Empower 3
Chromatography Data System for the Regulated Laboratory
Agenda

- Introduction
- Usability
- Applications
  - Content Uniformity using Custom Calculations
  - Organic Impurities and Related Substances
  - Dissolution/Elution
- Compliance
- Method Development
- Method Validation
- Architecture and Integration
Empower 3
Business Impact

- Napp Pharmaceutical - Background
  - QC and Stability Lab
  - 22 users and 54 systems
    - 34 with dissolution baths
    - Multiple vendors LCs
  - Excel for calculating results
  - Delays prevented product release which impacted revenue
  - Data security and integrity paramount as a compliant laboratory

- Solution
  - Network solution for system access
  - Managers reviewed reports from their own computers
  - Replaced Excel

EMPOWER 3 BENEFITS

- Easier sharing between labs
- Improved communication
- Removal of transcription errors
- Easier access to information
- Reduced errors because of a smoother and undistributed workflow
- Reduced bottlenecks in the lab workflow
- Increased sample throughput without compromising on release times
- Flexibility in staff allocation
- Reduced training costs
Empower Software Success

- 350,000+ Empower Software Licenses sold
- Over 3,500+ CDS Network installations
- 50 of the Top 50 Pharmaceutical Companies have deployed Empower Networks

Boehringer Ingelheim
Roche
Bayer
Novartis
GlaxoSmithKline
Boehringer Ingelheim
Sanofi Aventis
P&G
Baxter
Pfizer
Teva Pharmaceutical Industries Ltd.
Mylan Laboratories Inc.
Lilly
Abbott Laboratories
AstraZeneca
Merck
Usability
Multiple User Interfaces: Pro, Walk-up, and QuickStart
Guided Workflow Wizard
Show Me... Help in QuickStart

How To...

Perform sample operations
- Run samples
- View and process samples
- Report samples
- Export and e-mail samples

Perform other procedures
- Create or Modify a method
- Manage Empower
Tools to Streamline Workflows

- Over 15 wizards to assist with routine tasks
- Sequence wizard can adapt to different # of samples
  - Bracketing logic
Automatically Re-inject Failing Standards

- Assess System Suitability before injecting samples
  - Continue
  - Abort
  - Re-inject

- Samples
  - Continue
  - Abort
  - Re-inject

Available since 2002

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Find Data Easily with View Filters

- Query based on any combination of meta data
  - Personalized based on users
  - Can choose to share with other users
  - Wildcards
  - Date ranges
Right-click context menu allows you to find related information

- "View As..."
  - Sequences
  - Injections
  - Unprocessed chromatograms
  - Results
  - Calibration curves
  - Integration settings
  - Instrument method
  - eSignatures
Single User Experience for Equipment from Many Vendors

- All Major HPLC
- All Major GC
- UPLC
- UPC²
- APC
- CE
- Dissolution
Waters Empower Mobile provides mobile access to targeted Empower functionality for specific users, tasks and workflows.

**BENEFITS OF EMPOWER MOBILE**

- Increase laboratory efficiency
- Increase staff flexibility
- Easily find and share results remotely
- Expedite workflow for signoff on reports
- Lower operating costs for system administration tasks
Empower 3 Software Laboratory Analytics

- Empower 3 Software Laboratory Analytics offers five prebuilt dashboard types:
  - System summary
  - System usage
  - Project usage analysis
  - User analysis (optional)
  - Methods analysis

EMPOWER 3 LABORATORY ANALYTICS LETS YOU

- Access critical system usage information
- Maximize system utilization
- Manage resources
- Identify training needs
- Identify error messages that affect your workflows
- Identify non-robust processing methods
- Plan for capital expenditures
- Identify opportunities to shorten run times with UPLC® technology

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Content Uniformity
Using Custom Calculations and Reports
Automated Calculations

The image shows a software interface for automated calculations, specifically for analyzing chromatographic data. The software window displays a graph with a chemical structure annotation. Below the graph, a table lists the following columns: Name, Retention Time (min), Area (μV*sec), Amount (μg/mL), Structure 1 Name, Structure 1 Mol Wt, Structure 1 Formula, and % Label Claim. The first row of the table shows the following data for Methamphetamine:

- Name: Methamphetamine
- Retention Time: 8.649 min
- Area: 10088680
- Amount: 78.510 μg/mL
- Structure 1 Name: Methamphetamine
- Structure 1 Mol Wt: 149.230
- Structure 1 Formula: C10 H15 N
- % Label Claim: 94.590

The table and graph together provide a detailed analysis of the chemical compounds being studied.
Example Custom Fields
Suitability Acceptance

<table>
<thead>
<tr>
<th>SampleName</th>
<th>In</th>
<th>Vial</th>
<th>Area (μV·sec)</th>
<th>Amount</th>
<th>Label Claim</th>
<th>% Label Claim</th>
<th>Pass?</th>
</tr>
</thead>
<tbody>
<tr>
<td>501206-80mg-CU1</td>
<td>1</td>
<td>5</td>
<td>1013794</td>
<td>79.266</td>
<td>81.000</td>
<td>97.859</td>
<td>Pass</td>
</tr>
<tr>
<td>501206-80mg-CU2</td>
<td>1</td>
<td>6</td>
<td>10384359</td>
<td>80.827</td>
<td>82.000</td>
<td>98.570</td>
<td>Pass</td>
</tr>
<tr>
<td>501206-80mg-CU3</td>
<td>1</td>
<td>7</td>
<td>10354676</td>
<td>80.596</td>
<td>79.000</td>
<td>102.020</td>
<td>Pass</td>
</tr>
<tr>
<td>501206-80mg-CU4</td>
<td>1</td>
<td>8</td>
<td>10197301</td>
<td>79.871</td>
<td>80.000</td>
<td>99.214</td>
<td>Pass</td>
</tr>
<tr>
<td>501206-80mg-CU5</td>
<td>1</td>
<td>9</td>
<td>10088680</td>
<td>78.510</td>
<td>83.000</td>
<td><strong>94.590</strong></td>
<td>Fail</td>
</tr>
<tr>
<td>501206-80mg-CU6</td>
<td>1</td>
<td>10</td>
<td>10336367</td>
<td>80.666</td>
<td>78.000</td>
<td>103.418</td>
<td>Pass</td>
</tr>
<tr>
<td>501206-80mg-CU7</td>
<td>1</td>
<td>11</td>
<td>10305642</td>
<td>80.245</td>
<td>80.500</td>
<td>99.684</td>
<td>Pass</td>
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<td>501206-80mg-CU8</td>
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<td>12</td>
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<td>81.007</td>
<td>82.000</td>
<td>98.789</td>
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<tr>
<td>501206-80mg-CU9</td>
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<td>81.000</td>
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<td>501206-80mg-CU10</td>
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<td>14</td>
<td>10215891</td>
<td>79.516</td>
<td>79.000</td>
<td>100.653</td>
<td>Pass</td>
</tr>
</tbody>
</table>

Mean: 10286305, 79.9
Std. Dev.: 110942.481, 0.864
% RSD: 1.1, 1.1
## Calculation and Report of Mean, SD, RSD

### Result Set Report 2 in Pharmaceutical2 as System/Administrator - QuickStart - [Preview Data]

**Overall Acceptability: Pass**

<table>
<thead>
<tr>
<th>SampleName</th>
<th>Int</th>
<th>Vial</th>
<th>Area (µV*sec)</th>
<th>Amount</th>
<th>Label Claim</th>
<th>% Label Claim</th>
<th>Pass?</th>
</tr>
</thead>
<tbody>
<tr>
<td>501206-80mg-CU1</td>
<td>1</td>
<td>5</td>
<td>10183794</td>
<td>79.296</td>
<td>81.000</td>
<td>97.859</td>
<td>Pass</td>
</tr>
<tr>
<td>501206-80mg-CU2</td>
<td>1</td>
<td>6</td>
<td>10384359</td>
<td>80.827</td>
<td>82.000</td>
<td>98.570</td>
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</tr>
<tr>
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<td>1</td>
<td>7</td>
<td>10354676</td>
<td>80.596</td>
<td>79.000</td>
<td>102.020</td>
<td>Pass</td>
</tr>
</tbody>
</table>

### Table

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Mean</th>
<th>Std. Dev.</th>
<th>% RSD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>10266305</td>
<td>110942.481</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>79.9</td>
<td>0.864</td>
<td>1.1</td>
</tr>
</tbody>
</table>

- **Mean**: 10266305, 79.9
- **Std. Dev.**: 110942.481, 0.864
- **% RSD**: 1.1, 1.1
Organic Impurities and Related Substances
Common Inefficiencies in Impurity Analyses

- Trending results over time
  - Checking for out-of-specification or out-of-trend results
- Calculating the impurity content
  - Correcting the % area value for unrelated peaks
  - External calibration
- Consistent peak assignment
  - New, unexpected peaks arise over time
  - Different time points, multiple Chemists, changes in formulations
- Consistent peak detection
  - Poorly resolved peaks
  - Reliable baseline for peaks with small signal-to-noise
Impurity Processing

- Calculate impurity values
  - Exclude certain peaks (matrix, excipient, etc.)
  - Report total impurities and maximum impurity
  - Include ICH limits

- Identify unnamed component peaks with relative retention time (RRT) based on main component

Replace spreadsheets with embedded Empower processing & reporting
Replace Spreadsheets with Embedded Empower Reporting
Choice of bar, line or scatter plot including fit or mean
Consistently Detect Shoulders using ApexTrack Integration Algorithm
Reproducibly Detect Small Peaks with ApexTrack Integration Algorithm
Dissolution/Elution
Integrated Online Dissolution System

Transfer Time (min)

Q FactorA

%
“Turn on” Options Prevent the Need to Reinstall Software
Flat File Environment or Database?
21 CFR Part 11 Compliance - Ready

- Event logs and audit trails collected automatically in the background
- Comments
  - Optionally required
  - Default comments
  - Free-flow text
- Can require password
View Results and Associated Audit Trail Information in the Result Audit Viewer

Differences in the results are in blue. Results outside limits are in red.

Manual integration noted in Integration Type field.

New in Feature Release 2
Compare Differences in Method Versions in the Result Audit Viewer

### Methods Differences

<table>
<thead>
<tr>
<th>Group</th>
<th>Value Name</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integration Parameters</td>
<td>Peak Width</td>
<td>2.04</td>
</tr>
<tr>
<td></td>
<td>Detection Threshold</td>
<td>1.400e+002</td>
</tr>
<tr>
<td>Component</td>
<td>Retention Time</td>
<td>1.761</td>
</tr>
<tr>
<td>System Suitability</td>
<td>Field Name</td>
<td>% Adjusted Area</td>
</tr>
</tbody>
</table>

#### New in Feature Release 2!

- **Compare Differences in Method Versions in the Result Audit Viewer**
- **Methods differences shown in separate tab**
- **Differences have text search**
Control System Permissions

User Type Name
1. Administrator
2. Analyst
3. Chemist
4. Guest
5. Instrument_Owner
6. Method Validation Administrator
7. Method Validation Chemist
8. Method_Developer
9. Super_User

Privileges
- Administrator
- Archive and Remove Sample/Project Archives
- View Audit Trails
- Archive System Audit Trails
- Clear/Restore Offline System Audit Trails
- Clear/Restore Offline Project/Sample Archives
- Restore AutoArchived Projects
- Paste Shallow Copies
- Lock Channels
- Unlock Channels
- Alter Custom Fields
- Create Custom Field
- Delete Custom Field
- Lock Custom Field
- Unlock Custom Field
- Alter Default Strings

Check All  UnCheck All  Print
OK  Cancel  Apply  Help
Eliminate Paper and Ensure Compliance with Electronic Signatures

Chromatograms can be “locked” to prevent changes to results.
Method Development
A QbD-Based Approach to Method Development

Fusion QbD Method Development Approach to Robustness

Method Screening
Select column & solvent using quantitative Trend Responses

Formal Method Development & Optimization
Characterize and model ALL study parameter effects on ALL critical method performance attributes

Mean Method Performance Models
• Establish ICH Design Space
• Identify Optimal Method
• Establish Operating Space

Method Robustness Models

Method Validation
Formal experiments to demonstrate method robustness

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Automatically Build Experimental Design in Empower as Ready-to-Run Sample Set(s)

Creates instrument methods and method sets within Empower CDS
Optimum Method Performance

Method Performs in 2 Regions
Optimum Method Performance and Robustness

Design Space of Robust Method

Confidential
Optimum Method Performance and Robustness

ACQUITY UPLC
- 3 columns
- Gradient conditions
- Gradient slopes
- Mobile phase compositions
- pH
- Pump flow rate

HPLC
- 10 columns
- Isocratic & gradient conditions
- Gradient slopes
- Mobile phase compositions

45 days

2 days
View UV and MS Spectra in a Single View with the Mass Analysis Window

New in Feature Release 2

Confidential

UV and MS spectra visible in one view

UV peaks labeled with m/z
Method Validation Manager

- Run Samples
- Edit Sample Set
- Alter Sample
- Review
- Process
- Validation Process
- Validation Review
- Preview
- Approve Data
- Update
Manage Method Validation Workflows

Reproducibility Data

Accuracy Data

Linearity Data

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Architecture and Integration
Designed for the Enterprise

- Centrally stored data
  - Single source of raw and processed data
  - Multiple users access simultaneously
- Data Security
  - Physical security
- Simpler Administration
  - Single management of users, permissions, policies
  - Convenient for archival, maintenance
Empower 3 Network Environment

**Workstations**
*Systems must be individually accessed in the Lab*

**Network**
*All systems and data available simultaneously to users inside and outside the Lab*

- **Client**
- **Client**
- **Client**
- **Client**
- **Application Server**
- **Raw Data Server**

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Common CDS Platform

Europe

USA

Latin America

Asia
Accessing Legacy Data: Waters Data Converter
Benefits Empower Software

- Business Benefits
  - Improved laboratory productivity and effectiveness
- Laboratory Benefits
  - Consistency of data storage, audit trails, tools and techniques
  - Intuitive chromatographic data handling and processing
  - Easy generation of reports
  - Flexible integration of chromatographic equipment
  - Streamlined Method Development and Validation
- Compliance
  - 21 CFR Part 11 compliance - ready
  - Minimized inspection time