Review and Approve Results in Empower

Data, Meta Data and Audit Trails
What is an audit trail?

- Systematic “story” of the data from creation, through interpretation and final assessment and reporting
- Easily confused as: Log of everything that happens in my system
  - Recent quote: “We switched on audit trails of everything at the beginning” and......
Process Understanding

- Key to determine the true audit trail
  - How is data recorded, where and when
  - What additional records are created along the way
  - How are these connected and what traceability is there between them
  - If records are not editable, do you need a traditional audit trail functionality?
  - Can you create a paper audit trail / change control?

- Using the answers to these questions the criticality of the audit trail can be determined and a sensible review process designed.
Critical Audit trails

- At each step, where are records created?
- Can they be modified? By whom? And how is this traced?
- How is data passed from one system to another?
  - Automatically and validated
  - Manually and Four eyes checked?
Annex 11: Prompting the question of audit trail review
Four new key areas in Annex 11

- Supplier Audits: including the requirement to share a summary of your assessment
  - Be sure this is agreed in your vendor NDA agreement
- Qualification of IT Infrastructure
  - And a formal agreement with IT departments
- Inclusion of Risk Management
  - In Regulation rather than in Guidance
- Review of Audit Trails
  - Specifically mentioned
Accurate and Traceable Data Entry - Audit Trails

- Annex 11§9
  - Based on Risk
    - Record of all GMP relevant changes and deletions
    - Reasons should be included
    - Convertible to human readable form and regularly reviewed.

- Additionally 11§8.2
  - Ability to “generate printouts indicating if any data changed since original entry”
Review of Audit Trails

- **Audit trails** need to be available and convertible to a generally intelligible form and *regularly reviewed*. (A11§9)
  - Part 11 “agency review”

- From a NIST publication*
  - Audit trails are a technical mechanism that *help managers maintain individual accountability*. ..Users are less likely to attempt to circumvent security policy if they know that their actions will be recorded in an audit log.
  - “Determine how much review of audit trail records is necessary”

- Increased appearance of Warning Letter observations

---

* Introduction to Computer Security: The NIST Handbook
Gulf Pharmaceutical Industries Feb 2012
- We also note that your SOP does not have provisions for any audit trail reviews to ensure that deletions and/or modifications do not occur.

Banner Pharmacaps Sept 2006:
- A second person must review these audit trails, particularly given the lack of controls for preventing data manipulation. **Such an audit may well have detected the data manipulation which was occurring at your facility.**

Sunrise Jan 2010:
- In addition, your firm's review of laboratory data does not include a review of an audit trail or revision history to determine if unapproved changes have been made.
## Recent Cases of Deliberate Fraud Using e-Records...

<table>
<thead>
<tr>
<th>Product /Batch Number</th>
<th>Lack of Complete Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Products and batches listed in FDA-483, point # 2</td>
<td>OOS results not documented in laboratory records. Unreported OOS results found in electronic data files.</td>
</tr>
<tr>
<td>Propoxyphene Napsylate and APAP Tablets, 100/650mg Batch 303110A</td>
<td>Changed chromatogram headers by cutting and pasting, so during review all sample injections would appear to be in sequence, for Dissolution Testing of Tablets D1 and D5.</td>
</tr>
<tr>
<td>Propoxyphene Napsylate and APAP Tablets, 100/650mg Batch 104026B Validation Batch</td>
<td>Original Sample Weights not recorded in notebook. Sample weights were changed by the analyst until a passing result was obtained for Assay (A2)</td>
</tr>
<tr>
<td>Acetaminophen &amp; Codeine Phosphate Tablets, 300/30mg Batch 407148</td>
<td>Processing methods changed by analyst until the processing method resulted in a passing result. Original processing method not recorded in laboratory notebook.</td>
</tr>
</tbody>
</table>
Empower Compliance Features:
Audit Trails
Biggest Compliance feature in Empower??

- The built in Empower Database
  - Enables every object to be uniquely referenced
  - Can never overwrite data
  - Can never mistake which data went with which method
  - Ensures easy and accurate data review

- Automatic versioning for results / methods
  - With full computer generated audit trail
  - WHO changed WHAT (before and after values) WHEN…. And WHY?)
Empower Audit Trails ID numbers

- Empower is built into an Oracle Database
- This database gives each object or result a Unique Identifier for tracking the values and records
- This identifier is unique within each project.
- Modification of any database object results in a NEW record with NEW identifiers

- Many users of Empower use these ID numbers to prove and identify results to auditors
  - Also to track for their own purposes
Assigns Unique ID # for All Entries

- **Raw Data ID’s**
  - Missing numbers from:
    - Channel
    - Assignment to Calibration
  - Assigned to Vial: 1142, 1143, 1144, 1145, 1146?

<table>
<thead>
<tr>
<th>Sample Name</th>
<th>Vial</th>
<th>Vial Id (Result)</th>
<th>Injection</th>
<th>Injection Id</th>
<th>Channel Id</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 System Suitability</td>
<td>1:A,1</td>
<td>1062</td>
<td>1</td>
<td>1064</td>
<td>1065</td>
</tr>
<tr>
<td>2 System Suitability</td>
<td>1:A,1</td>
<td>1062</td>
<td>2</td>
<td>1069</td>
<td>1070</td>
</tr>
<tr>
<td>3 System Suitability</td>
<td>1:A,1</td>
<td>1062</td>
<td>3</td>
<td>1071</td>
<td>1072</td>
</tr>
<tr>
<td>4 System Suitability</td>
<td>1:A,1</td>
<td>1062</td>
<td>4</td>
<td>1073</td>
<td>1074</td>
</tr>
<tr>
<td>5 System Suitability</td>
<td>1:A,1</td>
<td>1062</td>
<td>5</td>
<td>1075</td>
<td>1076</td>
</tr>
<tr>
<td>6 AG Standard 1</td>
<td>1:A,2</td>
<td>1077</td>
<td>1</td>
<td>1078</td>
<td>1079</td>
</tr>
<tr>
<td>7 AG Standard 2</td>
<td>1:A,3</td>
<td>1080</td>
<td>1</td>
<td>1081</td>
<td>1082</td>
</tr>
<tr>
<td>8 AG Standard 3</td>
<td>1:A,4</td>
<td>1083</td>
<td>1</td>
<td>1084</td>
<td>1085</td>
</tr>
<tr>
<td>9 AG Standard 4</td>
<td>1:A,5</td>
<td>1086</td>
<td>1</td>
<td>1087</td>
<td>1088</td>
</tr>
<tr>
<td>10 AG Standard 5</td>
<td>1:A,6</td>
<td>1089</td>
<td>1</td>
<td>1090</td>
<td>1091</td>
</tr>
<tr>
<td>11 AG Sample 1</td>
<td>1:A,7</td>
<td>1092</td>
<td>1</td>
<td>1093</td>
<td>1094</td>
</tr>
<tr>
<td>12 AG Sample 2</td>
<td>1:A,8</td>
<td>1095</td>
<td>1</td>
<td>1096</td>
<td>1097</td>
</tr>
<tr>
<td>13 AG Sample 3</td>
<td>1:B,1</td>
<td>1098</td>
<td>1</td>
<td>1099</td>
<td>1100</td>
</tr>
<tr>
<td>14 AG Sample 4</td>
<td>1:B,2</td>
<td>1101</td>
<td>1</td>
<td>1102</td>
<td>1103</td>
</tr>
<tr>
<td>15 AG Sample 5</td>
<td>1:B,3</td>
<td>1104</td>
<td>1</td>
<td>1105</td>
<td>1106</td>
</tr>
<tr>
<td>16 AG Sample 6</td>
<td>1:B,4</td>
<td>1107</td>
<td>1</td>
<td>1108</td>
<td>1109</td>
</tr>
<tr>
<td>17 AG Sample 7</td>
<td>1:B,5</td>
<td>1110</td>
<td>1</td>
<td>1111</td>
<td>1112</td>
</tr>
<tr>
<td>18 AG Sample 8</td>
<td>1:B,6</td>
<td>1113</td>
<td>1</td>
<td>1114</td>
<td>1115</td>
</tr>
<tr>
<td>19 AG Sample 9</td>
<td>1:B,7</td>
<td>1116</td>
<td>1</td>
<td>1117</td>
<td>1118</td>
</tr>
</tbody>
</table>
### IDs assigned to Cal Curve in Peak View

<table>
<thead>
<tr>
<th>Sample Name</th>
<th>Vial</th>
<th>Vial Id (Result)</th>
<th>Injection</th>
<th>Injection Id</th>
<th>Channel Id</th>
<th>Result Id</th>
<th>Calibration Id</th>
<th>Name</th>
<th>Curve Id</th>
<th>Retention Time (min)</th>
<th>Area (μV*sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>1</td>
<td>1064</td>
<td>1065</td>
<td>1147</td>
<td>1141</td>
<td>Acetaminophen</td>
<td>1142</td>
<td>0.871</td>
<td>68955</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>1</td>
<td>1064</td>
<td>1065</td>
<td>1147</td>
<td>1141</td>
<td>Caffeine</td>
<td>1143</td>
<td>1.213</td>
<td>90121</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>1</td>
<td>1064</td>
<td>1065</td>
<td>1147</td>
<td>1141</td>
<td>Acetanilide</td>
<td>1144</td>
<td>1.499</td>
<td>99000</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>1</td>
<td>1064</td>
<td>1065</td>
<td>1147</td>
<td>1141</td>
<td>Acetylsalicylic Acid</td>
<td>1145</td>
<td>1.664</td>
<td>109067</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>1</td>
<td>1064</td>
<td>1065</td>
<td>1147</td>
<td>1141</td>
<td>Acetylsalicylic Acid</td>
<td>1145</td>
<td>2.098</td>
<td>39798</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>1</td>
<td>1064</td>
<td>1065</td>
<td>1147</td>
<td>1141</td>
<td>Acetylsalicylic Acid</td>
<td>1145</td>
<td>2.785</td>
<td>59302</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>1</td>
<td>1064</td>
<td>1065</td>
<td>1147</td>
<td>1141</td>
<td>Phencetin</td>
<td>1146</td>
<td>2.829</td>
<td>89074</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>1</td>
<td>1064</td>
<td>1065</td>
<td>1147</td>
<td>1141</td>
<td>Phencetin</td>
<td>1146</td>
<td>3.102</td>
<td>63820</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>2</td>
<td>1069</td>
<td>1070</td>
<td>1148</td>
<td>1141</td>
<td>Acetylsalicylic Acid</td>
<td>1145</td>
<td>2.831</td>
<td>69341</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>2</td>
<td>1069</td>
<td>1070</td>
<td>1148</td>
<td>1141</td>
<td>Acetylsalicylic Acid</td>
<td>1145</td>
<td>2.831</td>
<td>89512</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>2</td>
<td>1069</td>
<td>1070</td>
<td>1148</td>
<td>1141</td>
<td>Caffeine</td>
<td>1143</td>
<td>1.211</td>
<td>90589</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>2</td>
<td>1069</td>
<td>1070</td>
<td>1148</td>
<td>1141</td>
<td>Caffeine</td>
<td>1143</td>
<td>1.497</td>
<td>99962</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>2</td>
<td>1069</td>
<td>1070</td>
<td>1148</td>
<td>1141</td>
<td>Caffeine</td>
<td>1143</td>
<td>1.664</td>
<td>110371</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>2</td>
<td>1069</td>
<td>1070</td>
<td>1148</td>
<td>1141</td>
<td>Acetylsalicylic Acid</td>
<td>1145</td>
<td>2.098</td>
<td>40193</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>2</td>
<td>1069</td>
<td>1070</td>
<td>1148</td>
<td>1141</td>
<td>Acetylsalicylic Acid</td>
<td>1145</td>
<td>2.788</td>
<td>61222</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>2</td>
<td>1069</td>
<td>1070</td>
<td>1148</td>
<td>1141</td>
<td>Acetylsalicylic Acid</td>
<td>1145</td>
<td>2.831</td>
<td>89512</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>2</td>
<td>1069</td>
<td>1070</td>
<td>1148</td>
<td>1141</td>
<td>Phenacetin</td>
<td>1146</td>
<td>3.106</td>
<td>65476</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>2</td>
<td>1069</td>
<td>1070</td>
<td>1148</td>
<td>1141</td>
<td>Phenacetin</td>
<td>1146</td>
<td>2.938</td>
<td>60289</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>2</td>
<td>1069</td>
<td>1070</td>
<td>1148</td>
<td>1141</td>
<td>Phenacetin</td>
<td>1146</td>
<td>3.064</td>
<td>88351</td>
</tr>
<tr>
<td>System Suitability test</td>
<td>1:A,1</td>
<td>1062</td>
<td>2</td>
<td>1069</td>
<td>1070</td>
<td>1148</td>
<td>1141</td>
<td>Phenacetin</td>
<td>1146</td>
<td>3.225</td>
<td>65641</td>
</tr>
</tbody>
</table>

©2013 Waters Corporation
Method ID, Version and 'Locked'
Result Audit Trail... more than a table of changes

Sample Sets

Standards used for Calibration

Calibration Curves

Unchanged Raw Data File

Who Collected
Who Processed
Who Reviewed
Who Approved

When
What
Why

Original Processing Method

Original Instrument Method

E-cord information

LC/GC System Used

Product Code/Stage Reagent LIMS ID

Unique Result

Processing Method

Instrument Method

Processing Method

Instrument Method
Built in Audit Trails in Empower

- It is not possible to create, manipulate, modify or delete data inside Empower without creating an audit trail entry.
- All user actions are logged in various audit trails and associated with the logged in USERNAME
  - Assumes all users have unique User Account
- Multiple “modes” of audit trail
  - Silent
  - Full – Includes the requirement to enter a reason “Why?”
    - With free form reasons
    - With predefined reasons only (Default Strings)
  - Reauthentication (re entry of password to confirm identity)
- Empower Audit trails are not editable or modifiable by ANY USER
Empower Audit Trails

- Sample Audit Trail
  - Tracks changes to entered data about each sample

- Result Audit Trail
  - Links results to instruments, samplesets, methods, calibration curves and standards used in calibration.
  - Also traces any manual manipulation of data

- Method Audit Trail
  - Keeps all versions of method for recreation of results
  - Audit Trail monitors each change, before and after values, who when and why
  - Different versions can be compared to identify the differences
Empower Audit Trails

- **Project Audit Trail**
  - Gives overview of all changes in a project
  - Includes details of method / data deletion

- **System Audit Trail**
  - shows changes to system objects and system policies
  - details archive activity
  - notes all changes to security (users, user types etc)
  - documents all successful and unsuccessful logins
    - you have a history of who was logged into the application at any time
    - you have information about system break in attempts
    - includes the client the login/login attempt occurred at
Empower Sample Audit Trail

### Sample History

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>User: mharoinski Date: 5/3/2002 12:49:16 AM Reason: All sample information not known at time of analysis</td>
</tr>
<tr>
<td>2</td>
<td>Modified Vial(Lot_No): &lt;No Value&gt; -&gt; SS 4Comp</td>
</tr>
<tr>
<td>4</td>
<td>Modified Vial(Sample/Weight): 1.00000 -&gt; 23.40000</td>
</tr>
</tbody>
</table>

For Help, press F1

©2013 Waters Corporation
Method Properties and Audit Trail

Method Properties:
- Name: Methamphetamine 2
- Type: Processing
- Last Modified By: Employee_00789

Audit Trail - Methamphetamine 2:
1. Version 5 5/2/2013 8:10:38 AM EDT User Employee_00789 forgot peak label
2. Version 4 4/24/2013 9:12:47 AM EDT User System Method (/Waters-s4ehz1/PharmaceuticalPharmDev...
3. Version 4 24/01/2003 16:23:50 User HLongden Method (/HLongden/PharmaceuticalQA : 1282) copied into ...
<table>
<thead>
<tr>
<th>Group</th>
<th>Value Name</th>
<th>Method (Methamphetamine 2 : 5/2/2013 8:10:38 AM EDT (Ver. 5))</th>
<th>Method (Methamphetamine 2 : 4/24/2013 9:12:47 AM EDT (Ver. 4))</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>Method Revision</td>
<td>Version 1 7/14/2002 10:48:19 AM User SSmith Created</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>« Expected Mass »</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Component Name</td>
<td>Methamphetamine</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>Retention Time</td>
<td>0.658</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Expected Mass 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Expected Intensity 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Expected Mass 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Expected Intensity 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>Expected Mass 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>Expected Intensity 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>Expected Mass 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>Expected Intensity 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>Expected Mass 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>Expected Intensity 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>« Component »</td>
<td></td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>Peak Label</td>
<td>MethA</td>
<td></td>
</tr>
</tbody>
</table>
How to Review Audit Trails
Reviewing Audit Trails

- **Purpose**
  - To uncover possible cases of fraudulent behaviour
    - Multiple processing data
    - Altering metadata to make results pass
    - Hiding or altering meta data on reports sent to QA
    - Uncovering persistent suspicious behaviour around security of data
    - Ensuring only authorised users have access to certain functionality
    - Deletion of data
    - Altering system policies / configuration / settings without change control procedures

- **How?**
  - Two possible procedures:
    - Review of relevant audit trails as part of data review
    - Periodic review of system level audit trails by admin
Review of Audit trails

- Review audit trails as part of data review process
  - Find anomalies before batch release
  - Focus of user behaviour that affect results
  - Peer Review / Manager review / QA review?

- Periodic Review of overall Audit trails
  - Looking for system level activity without correct documentation, change control, testing or approval
    - Eg changing system policies, user access or deletion of data

- Biggest issue: Audit trails are often more a log of all activity (to comply) and not designed for easy review
  - But it is expected that inspectors will look at the audit trails
How to Review Audit Trails in Empower?

- Use the Preview and Sign off tools
  - Inform regulatory bodies that electronic signatures are being used in your company
  - Set up system policies to control signature processes
  - Create reports including all relevant meta data and include the Sign Off property
    - Sample Set, Method details, All versions of Results and all Audit trails
  - Review all pages of report
  - Sign report
Using Reports and E-Signatures to review and approve results
Selecting policies for GXP and eSigs

- Result Sign off tab
  - Sign off Inactivity delay
  - Clear password
  - Enforce single logon
  - Allow lock channels
  - Save report image as pdf
  - Multiple sign off behavior
  - Enforce sign off 1 before sign off 2

Warning: By selecting “cancel”, changes made in ALL tabs, including changes made to the LDAP domains, will be undone.
Report methods to be used for electronic signatures must have ‘Allow this method to be used in sign off’ checked.

If the content of the method is changed this check box will be automatically deselected and must be selected again before the method can be used for electronic signatures.
Report methods for electronic Signatures

- Viewing sign off information in the report
- Add the sign off table to the method
Signing reports

- Report is viewed as normal
- Signature table is displayed
Signing reports

- Review the report and if suitable
- Click the sign off button

Note

- Sign off button is greyed out until all the pages of the report have been displayed
Signing reports

- Sign off dialogue box is displayed
- Enter
  - User name
  - Password
  - Reason
- Click sign off
- If signing of for ‘Sign off 2’
  - Can lock channels
Signing reports

- Report now contains sign off information
What should be included in an Electronic Signature report
What should be included in an Electronic Signature report

- Should I use a report to review data
- What should go on that report
  - As much as possible
  - Only what is essential

What is essential?
What should be included in an Electronic Signature report

- Individual Reports or Summary?
Individual or Summary Reports

- **Individual**: Each result is signed individual date/time
  - Can reject one result out of a batch
- **Summary**: One signature applies to each individual result
  - Same date and time
  - Simplify the signature box on reports with single signing action

- **What to do with results which are not signed?**
  - Are they superseded results?
  - Do you need to sign as “rejected”?
  - What will you say to an auditor who asks about these results?
What should be included in an Electronic Signature report

- Chromatogram
  - One... Some... All... None
  - Full
  - Expanded base line
  - Thumb nail

- How useful is this for scientific review?
  - No zoom on integration

- Could annotations have obscured data?
  - Only show up on printed reports, not electronic reports
What should be included in an Electronic Signature report

- Method data
  - Processing… Instrument… Method Set… Sample Set… None
  - Some… All…
  - History
  - ID
  - Version
- Compare Methods
- Train reviewer on Empower traceability
What should be included in an Electronic Signature report

- Sample Set Method?
- Sample Set?
- Channel Information (is it complete? Test injections?)
  - Samples... Standards... Controls... Blanks... None
  - Some... All...
  - Sequence, ID, Channel name

<table>
<thead>
<tr>
<th>SampleName</th>
<th>Sample Type</th>
<th>Val</th>
<th>Inj#</th>
<th>Run Time (Minutes)</th>
<th>Injection Volume (ul)</th>
<th>Acquisition Method Set</th>
<th>Sample Weight</th>
<th>Processed Channel Descr.</th>
<th>Injection Id</th>
</tr>
</thead>
<tbody>
<tr>
<td>PQ Std 2.5x</td>
<td>Standard</td>
<td>1</td>
<td>1</td>
<td>6.0C</td>
<td>20.00</td>
<td>LC Demo Method Set</td>
<td>1.00000</td>
<td>254nm</td>
<td>1007</td>
</tr>
<tr>
<td>PQ Std 5.0x</td>
<td>Standard</td>
<td>2</td>
<td>1</td>
<td>6.0C</td>
<td>20.00</td>
<td>LC Demo Method Set</td>
<td>1.00000</td>
<td>254nm</td>
<td>1023</td>
</tr>
<tr>
<td>PQ Std 10x</td>
<td>Standard</td>
<td>3</td>
<td>1</td>
<td>6.0C</td>
<td>20.00</td>
<td>LC Demo Method Set</td>
<td>1.00000</td>
<td>254nm</td>
<td>1027</td>
</tr>
<tr>
<td>PQ Unk. 1</td>
<td>Unknown</td>
<td>4</td>
<td>1</td>
<td>6.0C</td>
<td>20.00</td>
<td>LC Demo Method Set</td>
<td>1.00000</td>
<td>254nm</td>
<td>1031</td>
</tr>
<tr>
<td>PQ Unk. 2</td>
<td>Unknown</td>
<td>5</td>
<td>1</td>
<td>6.0C</td>
<td>20.00</td>
<td>LC Demo Method Set</td>
<td>1.00000</td>
<td>254nm</td>
<td>1035</td>
</tr>
<tr>
<td>PQ Unk. 3</td>
<td>Unknown</td>
<td>6</td>
<td>1</td>
<td>6.0C</td>
<td>20.00</td>
<td>LC Demo Method Set</td>
<td>1.00000</td>
<td>254nm</td>
<td>1036</td>
</tr>
<tr>
<td>PQ Unk. 4</td>
<td>Unknown</td>
<td>7</td>
<td>1</td>
<td>6.0C</td>
<td>20.00</td>
<td>LC Demo Method Set</td>
<td>1.00000</td>
<td>254nm</td>
<td>1043</td>
</tr>
</tbody>
</table>
What should be included in an Electronic Signature report

- Result Information
  - Samples... Standards... Controls... Blanks... None
  - Some... All...
  - ID
  - Result Set Name
  - Result Set ID
  - Altered
  - Manual
  - Peak Codes
What should be included in an Electronic Signature report

- Calibration information
  - One... Some... All... None
  - Curve plot
  - Equation
  - Calculations
  - ID
What should be included in an Electronic Signature report

- Audit trails
  - Samples... Standards... Controls... Blanks... None
  - Some... All...
  - Sample History
  - Method History
  - Method Versions
How to Review Audit Trails in Preview and Reports?

- **Advantage:** Evidence of “review”
- **Issues:**
  - Just because they are on the reports and you looked at the at page, did you actually see anything irregular?
  - Can you pick out “normal” audit records from “non normal”?
  - What real value does this bring to the review process?
  - Creating huge reports for each run, effectively a new “copy” of the electronic data.
How to Review Audit Trails in Empower?

- Review chromatograms, methods and relevant Audit Trails in Empower application
  - Sign a report to document that you have followed the review SOP

  I sign this data to attest that I performed/ reviewed / approved this data according to SOP 12345
  This includes review of all manual entry of meta data (eg weights, dilution and other factors and also the relevant audit trails.)

  - Mimics the review of many other aspects of a method execution
    - Sampling / solution creation/ standard creation
      - No true recording of activity
How to review data in Empower

- Use the Empower project name to open the correct Empower project
- In the result or result set tab search for the ID
How to review data in Empower

- Use right click “View as...” to select
  - Sample Sets
  - Results
  - Peaks
  - Processing methods
  - Instrument Methods
  - Sample Set methods
  - Audit Records
How to review data in Empower

- In Results tab
  - Result ID, Processed Manually, number of results for channel, result number, processed by, processed date, Processing method, date acquired, channel, vial, injection, system, label, sampleset id, run time, custom fields, faults, blank, comments, peak codes, number of sign offs, sample name......
How to review data in Empower

- In Sample Set use alter sample
- See if a sample has been altered then right click and Select view
  - Sample History
  - SampleSet method History
How to review data in Empower

- Sample History
  - Who
  - What
  - When
  - Why

![Sample History Window](image-url)
How to review data in Empower

- SampleSet/Instrument/Processing Method History
  - Name
  - Date
  - ID
  - Version
  - Audit Trail
  - Check differences between version
How to Review Audit Trails in Empower?

- Concerns
  - Difficult to FIND all audit records in Empower
  - Complicated SOP to follow
    - Even for experienced Empower users
    - Difficult for non/ new/ infrequent users like QA
  - No automatic documentation of the review process
The Review Tool

- Access to integrated chromatograms/results
  - All integration positions
  - Ability to zoom in to examine without reprocessing
- Peak and Result level values
- Instrument Method
- Processing Method
- Calibration Curves
- NOW Direct access Sample Set
- All that was missing was the audit trails
Reviewing Audit Trails: A New tool in FR2

- Designed to make the requirement to review Audit trails simpler
  - Annex 11 and various warning letters
- Launched from Review
  - Where a manager would be looking at Results
- Brings into one window audit records from
  - Project window
  - Manual results
  - Method changes
    - Processing, Instrument, Sample Set (alter sample) and Method Set
    - Allows multiple methods to be compares
- Compares results from superceded results
  - Where results have been reprocessed
  - Compares Areas, RT, Amount etc between two results
Enhanced Data Review
New Result Audit Viewer (RAV)
Result History Table

- Searches the multiple Audit trails for data related to the selected injection
  - Acquisition Log
  - Injection Log
  - Sample Set History (Includes sample set level history, sample level history and method changes)
  - Sample History
  - Method History
  - Audit Trail Records

- Merges data, with different columns and information, into one easy to search table.
  - Some logs are missing ACTION REASON or type... So a N/A is entered
  - Blank columns really were not populated
# Enhanced Data Review

## New Result Audit Viewer

### Result History

<table>
<thead>
<tr>
<th>Result Id</th>
<th>Visual</th>
<th>Sample Set Id (Result)</th>
<th>Sample Name</th>
<th>Visit</th>
<th>Injection</th>
<th>Date Processed</th>
<th>Processing Method</th>
<th>Result Codes</th>
<th>Result Type</th>
<th>Channel Name</th>
<th>Channel Device</th>
<th>Integration Algorithm</th>
<th>Software Version</th>
<th>Source SAP Info</th>
<th>Result Audit Viewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2169</td>
<td>2121</td>
<td>Blank</td>
<td>S,A,L</td>
<td>1</td>
<td>1/22/2013 9:31 AM EST</td>
<td>Soft Drink Assay</td>
<td>S02</td>
<td>LC</td>
<td>ACQUITY TUV OVA</td>
<td>ACQUITY TUV OVA 2140mm</td>
<td>Empower 3</td>
<td>Empower: 3 Software Build 3471 SP3 Installed, Feature Release 2 DB ID: 2200645534</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2169</td>
<td>2121</td>
<td>Reference</td>
<td>S,A,L</td>
<td>1</td>
<td>1/22/2013 9:31 AM EST</td>
<td>Soft Drink Assay</td>
<td>S02</td>
<td>LC</td>
<td>ACQUITY TUV OVA</td>
<td>ACQUITY TUV OVA 2140mm</td>
<td>Empower 3</td>
<td>Empower: 3 Software Build 3471 SP3 Installed, Feature Release 2 DB ID: 2200645534</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2169</td>
<td>2121</td>
<td>Syr Sulf</td>
<td>S,A,L</td>
<td>1</td>
<td>1/22/2013 9:31 AM EST</td>
<td>Soft Drink Assay</td>
<td>S02</td>
<td>LC</td>
<td>ACQUITY TUV OVA</td>
<td>ACQUITY TUV OVA 2140mm</td>
<td>Empower 3</td>
<td>Empower: 3 Software Build 3471 SP3 Installed, Feature Release 2 DB ID: 2200645534</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Screenshot:

- **Result History**
  - **vonderwoman/ Administrator**: Audit Trail Record
  - **Belle**: Processing Method Properties
    - N/A
    - Optimized integration
    - Modified Sample Name/Amount/Values
    - Corrected bracketing
    - Corrected bracketing
    - Corrected bracketing
  - **Belle**: Sample Set History
    - N/A
    - Added processing method
    - Optimized integration
  - **Belle**: Method Set Properties
    - N/A
  - **Belle**: Processing Method Properties
    - N/A
    - Optimized integration
    - Corrected bracketing
    - Corrected bracketing
    - Corrected bracketing
  - **Belle**: Sample Set Method Properties
    - N/A
    - Corrected bracketing
  - **Belle**: Sample Set Method Properties
    - N/A
    - Optimized integration

For Help, press F1

© 2013 Waters Corporation
Result Differences

- Middle table show all superseded results that are stored in the CURRENT result set
  - Individual results can be selected and brought into review to see "lone results or across result sets"
- Selecting these results will compare to the most recent result
  - Selected in the top table
- Select a peak to see peak values and compare across results
  - Faults are still highlighted
  - Differences can be highlighted
  - Can select to ONLY show differences
    - All can be saved as preferences, along with column selection and order
### Result Differences

#### Results Table

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Sample Name</th>
<th>Manual</th>
<th>Result Comments</th>
<th>Faults</th>
<th>Summary Faults</th>
<th>Result #</th>
<th>Result Superseded</th>
<th>View</th>
<th>Injection</th>
<th>Data Processed</th>
</tr>
</thead>
<tbody>
<tr>
<td>2481</td>
<td>501206-80mg-CUS</td>
<td>✔</td>
<td>required to catch the end of the tail for peak</td>
<td></td>
<td></td>
<td>38</td>
<td></td>
<td>9</td>
<td>1</td>
<td>4/24/2013 9:29:55 AM EDT</td>
</tr>
<tr>
<td>2474</td>
<td>501206-80mg-CUS</td>
<td></td>
<td>Required reprocessing after altering sample information</td>
<td></td>
<td></td>
<td>35</td>
<td></td>
<td>10</td>
<td>1</td>
<td>4/24/2013 9:17:24 AM EDT</td>
</tr>
</tbody>
</table>

#### Superseded Results

<table>
<thead>
<tr>
<th>Selected</th>
<th>Result ID</th>
<th>Sample Name</th>
<th>Manual</th>
<th>Result Comments</th>
<th>Faults</th>
<th>Summary Faults</th>
<th>Result #</th>
<th>Result Superseded</th>
<th>View</th>
<th>Injection</th>
<th>Data Processed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2480</td>
<td>501206-80mg-CUS</td>
<td>✔</td>
<td>integration improved manually</td>
<td>✔</td>
<td></td>
<td>37</td>
<td></td>
<td>9</td>
<td>1</td>
<td>4/24/2013 9:23:43 AM EDT</td>
</tr>
<tr>
<td></td>
<td>2474</td>
<td>501206-80mg-CUS</td>
<td></td>
<td>Required reprocessing after altering sample information</td>
<td></td>
<td></td>
<td>36</td>
<td></td>
<td>9</td>
<td>1</td>
<td>4/24/2013 9:17:24 AM EDT</td>
</tr>
</tbody>
</table>

### Methamphetamine

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Name</th>
<th>Area (μm²/sec)</th>
<th>Amount</th>
<th>Int Type</th>
<th>Curve Id</th>
<th>Peak Label</th>
<th>Retention Time (min)</th>
<th>% Area</th>
<th>Height (μV)</th>
<th>Units</th>
<th>Peak Type</th>
<th>Relative RT (min)</th>
<th>RT Ratio</th>
<th>Start Time (min)</th>
<th>End Time (min)</th>
<th>Baseline (μV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2481</td>
<td>Methamphetamine</td>
<td>10115635</td>
<td>98.112</td>
<td>bb</td>
<td>2465</td>
<td></td>
<td>8.649</td>
<td>100.00</td>
<td>542890</td>
<td>Found</td>
<td></td>
<td>7.700</td>
<td>11.283</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2480</td>
<td>Methamphetamine</td>
<td>10100900</td>
<td>97.962</td>
<td>Bb</td>
<td>2465</td>
<td></td>
<td>8.649</td>
<td>100.00</td>
<td>542805</td>
<td>Found</td>
<td></td>
<td>7.867</td>
<td>9.917</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2474</td>
<td>Methamphetamine</td>
<td>10086680</td>
<td>97.832</td>
<td>BB</td>
<td>2465</td>
<td></td>
<td>8.649</td>
<td>100.00</td>
<td>542897</td>
<td>Found</td>
<td></td>
<td>7.867</td>
<td>9.525</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Differences in the results are in blue. Results outside limits are in red.

Manual integration noted in Integration Type field.
Method Information and Differences

- Selecting a result in the TOP table will search and display the associated methods in the middle table.
- For each type of method an entire method history can be displayed in the middle table.
  - Although easier to see in Review graphically.
- The bottom table displays the contents of the method version selected.
- Selecting two method versions allows methods to be compared.
  - Uses the regular “Method Differences” functionality.
    - Show Only or Highlight differences.
  - Can only compare two methods at one time.
  - NB for details of change, use the Result History tab.

©2013 Waters Corporation
## Processing Method Comparison

### Results

<table>
<thead>
<tr>
<th>Result Id</th>
<th>Sample Name</th>
<th>Manual</th>
<th>Result Comments</th>
<th>Faults</th>
<th>Summary Faults</th>
<th>Result #</th>
<th>Result Superseded</th>
<th>Val</th>
<th>Injection</th>
<th>Date Processed</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>2481 501206-80mg-CU5</td>
<td>✓</td>
<td>required to catch the end of the tail for peak</td>
<td></td>
<td></td>
<td>38</td>
<td></td>
<td>9</td>
<td>1</td>
<td>4/24/2013 9:29:55 AM EDT</td>
</tr>
<tr>
<td>16</td>
<td>2475 501206-80mg-CU6</td>
<td></td>
<td>Required reprocessing after altering sample information</td>
<td></td>
<td></td>
<td>38</td>
<td></td>
<td>10</td>
<td>1</td>
<td>4/24/2013 9:17:24 AM EDT</td>
</tr>
</tbody>
</table>

### Method History

<table>
<thead>
<tr>
<th>Method Id</th>
<th>Method Comments</th>
<th>Method Version</th>
<th>Method Locked</th>
<th>Method Date</th>
<th>Method Modified User</th>
<th>Method Name</th>
<th>Method Type</th>
<th>Old Id</th>
<th>Source SAW Info</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>New Method</td>
<td>4</td>
<td></td>
<td>4/24/2013 9:12:47 AM EDT</td>
<td>HLongden</td>
<td>Methamphetamine 2</td>
<td>Processing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>New Method</td>
<td>3</td>
<td></td>
<td>4/24/2013 9:12:47 AM EDT</td>
<td>HLongden</td>
<td>Methamphetamine 2</td>
<td>Processing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>New Method</td>
<td>2</td>
<td></td>
<td>4/24/2013 9:12:47 AM EDT</td>
<td>HLongden</td>
<td>Methamphetamine 2</td>
<td>Processing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>New Method</td>
<td>1</td>
<td></td>
<td>4/24/2013 9:12:47 AM EDT</td>
<td>HLongden</td>
<td>Methamphetamine 2</td>
<td>Processing</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Method Differences

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>Method Revision</td>
<td>Version 1 7/14/2002 16:49:19 AM User SSmith</td>
<td>Created method Methamphetamine 2</td>
</tr>
<tr>
<td>13</td>
<td>&lt; System Suitability Limits &gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Lower Error Limit (LCL)</td>
<td></td>
<td>98.00</td>
</tr>
<tr>
<td>15</td>
<td>Warning %</td>
<td></td>
<td>98.00</td>
</tr>
<tr>
<td>16</td>
<td>Lower Warning Limit</td>
<td></td>
<td>98.00</td>
</tr>
</tbody>
</table>
### Result Audit Viewer

#### Method/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 Limits</td>
<td>Field Name</td>
<td>% Adjusted Area</td>
</tr>
<tr>
<td>Upper Error Limit (UEL)</td>
<td>UEL</td>
<td>1.200</td>
</tr>
</tbody>
</table>

- Methods differences shown in separate tab
- Differences have text search

©2013 Waters Corporation
Questions How would you use this?

- As part of Chromatogram review for all chromatograms?
- Only to investigate where odd integration is seen,
  - Where Manual integration is done?
  - Where data faults or is close to a fault?
- On a random number of samples?

- Would you update SOPs to use this tool?
  - Would you test them
  - And that they were being followed?

- Would you want more information in here?
- How would you document that Audit trail review was done?
- Could we add more tools?