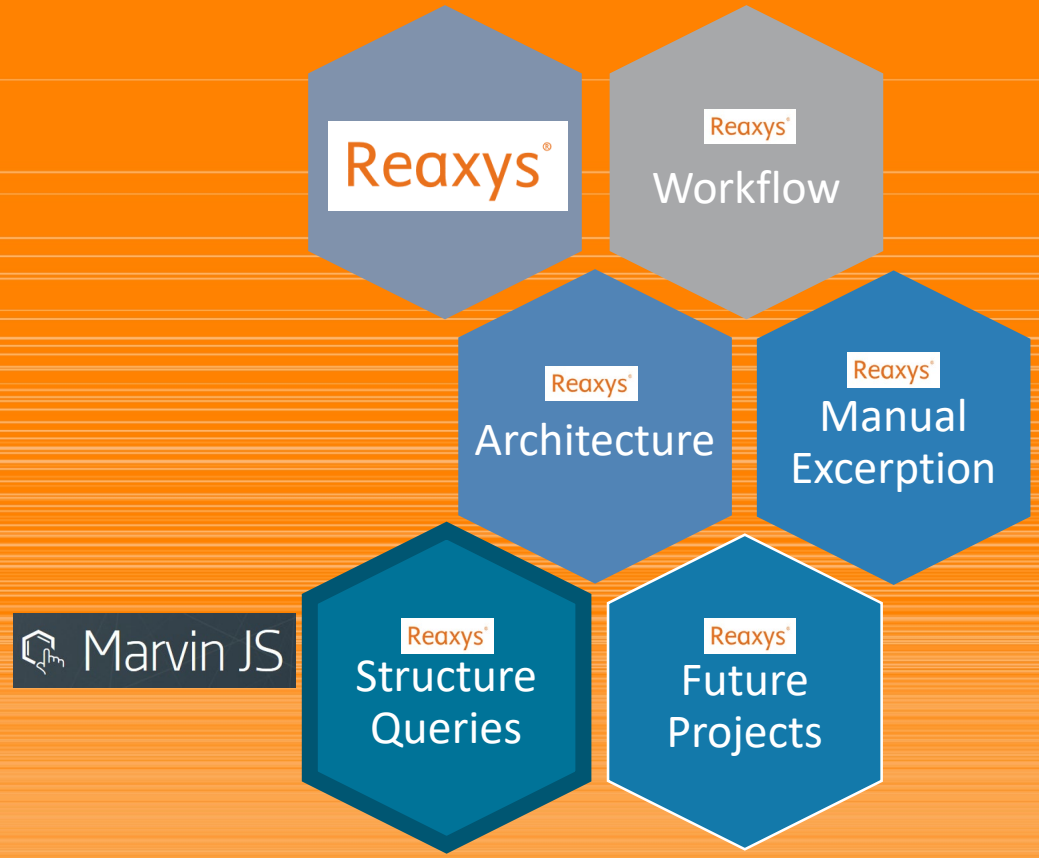


Marvin JS

JChem Web Services

MolPrinter

ChemAxon's technology in Reaxys

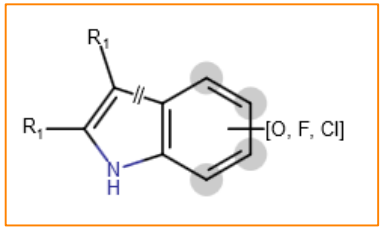


ChemAxon

Key Reaxys Use Case: Reaction Searching and Synthesis Planning

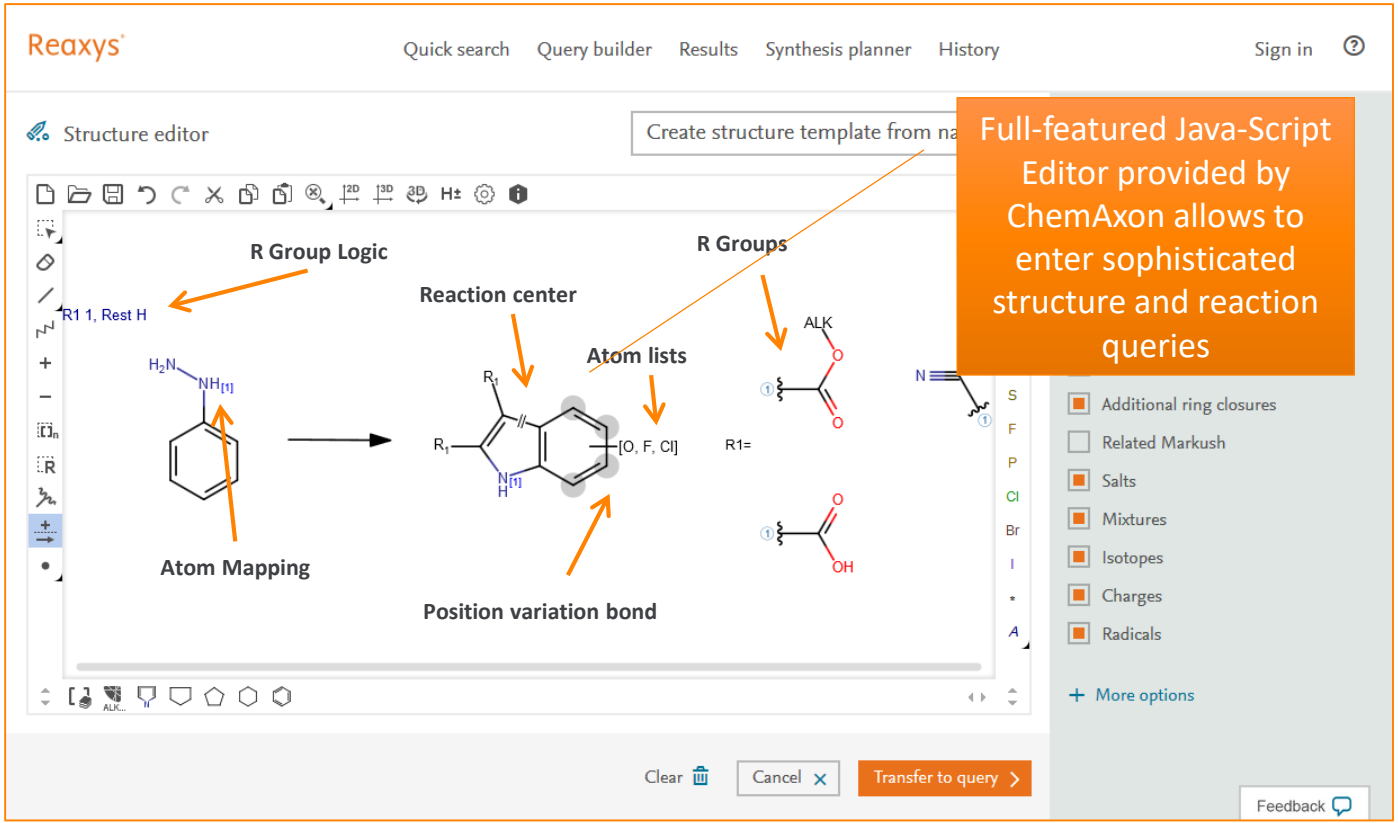
Marvin JS

- **Using MarvinJS to enter even complex reaction queries**
  - Find preparations for a substituted indole based on a sophisticated substructure query



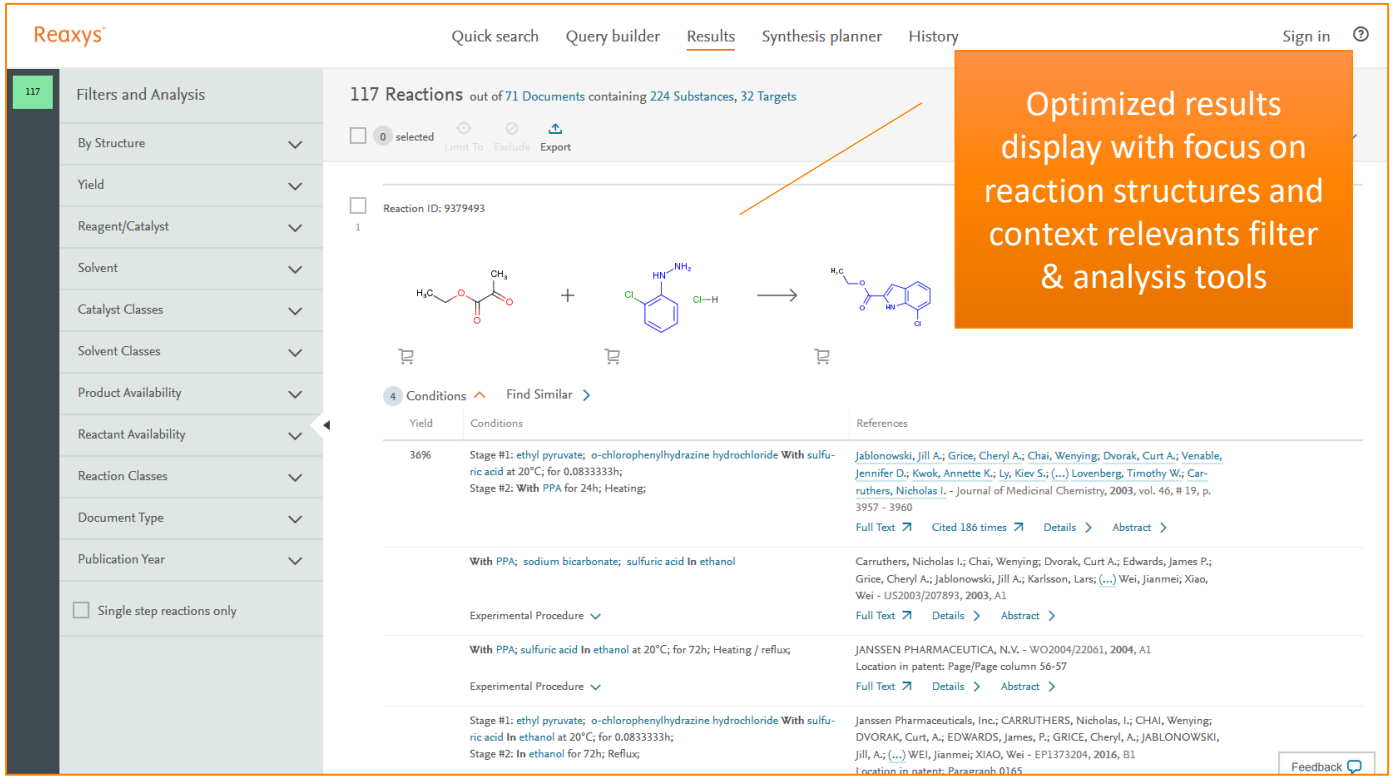
Key Reaxys Use Case: Reaction Searching

Marvin JS



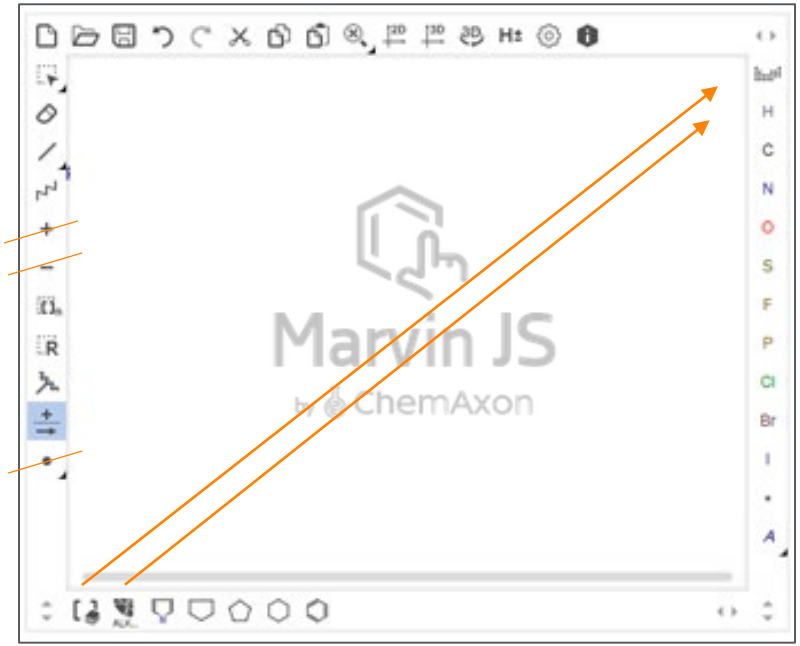
Key Reaxys Use Case: Reaction Searching

MolPrinter

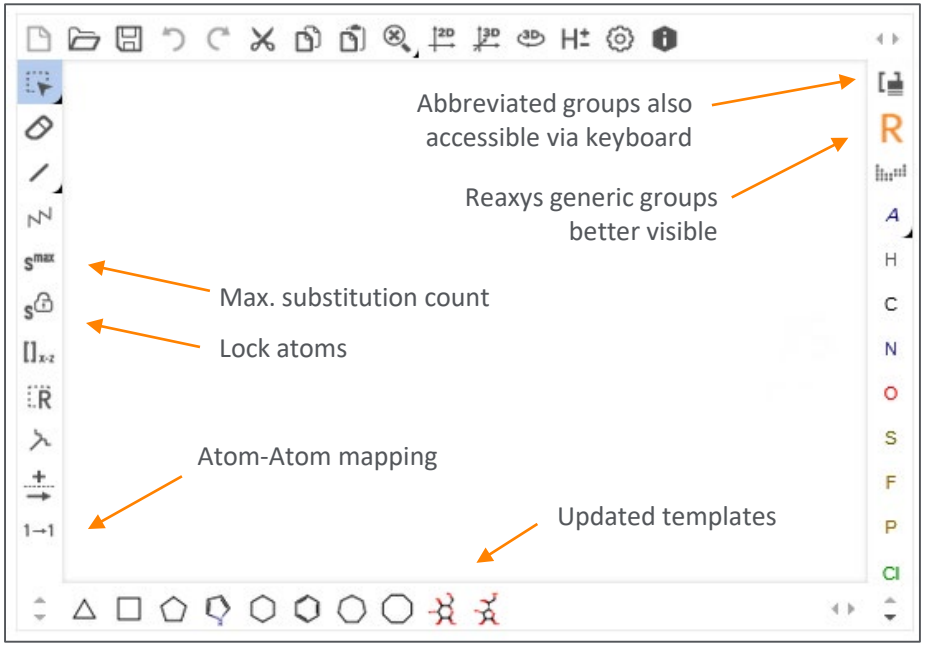


MarvinJS Usability Improvement Project

- **Originally integrated MarvinJS version was not optimized for Reaxys users**
  - ChemAxon and Elsevier exchanged end users feedback and came up with an improvement plan

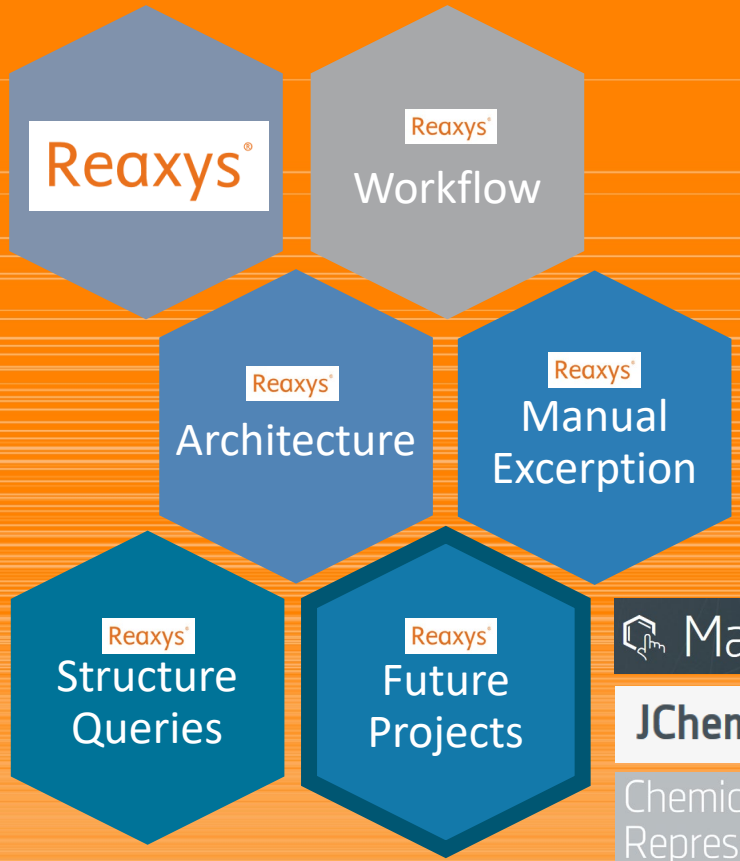


Old version



New version

ChemAxon's technology in Reaxys



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ChemAxon

Ongoing & Future Projects – Predictive Tools

Marvin JS

MolPrinter

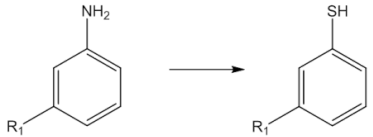
JChem Web Services

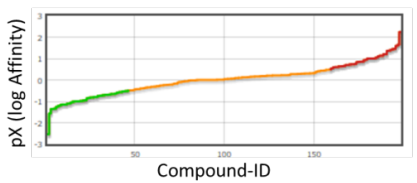
Chemical Structure Representation Toolkit

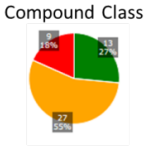
Using Reaxys Medicinal Chemistry bioactivity data to build predictive tools

- **Bioisosteric replacements**
  - Enhance affinity
  - Correct an ADME problem
  - Overcome an IP issue

"What should we make next?"

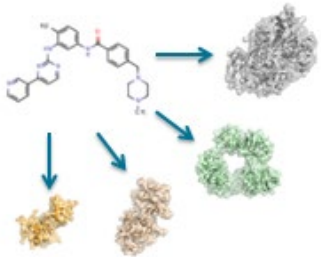






- **Target prediction**
  - Primary activity
  - (un)favourable side effects
  - Drug repurposing

"What can we expect from our compound?"



- Use of **Marvin JS** for rendering chemical structures and for formulating the chemical structure on the query page
- Use of **ChemAxon Server Tools** for transforming molecular sketches into SMILES and 3D structures, handling molecular topologies and creating molecular images

ChemAxon’s technology in Reaxys

Thanks for your attention!

Thanks to Elena Herzog, Stefan Roller, Olivier Barberan, Rosalind Sankey, Jürgen Swienty-Busch, and Pieder Caduff

Ralph Hössel

ChemAxon’s technology in Reaxys

Next slide is the abstract

Abstract

ChemAxon's technology supporting Reaxys and Reaxys Medicinal Chemistry (RMC) production, searching and visualization workflows

Ralph Hössel[1], Elena Herzog[1], Stefan Roller[1], Olivier Barberan[1], Rosalind Sankey[1], Jürgen Swienty-Busch[1], Christian Böhm[1] and Pieder Caduff[2],

[1] Elsevier Information Systems, Frankfurt am Main, Germany, [2] Elsevier Life Sciences IP Ltd, UK

Reaxys and Reaxys Medicinal Chemistry (RMC) is a first-class chemistry solution designed to support chemistry, pharma, environmental & material research. Its user-friendly and intuitive interface offers retrieval of a wide range of chemistry data which is stored & managed in a robust database. This is supported by a wide range of chemistry related search functionalities, including structure and reaction search, property search and NLP supported text search based on continuously updated and expanded taxonomies focused on chemistry and pharmacology disciplines.

Reaxys and RMC's end-to-end processing workflow embeds and employs ChemAxon's technology in various stages and processes; from supporting manual excerption of factual data from full text publications (literature articles or patents), for chemical entity visualization, annotation and enumeration, and for advanced structure search and retrieval functionalities. ChemAxon's technology also provides presentation of structures and molecules to the end-user on the Reaxys and RMC's User Interface. The focus of the presentation will be on demonstration and usage of ChemAxon's cheminformatics tools and applications in Reaxys and Reaxys Medicinal Chemistry.

intuitive Excerption Interface - iEI

- **iEI (intuitive Excerption Interface) is a Windows-based, locally installed software for manual excerption of chemistry and MedChem data**
- **iEI is embedded in the overall Reaxys and RMC workflow**
- **iEI ensures high data quality by…**
  - using **taxonomies** or completely fixed vocabularies (185) for nearly all text fields
  - well organized excerption masks
  - More than 1000 check rules, 150 of them purely for Reaxys MedChem, 50 purely for chemical structure issues
- **iEI ensures high efficiency in excerption by…**
  - providing hyperlinks between related objects (e.g. between assays and data points, or compounds and reactions etc)
  - providing several overviews from different angles (compounds, pharmacological data, physical data, reactions, etc)
  - providing tabular views for quick entry of similar data sets
  - various copy and paste features
- **iEI exports the final data set in a way that it can be loaded into the Reaxys data base, ensuring that all checks have been run**