Automated Workflow for Building a Compound Structure Database Using ACD/Spectrus Platform

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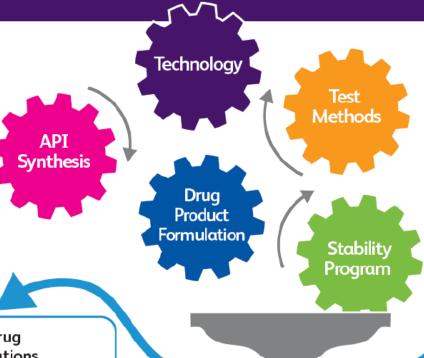




# PHARMSCI **SMALL MOLECULE**

Leader in the design, development and clinical manufacture of innovative medicines

Ensuring robustness and repeatability throughout the development process to deliver new medicines to patients across the globe



Designing the final Drug Product is an iterative operation where optimization of any component can impact the other components

### New Drug Applications

Chemistry, Manufacturing and Controls

- Define acceptable composition
- · Demonstrate Retention of quality over time
- · Define Methods for ensuring quality
- · Provide Manufacturing 'Recipes'
- · Specify Qualified Manufacturer(s)
- Demonstrate the suitability of methodology for manufacturing & testing
- · Provide actual samples of API and DP

### Active Pharmaceutical Ingredient (API)

Organic Chemistry & Manufacturing Science

 Develop recipes for scaling up manufacturing to produce required quantities that are safe to run while minimizing impurities

#### Drug Product

Formulation Design

 Develop a dosage formulation that ensures uniform and precise distribution of the active ingredient with other inert components to deliver the desired response upon dosing

# Clinical Supplies

Clinical Supply Manufacture

- · Acquire Starting Materials
- Manufacture API and DP
- Complete quality testing at each step of the process
- Store bulk dinical supplies until needed for a Clinical Trial
- Dispense and distribute Drug Product for Packaging & Labeling

### Process, Product & Analytical Development

Processes are designed, developed and constantly tweaked to yield a safe, reproducible, cost effect path to a stable, manufacturable Drug Product Formulation with optimal bioperformance. Developing technologies are utilized in all aspects of the development process, while scientific knowledge in these areas is utilized to aid in the selection of the final drug molecule.

#### Manufacturing

Requires identification and sourcing of Raw Materials, execution of multiple organic synthesis and formulation steps and in-process analysis to ensure the manufacture is proceeding as expected.

#### **Analytical Test Methods**

Developed to match each step of the manufacturing process, testing is utilized to confirm quality of a drug and its precursors. Approximately 70 tests are completed for each Drug Product lot released.

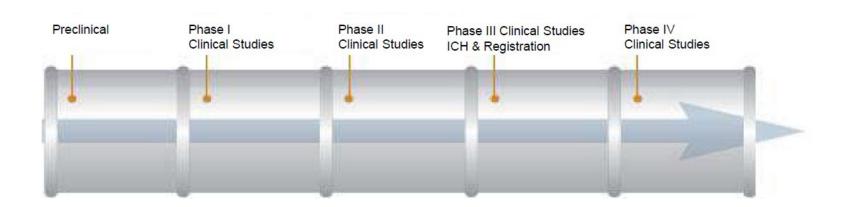
#### **Stability Program**

Allows for identification of degradation products and the pathways that create them for both API and Drug Product.
Also yields information regarding the usable lifespan of a manufactured dose.



### Analytical Research and Development (ARD)

- Development of analytical methods
- Characterization of structures
- Specifications and control strategies to enable API & drug product development
- Clinical supply release testing, and shelf-life assignment
- Support for all phases of development





### Pfizer Structure Elucidation Group (SEG)

- Global partners in small molecule Structure characterization
- Active pharmaceutical ingredients (APIs), synthetic intermediates, byproducts, process related impurities and degradants.
- Support through discovery, development, late stage, and manufacturing
- Two sites, Groton US and Sandwich UK



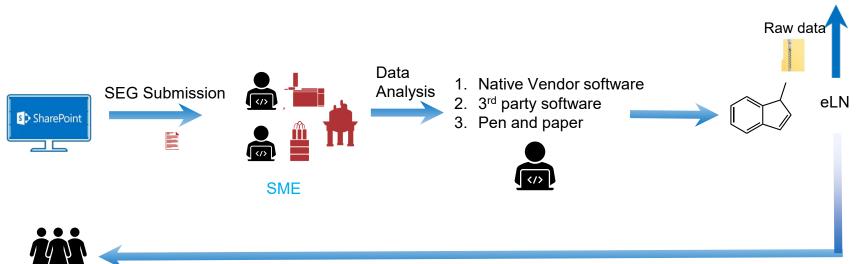
- Purification, MS, NMR, enabling technologies
- >600 structure elucidation requests per year





### **SEG Workflow**

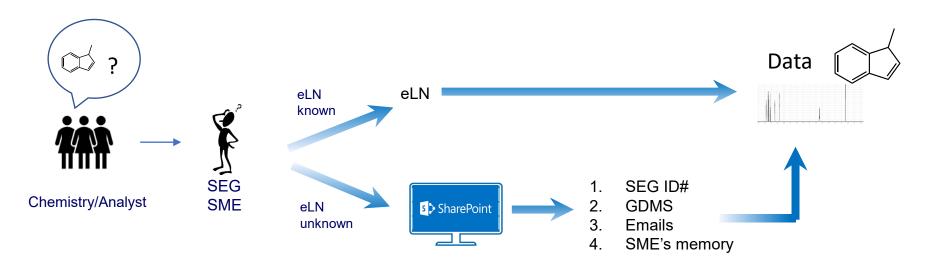






Chemist/Analyst

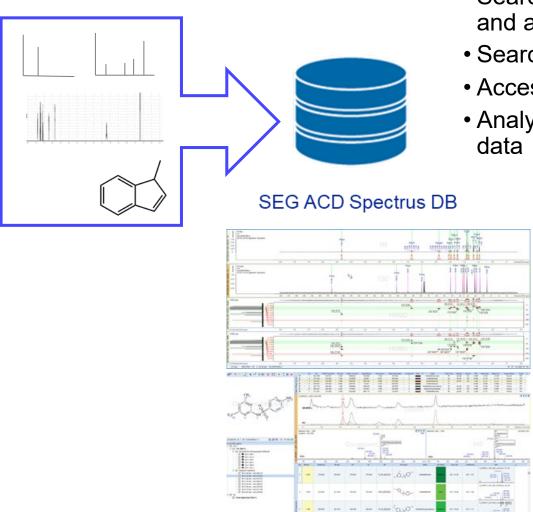
# Challenges



- Limited data searchability
- Inefficient process to respond to queries, and data investigations
- Duplication of structure elucidation efforts
- Limited data sharing between sites
- Multiple data formats



### Solution: Structure Database



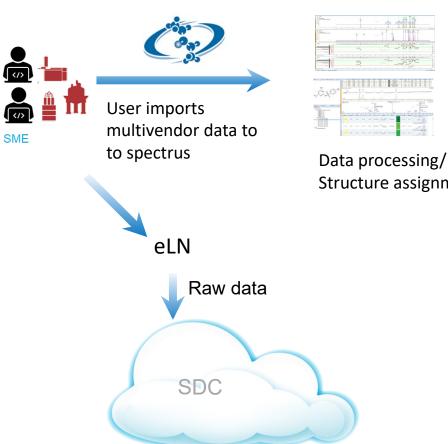
- Search by structure, PF-# and any other meta data
- Search by spectra
- Access to other site's data
- Analyst/chemist access to data

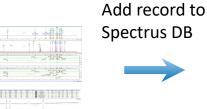






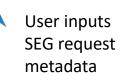
# ACD Spectrus DB workflow





Structure assignments











### **Implementation**

- Slow process
  - Users must perform several extra steps to add data to DB
- Up to user how much metadata is captured in records
  - Inconsistences across record set leads to impaired searching
- Still one DB per site
  - Different workflows
  - Different metadata captured

Need for automation





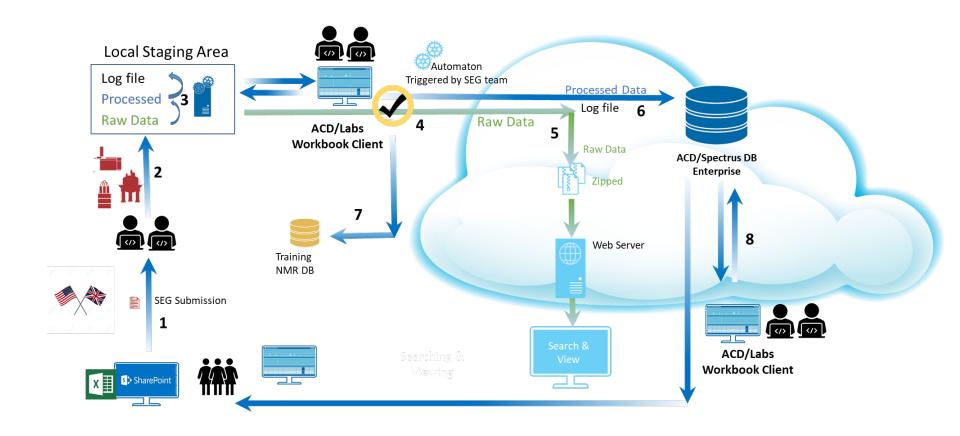
### **Goals for Automation**

- Harmonization of SEG workflows (Global SEG DB)
- Sample submission metadata automatically captured
- Raw data automatically converted to spectrus files for data processing
- Results uploaded to global DB via push of a button
- MS, NMR data, and sample submission metadata married into one record for each structure
- Raw data, full spectrus files, and processed spectrus files automatically transferred to SDC
- Selected gold standard NMR data added to an NMR prediction training DB
- Access to spectrus data in SDC via web viewer.



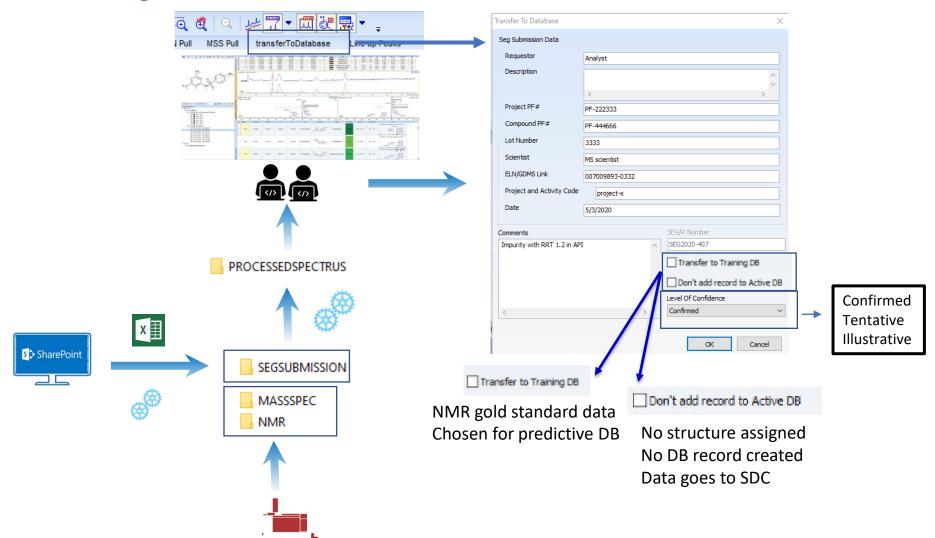


### **Automated Workflow Overview**





# Zooming in



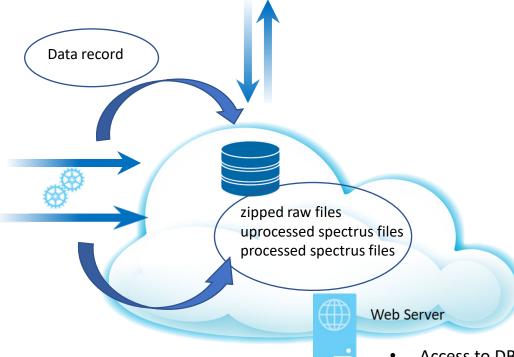


# Zooming in

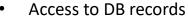
Transfer to DB triggers all data transfer to SDC



# ACD/Labs Workbook Client



Data viewing

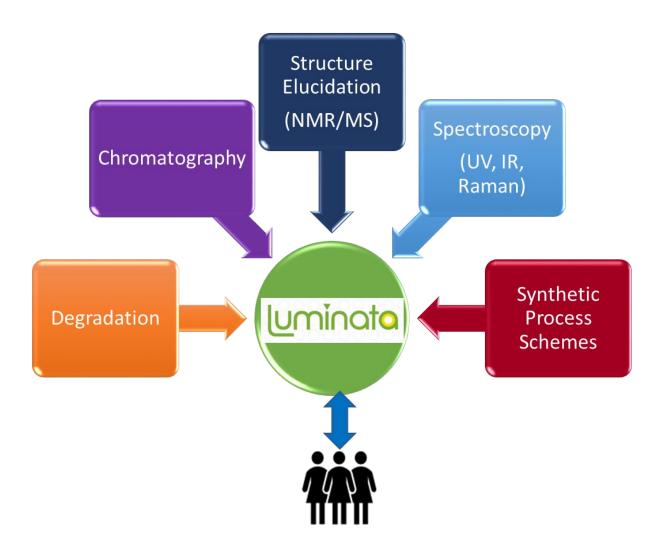


- Ability to search data
- Viewing of raw data via spectrus files





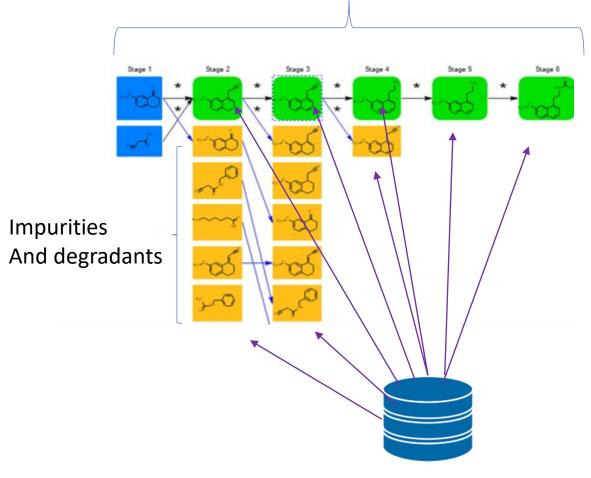
# **Looking Forward**





# Global SEG DB Integrated with all Project data

Synthetic scheme



Global Compound Database (SEG)



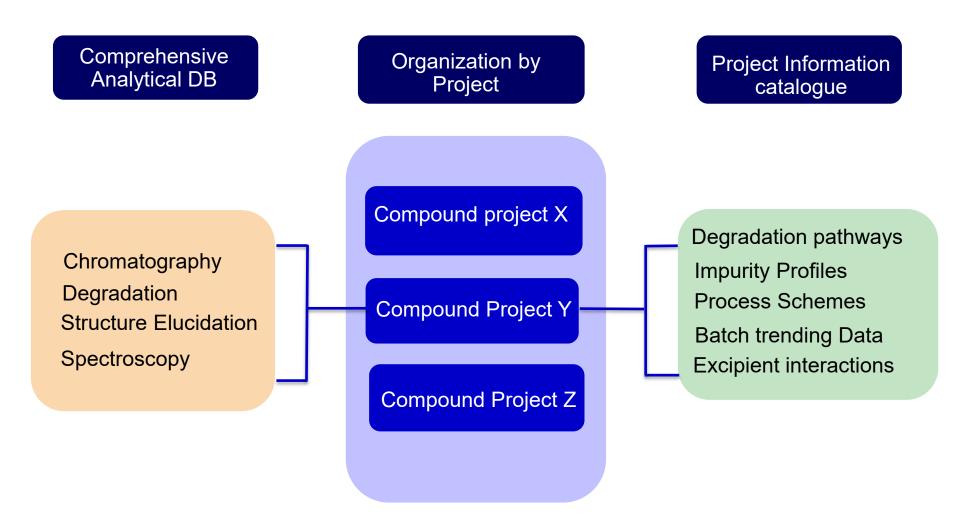


### Luminata





# **Information Library**





### Acknowledgements

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