

Auditing a Regulated Study Utilizing an Electronic Laboratory Notebook (ELN)

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Objective

The steps for auditing always will be an exercise in puzzle-assembly – but now we have electronic tools (eTools) for assistance. Assembly of all the pieces that constitute a study occur within the laboratory, various electronic systems, and culminate within the ELN. The ELN serves as both a traditional laboratory notebook, allowing the flexibility to capture and/or attach any necessary data, as well as a virtual file cabinet with unlimited storage of all documentation. Permission-based visibility to all study and support data is granted to the auditor allowing real-time access to critical pieces of study information. With all information available at an individual's fingertips, a study could progress from sample receipt all the way through to a final report, complete with finalized audit reports and a Quality statement, in an amount of time that is unheard of in the industry- days, not months. The utilization of eTools is critical in order to accomplish this drastic reduction in turnaround time.

Auditing Process

Audit eTools: system checks, audit trails, version history, and electronic reports

System checks are *customized* background checks, set up to verify a multitude of information types- from calculations to correct version method use, as displayed in Figures 1 & 2. Each of these system checks are validated before use and include an executed test plan, reviewed by Quality and approved by Management. By incorporating quality and efficiency on the front-end, valuable time is saved on the back-end.

Figure 1- Automatic System Check
Correct BAM sponsor, study, version, and regulatory status verified; wrong BAM was used for this study. User Cannot proceed.

Instrumental_Analysis	
Is BAM Template Appropriate For This Sponsor?	Yes
Is BAM Template Appropriate For This Study?	No! Experiment must be opened with BAM Template from Approved BAM Templates Folder within the Study.
Correct BAM Version and Regulatory Status?	Yes
All Mandatory Fields Complete?	No
Passed All Field Checks?	No
System Suitability Acceptable?	No
Template Formulas Intact?	Yes

Figure 2- Automatic Calculation Check
Area/height count and retention time verified; area count is out of range.

System Suitability Results	
	Methodone
Area or Height Counts	10466
Retention Time (min.)	0.905
Issues_	Response Out of Range
Acceptable	No

Audit trails tend to be daunting, enormous, and cryptic. The key to utilizing audit trails in a meaningful and efficient manner is to identify and focus on entries posing the highest risk of being erroneous. In our validated ELN, human entries pose a higher risk than information auto-populated by the system. An example of the ELN audit trail is displayed in Figure 3.

An added bonus of audit trails is the elimination of a writing utensil; it is no longer necessary to attempt to decipher cross-outs due to bleeding ink through a dried blanket of solvent, shoddy penmanship, or miles of words crammed, and crawling along the edge of a page. Figures 4 and 5 compare information captured in a traditional notebook to the same information captured in the ELN.

Auditing Process (Cont.)

Figure 3- Audit trail example
system entries (blue arrows) v. human entries (red arrows)

Audit Log									
ID	Date	Time	User	Type	Description	Sheet	Source	Comment	
300	Apr 13, 2011	8:59:08 AM	bousuma	Data Changed	System updated Experiment Properties from E-Workbook	Experiment Properties			
301	Apr 13, 2011	8:59:17 AM	bousuma	Data Changed	Value changed from "Yes" to "No" in cell Audit Ready for Management Approval?	Status	Status	As Intended-Updated status table per test script 9.3	
302	Apr 13, 2011	8:59:20 AM	bousuma	Data Changed	Value changed from "No" to "Yes" in cell Audit Ready for Management Approval?	Status	Status	As Intended-Updated status table per test script 9.3	
303	Apr 13, 2011	9:26:32 AM	whitej	Data Changed	System updated Experiment Properties from E-Workbook	Experiment Properties			

Figure 4- Traditional Paper Lab Notebook Pages

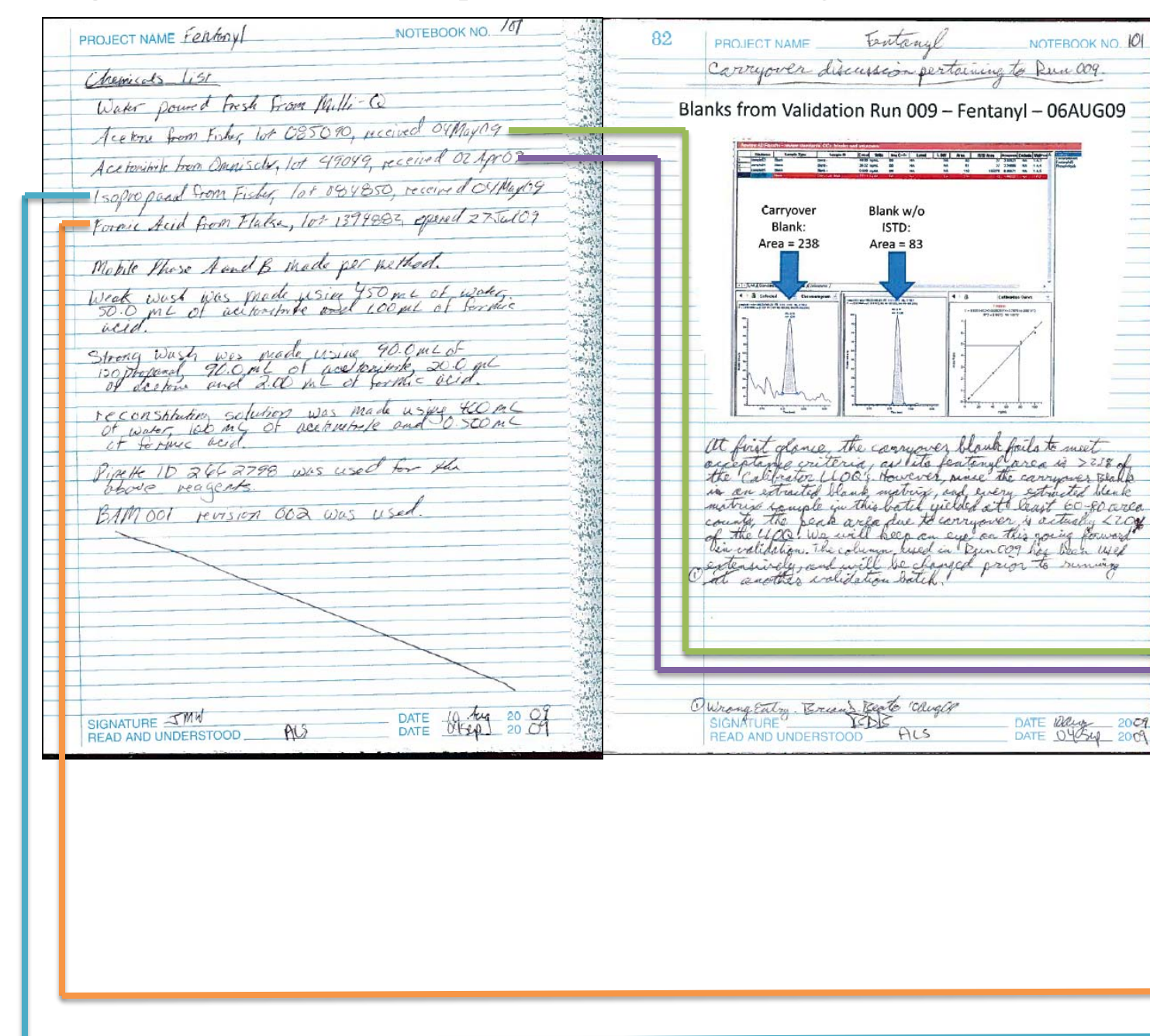


Figure 5- ELN Screen, Same Data Electronically Captured

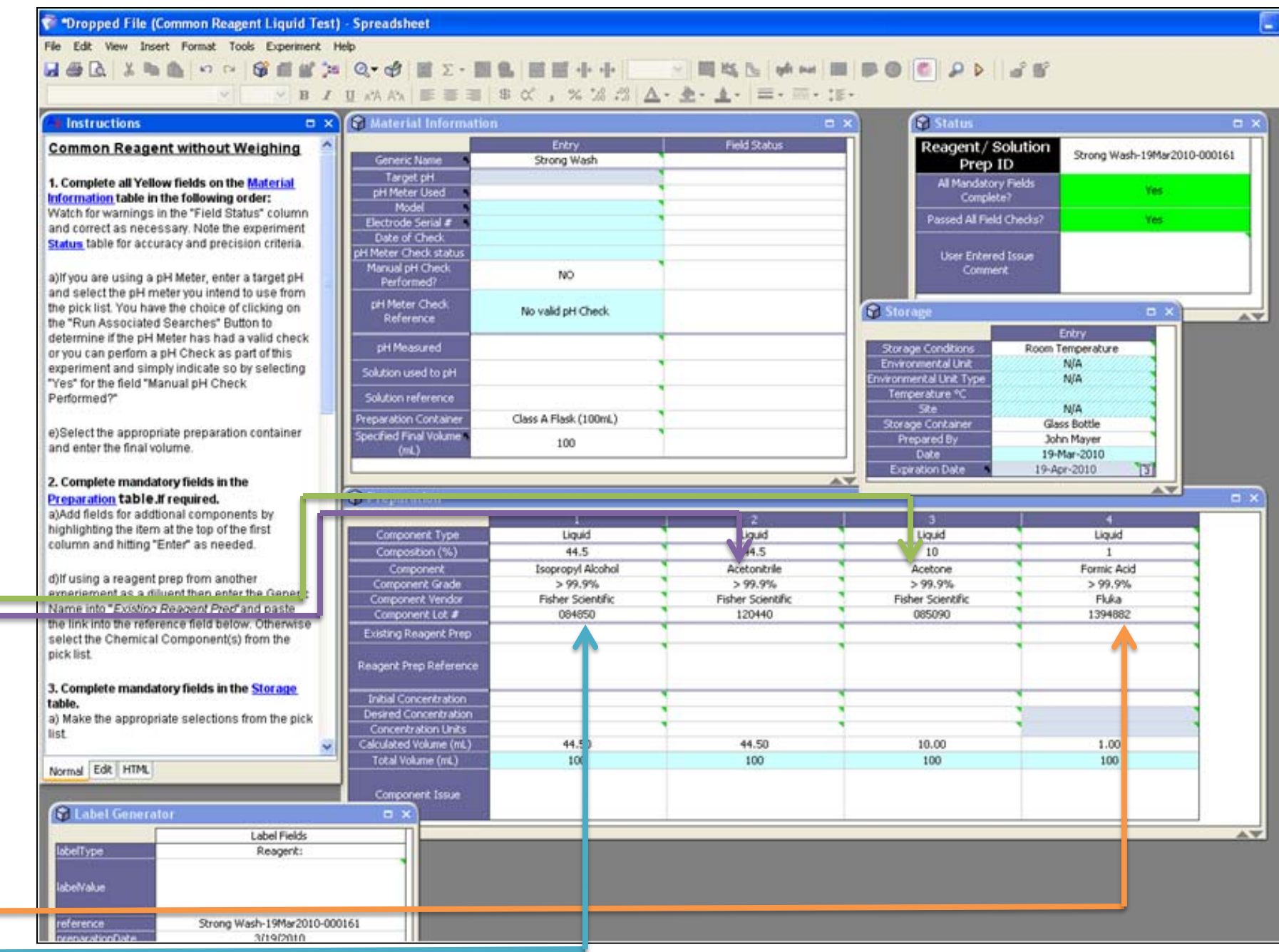


Figure 6- Version History: person making changes is identified in each version save. Commentary can be entered to indicate changes made.

Audit-0010-1061-Study Setup-20-Apr-2011-001 History	
Version 1, User: bousuma At: May 24, 2011 4:42	
Version 2, User: bousuma At: May 26, 2011 4:42	
Version 3, User: bousuma At: May 27, 2011 4:42	
Version 4, User: bousuma At: Jun 3, 2011 2:24	
Version 5, User: bousuma At: Jun 6, 2011 2:23	
Version 6, User: bousuma At: Jun 6, 2011 2:23	
Version 7, User: bousuma At: Jun 6, 2011 2:23	
Version 8, User: bousuma At: Jun 6, 2011 2:23	
Version 9, User: grevert At: Jun 8, 2011 6:1	
Version 10, User: grevert At: Jun 8, 2011 6:1	
Version 11, User: grevert At: Jun 8, 2011 6:2	
Version 12, User: grevert At: Jun 8, 2011 6:2	
Version 13, User: grevert At: Jun 8, 2011 6:2	
Version 14, User: grevert At: Jun 8, 2011 6:2	
Version 15, User: grevert At: Jun 8, 2011 6:2	
Version 16, User: grevert At: Jun 8, 2011 6:2	
Version 17, User: grevert At: Jun 8, 2011 6:2	
Version 18, User: grevert At: Jun 8, 2011 6:2	
Version 19, User: grevert At: Jun 8, 2011 6:2	
Version 20, User: grevert At: Jun 8, 2011 6:2	
Version 21, User: grevert At: Jun 8, 2011 6:2	
Version 22, User: grevert At: Jun 8, 2011 6:2	

Experiment ID: Audit-0010-1061-Study Setup-20-Apr-2011-001	
Template Approved For Use?	Yes
All Mandatory Fields Complete?	Yes
Template Formulas Intact?	Yes
All Findings Tables Complete?	Yes
Can Draft Report be sent out?	Yes
CAPA Number (if necessary)	N/A
CAPA Number Entered By (Auto-populated)	Tim Grever
Audit Ready for Management Approval?	Yes
Sent to Management By (Auto-populated)	Abby Bousum

The ELN retains a version history of all 'document saves' in perpetuity. It is not possible to make changes to an experiment that has approval signatures applied without a record of this occurring (Figure 6). Every version save can be restored for viewing purposes; this functionality is heavily utilized for testing and validation purposes. Each version save captures the testing performed in that particular version.

Results

Version history captures all 'document saves' in perpetuity. It is not possible to sneak back into a study unnoticed, after approval signatures have already been applied.

The ELN is also utilized to build the entire audit report (Figure 7). Within a single location in the ELN, Quality can capture findings (including hyperlinks to all e-findings) and allow the Principal Investigator (PI) and/or Management to respond to findings (Figures 7 and 8).

Figure 7- All Findings: Findings (including hyperlink) and Responses are captured in a single table. Findings are locked, so no changes can be made. All of the findings are discussed in a traditional audit report (orange arrow).

Experiment Hyperlink	Findings	Dates of Findings	Recommended Actions	Response Required?	Responded Required From Whom?	Responses	Data Impacted?	Initial	Date Responded	Any Additional Comments	Management Response (if necessary)
/Root/AIT/Bioscience/Sponsor/Node/0010/0010-1061/Study/Specific Protocols & Plans/BIO.VLP.0010-1061	Validation Plan is not "attested as exact copy"	20-Apr-2011	Have QA attest or indicate that this is an electronic file that has been dropped into the ELN.	Yes	BM	Attesting completed	No	BM	26-May-2011		

Figure 8- Corresponding Audit Report: Quality Submission of Findings, Responses, and Approvals are all electronically captured and include e-signatures.

(v2) QA Submission of Findings:
The following report is the result of a study setup audit w/ 24May2011. **A total of 5 findings and 3 observations** were the focus of this study. The following experiments/items were the focus of this study:
Study Summary Experiment
Validation Plan
Matrix Stability Experiment
Matson Study Setup

(v3) Response to Findings:
All findings have been addressed, and there was no impact on the study.
Digitally signed by Barbara Carel
Reason: Experiment Completed
Comment: updated per finding 2.1 in Study Setup Audit Statement: This is my electronic signature.
Date: Jun 6, 2011 3:49:00 PM

(v3) Management Approval/Comments of Audit:
Response to Findings and Observations is complete.
Digitally signed by Tim Grever
Reason: Management Reviewed and Approved
Statement: This is my electronic signature.
Date: Jun 9, 2011 9:14:15 AM

Conclusion

The days of auditing against paper checklists are gone. All too often in the CRO industry, the limiting factor in reporting final results isn't generating the lab data, it's the lengthy quality review that takes place after testing is complete. Cumbersome, paper-driven, reactive processes have been replaced with electronic, proactive processes. Utilizing tools available within the ELN, sophisticated bioanalytical laboratory processes can be matched with equally sophisticated QA techniques, resulting in a more efficient turnaround time.

