The value of ACD/Labs software to AstraZeneca

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A Changing Business Environment

Challenges
- External cost pressures
- R&D costs/productivity
- Regulatory pressures (incl. environmental)
- Patent cliff/generic competition

Opportunities
- Focus on Quality
- Faster development times
- Changing portfolio/Externalisation
- Increasing chemical complexity

AZ Strategic Priorities
- Achieve Scientific Leadership
- Return to growth
- Be a great place to work
The Drug Discovery and Development Process

1. Medicinal Chemistry
2. Automated Structure Verification
3. IP - Naming
4. Drug Metabolism and PharmacoKinetics (DMPK)
5. Pharmaceutical Development

Research  Early Clinical Development  Late Phase Development  Manufacture and Marketing
Discovering and developing Drugs in AstraZeneca

- Small Molecule Chemistry (MW < 600) plays a key role in AZ’s business
- ACD/Labs is a key tool used in AZ’s R&D Organisation

- Medicinal Chemistry
  - *Chemsketch; NMR Predictors; PhysChem prediction algorithms*
- Drug Metabolism and Pharmacokinetics (DMPK)
  - *Markush structures; ChemFolder/Spectrus*
- Intellectual Property (IP)
  - *ACD/Name*
- Safety
  - *PhysChem predictors (Toxicology Predictors)*
- Pharmaceutical Development
  - *Databasing products (e.g. Spectrus); NMR Prediction, and many more!*
1. Designing better drugs using ACD PhysChem

Discovery Medicinal Chemistry – AZ’s C-Lab

- C-Lab enables computer-based design of compounds with improved efficacy and safety
- C-Lab delivers ACD/PhysChem and AZ’s QSAR model predictions to designers
- C-Lab enables the highest *quality* drug candidates to be designed
2. Automated Structure Verification

Compound collection

Automated interpretation of NMR spectra

correct isomer

wrong isomer

Match 0.99

Match 0.00
3. Compound naming using ACD/Name

Intellectual Property Department

Evidence of Value

- ACD/Name was temporarily unavailable for <1 month when we moved to new Windows 7 PCs – more than 50% of patent attorneys noticed and complained during that time.

ACD/Name = Tool of Choice

- We have an obligation to include names that are unambiguous (and obviously correct) in our patent applications – we trust the ACD results.
- AZ’s IP Department use ACD Name as the default naming (structure-to-name) and “reverse engineering” (name-to-structure) tool.
- We also use ACD/Name for checking names that are provided to us by the chemists or from third parties in the literature.
  - ACD/Name will often produce results where other naming packages fail.

“This is a well used tool!”
Senior Patent Director, AZ-IPD, UK
4. Drug Metabolism and PharmacoKinetics

The Uses of ACD/Labs Tools

- **What is DMPK?**
  - Drug Metabolism and Pharmacokinetics is the study and understanding of what the BODY does to the DRUG
  - NB: Pharmacodynamics is the study and understanding of what the DRUG does to the BODY

- **What is the value of having a database of metabolites?**
  - Many drugs are metabolised post-administration; many metabolites have their own “pharmacodynamics”: bioactivity; side effects; interactions; etc.
  - It is vital that we know as much as we can about these metabolites so that we can be sure of our drugs’ safety and efficacy

- **Which ACD/Labs Products enabled this to happen?**
  - ChemSketch: Ability to manage and represent Markush structures
    - Needed when there is uncertainty about the absolute structure of a metabolite
  - ChemFolder Enterprise
    - The critical databasing product

- **What has been the impact/value to AZ-DMPK of having access to ACD/Labs tools?**
  - The value and impact of these tools on improving the effectiveness of our DMPK function will be described in more detail in Martin Hayes's talk on June 11th.
5. PharmDev: The Reality of Turning Data → Knowledge

DATA

Spectrus Processor
• NMR - ID and assay
• LCMS - ID

Autochrom and LC Simulator
• Method development

Spectrus Database
• Spectral data
• Structural data

Prediction
• Physchem
• NMR spectrum

ENSURING OUR PRODUCT SAFETY AND EFFICACY

Click to visit ACD/labs website
Scanned PDF
- Limited audit trail / file info
- No chemical shifts
- Only possible for visual comparison
- Poor quality

Knowledgebase
- Fully structure and shift searchable
- Meta data captured
- Access to associated structures and data

“Live” spectrum
- Full parameter details
- Clear annotation
- Full shift analysis

Key ACD/labs Tool: Spectrus Processor
- Rolled out in 2013 across Global Pharm Dev
- One common platform for users
- Ability to associate with structures and other related data
- Intelligent use of data with Database tools
Spectrus Database Pilot for Effective Knowledge Management in Chemical Development

Discovery
- Phase 1: Toxico logical testing
- Phase 2: Early clinical trials
First into man

Phase 2
- Phase 3 / Technology Transfer
- Full clinical trials
- Prepare for launch

Launch

Benefits
- Process understanding to develop Robust processes
- Control Strategy
- Development and Product registration
- Knowledge base for lifecycle management opportunities and manufacturing support

Limited impurity understanding → Impurity name and structure → Typical levels and spec limits → How the impurity is formed / removed

Typical levels and spec limits

Limited impurity understanding

Impurity name and structure

How the impurity is formed / removed

Typical levels and spec limits

Benefits
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Summary

• Brief overview of how we use ACD/Labs applications and the benefit we get

• Understanding of where we’re heading in terms of knowledge management

• Demonstrate the value AZ gets from ACD/Labs software

• Excellent interactions with ACD/Labs and AZ
  - Regular customer and vendor interactions
  - Seamless upgrade to new operating platform in AZ

• Fits with AZ Business model
  - Interested in off-the-shelf products and less inclined to customise bespoke products
The Future
Short video – Click → YouTube

https://www.youtube.com/watch?v=yvXumAMPoAQ
Thank you!

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