From Library Design to Compound Delivery – Data Management in a CRO Perspective

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ComInnex Overview

• 25 years of experience (as ComGenex/AMRI/ComInnex) in working with top pharma companies from US-Europe-Japan
• A drug discovery service provider for pharma, biotech and agrochemical industries:
  - Screening compound libraries
  - Novel scaffold design
  - FTE based custom chemistry and medchem
  - Fixed fee custom synthesis
• Unique combination of technologies and know-how
  - Technology-enabled chemistries
  - Integrated production IT system
  - High throughput chemistry and purification
Use Case: Compound Library Services

1. Small scale structure design
   - Focus on feasibility and novelty
   - Technology enabled aspects
2. Library building
   - KNIME workflow with ChemAxon tools
   - Data collected from the ELN and the new core design
3. Production of selected compounds
   - KNIME – ELN/LIMS connection
   - Standardization, uniqueness checking, capturing production info
4. Analysis-purification-assignment-delivery
   - „LIMS controlled”

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Library Design Strategy

• Traditional chemistry sequence ensures large chemo-type diversity among key intermediates and final libraries

• Technology-enabled step with proprietary synthetic know-how
  – Enhances IP security and novelty via unique technick
  – Increases synthetic scope and success rate
KNIME-based Workflows

Collecting building blocks, reagents
Library enumeration
Substructure filtering

Diversity filtering
Stereochemistry filtering
Phys chem property filtering

Cost optimization
Library generation
Reaction generation for the selected products

Database Read
Molecule Type
CactChem Fingerprint
Missing Value
already delivered compounds
Node 44
Node 40
Node 49

Fingerprint Similarity
Node 37
Node 30

CSV Reader
Number To String
Joiner
Column Filter
SDF Extractor
CSV Reader
Number To String
Joiner
Node 57
Node 54
Node 50
Node 58
Node 60

SDF Reader
scaffold-reagent info
Column Filter
CSV Reader

SDF Writer
processed VL to diversity calc

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Integration of Tools

- Library enumeration – Reactor
- Property filtering – Calc. plugins
- Substructure filtering – MolSearch
- Stereochemistry
- Diversity calculations

KNIME / RDKit-Python

- KNIME controls the design process
- Diversity calculations – custom Python module (to be incorporated in KNIME)
- “Chemistry know how” incorporated into the enumeration

„Chemistry know how“ incorporated into the enumeration
Production ELN/LIMS System

Standardization
Ordering of reagents
Production of compounds
NMR assignment
Qualitative analysis
Sample / vial / container handling
Delivery and/or storage
Components and Connection Points

Inventory and logistics: reagents, vials, orders, etc.

LIMS features: analytical requests, automation...

ELN features: procedures, stoichiometry, etc.

Reaction tree handling

Structure searches (duplicate, full fragment, substr.)

Non-chemical data management

JChem + Standardizer

Compound, production, reagent, inventory, analytical measurement data
Typical Lab Software Architecture

ComInnex aspects:
- Instrument data upload automated as much as possible
- Strict project handling
- Visualize the status of a production/container from its creation to delivery/storage
- Two-way integration with the design workflows:
  - New libraries automatically feed target reactions into the ELN
  - Selection of reagents based on previous usage, price, etc.
Summary

Powerful tools

Integration of the tools, minimal user intervention should be required

Guide/control the design/production process

Requirements
Thank you for your attention!