WHITE PAPER

Streamlining Bioanalytical Workflows and Enforcing Compliance

Key Benefits

- Reduced QA/Auditing Time
- Enforced Compliance with Established Methods
- Specific Bioanalytical Laboratory Workflows
- Integration with Watson LIMS

How E-Notebooks Make a Difference in Regulated Labs

Compliance with government regulations and other standards in a bioanalytical laboratory is critical, yet many labs have not yet taken full advantage of commercial software solutions that enforce compliance while increasing workflow efficiency. Many researchers continue to manually track and account for each experiment as it is planned and executed. In addition, the Quality Assurance teams responsible for compliance must sift through spreadsheets and paper logs to identify any problems with sample analysis runs. Software solutions reduce human error, automate steps to enforce compliance and create efficiencies through effective data management.

Even the most straightforward bioanalytical workflow includes numerous factors that require tracking. The treatment of subjects, collections of samples and analyses of samples must be carefully tracked and verified to prevent deviation from the prescribed method – or, if unavoidable, that such deviation is well-documented. This is a complex and demanding task. At all times, researchers must be able to account for the compound(s) under study, including their identification, preparation and characterization, and prove that the reagents or solutions involved were prepared according to approved methods. All equipment used in the study must be documented and properly maintained. A misstep as small as using a balance that wasn't calibrated within the last 24 hours can affect regulatory compliance. Finally, data analysis, calculations and results must be verifiable.

This white paper reviews the performance and benefits of PerkinElmer Informatics' E-Notebook BioAnalytical Module, a solution that streamlines the bioanalytical workflow, enforces compliance and enables scientists to plan, execute, review and publish their analyses more efficiently.

PerkinElmer
For the Better

Working with Thermo Scientific Watson LIMS

BioAnalytical E-Notebook from PerkinElmer partners perfectly with Thermo Scientific Watson LIMS. Within the bioanalytical workflow, E-Notebook directly targets all the functions that are not handled by Watson. Watson commonly tracks samples and computes concentrations from results. E-Notebook takes over to handle solution/material preparation, barcode printing and scanning, equipment management, study/run approval and reporting. Watson and E-Notebook directly and seamlessly interface, so that identifiers for Watson projects, studies and runs are queried from Watson and recorded into E-Notebook. Dynamic method validation calculations not handled by Watson can be handled by E-Notebook.

The focal integration point is sample analysis run data. This is pulled from the Watson database into the E-Notebook form. Links are established between E-Notebook and Watson at the Project, Study and Run levels to facilitate the identification and selection of the proper data sets. Once the data has been brought into E-Notebook, scientists may perform the necessary calculations. Supported calculations include:

- Recovery and Matrix Effect
- Stability
- Carryover
- Signal to Noise
- Internal Standard
- Immonogenicity Tier 1, 2 and 3

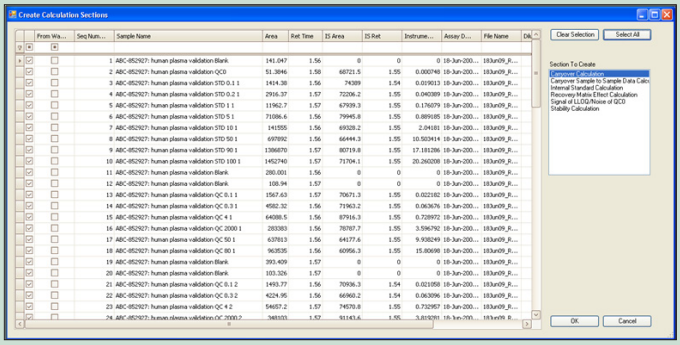


Figure 1: Method template listing the Equipment and Materials needed to carry out a Sample Analysis Run.

Calculations are executed "on-the-fly." This means a dedicated data form is created in E-Notebook when a calculation is launched. The appropriate data is then loaded into the form and the desired calculations are computed and results reported. Results of the calculations are clearly indicated in each form.

Organized for the Bioanalytical Workflow

Often scientists are reluctant to rely on commercial software because it can require them to adapt their processes to conform to out-of-the-box functionality. BioAnalytical E-Notebook, however, is able to translate existing lab methods so the software conforms to lab practices, instead. E-Notebook organization reflects the manner in which bioanalytical labs carry out their work. The highest levels of organization are: Lab Groups, Projects and Studies. Within a Study, data is further organized according to the species and matrix (tissue or fluid type) under analysis.

Because bioanalytical labs operate in a collaborative fashion, all sample analysis runs are performed under the Lab Group organization. This ensures consistent organization of data, even though the data may have been generated by several different people.

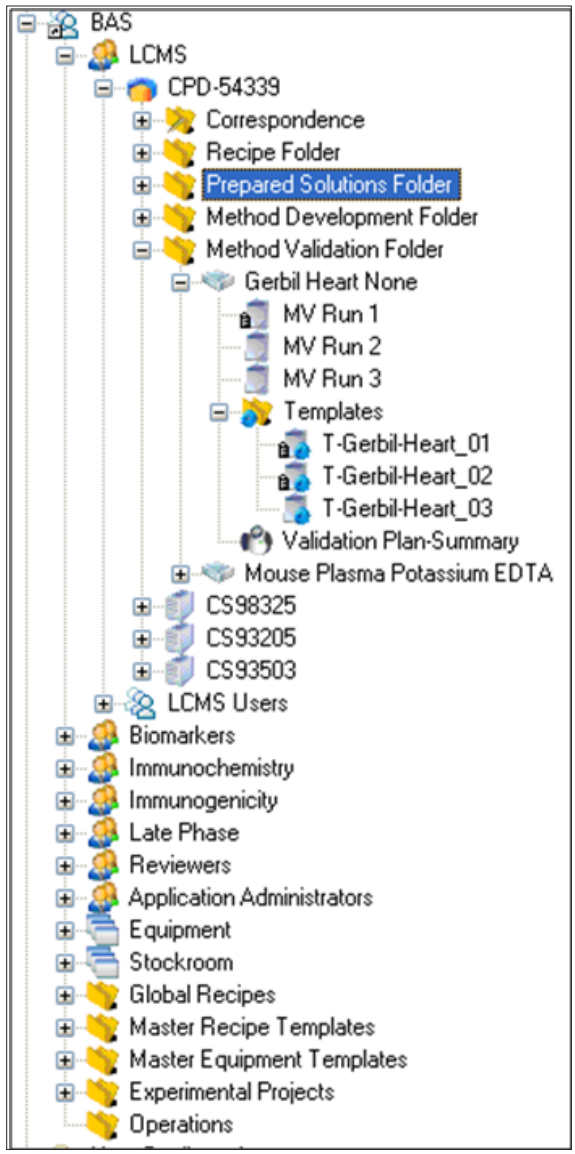


Figure 2: Organization of data in the BioAnalytical E-Notebook

To reflect the typical practice of preparing and consuming many solutions for a specific project, solutions and recipes (methods for solution preparation) are managed at the Project level.

The Global level manages items from common solvents and buffers to instruments and equipment that are shared by many people in the lab, regardless of Project. Equipment and instrumentation are typically not dedicated to a single Project.

Special Considerations for Sample Analysis

What if you could simply copy a suitable development method for use as the basis of your method validation work? With E-Notebook, this time-saving step is possible. BioAnalytical E-Notebook provides distinct, yet complementary, organizational sections for method development, method validation and study work. Workflows are consistent between these areas, yet the purpose of each is very different. E-Notebook provides a means of separating these activities. If, during method development, a particular method is deemed suitable for proceeding to the validation stages, that method can be easily copied and used during validation work. In the study execution phase, the scientist can select the appropriate validated method for analyzing samples.

High-level E-Notebook Sample Analysis Workflow:

• Create a method template to define the objective(s), types of experiment and materials to be used, laboratory procedures to be followed, analyses to be performed and details on how to perform them, and acceptance criteria.

• Submit the template for review and approval. Approval may only be given by a user of the system with the appropriate role assigned. This prevents the scientist from approving their own work and is enforced by the system.

• Create a Sample Analysis Run based on the approved template. The requirement for template approval is enforced by the system. The Sample Analysis Run captures the experimental data generated during execution of the method.

• Indicate the specific reagents, solutions and equipment used in the run. This may be done by scanning the barcodes on the solutions or equipment.

• Upload data for the sample analysis.

• Perform any necessary calculations as defined in the method template.

• Write up any necessary observations and/or conclusions for the run. Indicate whether the acceptance criteria were met.

• Submit the run for review and approval.

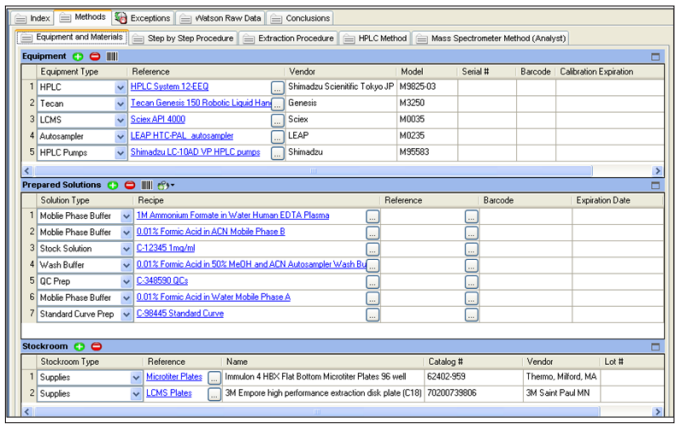


Figure 3: Creating a new calculation in the BioAnalytical E-Notebook

The review and approval process often involves back-and-forth communication between the experiment's author and the reviewer, as questions are raised, potential issues resolved and missing data added. In laboratories using paper notebooks, this communication is frequently handled with the use of paper "sticky notes" that can be removed once they are no longer needed. E-Notebook offers the same convenience with electronic sticky notes that both scientists and reviewers can use to attach transient notes to particular items. These notes are created and removed as necessary , and should be completely removed before the work receives final approval.

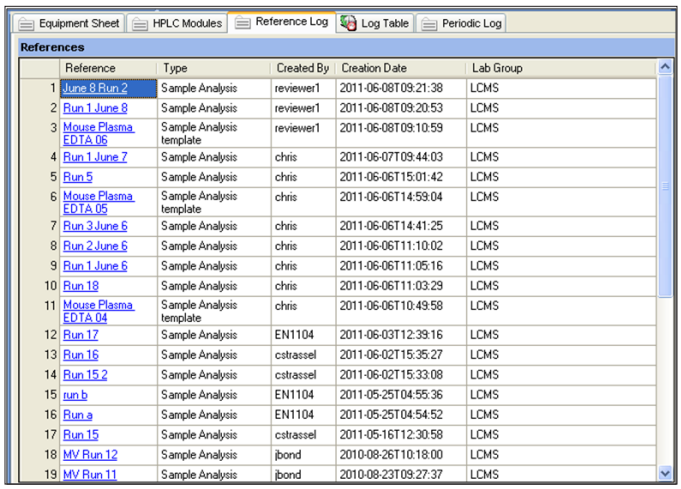
A Faster Way to Prevent, Document and Review Exceptions

Paper-based labs rely on diligent Quality Assurance teams to spend their time pouring through hundreds of pages of data in different sources simply to ensure that every step of every analysis is compliant. The QA reviewers scan lab notebooks, instrument log books and archived instrument data files. Compare this labor-intensive task to E-Notebook, which provides reports at several levels that flag for the reviewer any exceptions or changes to the data. A dashboard at the Project level, for example, displays all exceptions which might have occurred in any experiment under the project. If an exception is identified, the reviewer can access detailed information, such as materials and methods for a particular sample analysis run, with a single click. In addition, the reviewer may choose to open a detailed audit trail viewer that shows all modifications to a given item in the system. This view provides a granular "before and after" look at the data.

To reduce time spent identifying and addressing exceptions, E-Notebook automates the process of tracking the course of a sample analysis run. This involves many different reagents, lab equipment and other supplies. To remain within Good Laboratory Practice (GLP) guidelines, E-Notebook effortlessly helps the scientist ensure that each item used in the experiment is within its established usage parameters, such as solutions within their expiry date or equipment properly maintained and calibrated. The system checks that necessary compliance conditions are met and immediately notifies the scientist if any item is out of compliance. The scientist has the option to make a change, but if they

proceed, the exception will be logged in the audit trail along with a mandatory annotation from the scientist.

E-Notebook closely tracks all equipment and solutions usage. This allows a reviewer to quickly identify the potential scope of a problem. Consider the case where a reference compound solution is found to be contaminated: any work that involved that solution must be immediately identified and reviewed. With E-Notebook, the reviewer simply opens the record for that solution and reviews the Usage Log. This shows every instance where the solution was used, either as a reagent in an experiment or as a component in another solution. This would be impossible with a paper notebook system.



	Reference	Type	Created By	Creation Date	Lab Group
1	June 8 Run 2	Sample Analysis	reviewer1	2011-06-08T09:21:38	LCMS
2	Run 1 June 8	Sample Analysis	reviewer1	2011-06-08T09:20:53	LCMS
3	Mouse Plasma EDTA 06	Sample Analysis template	reviewer1	2011-06-08T09:10:59	LCMS
4	Run 1 June 7	Sample Analysis	chris	2011-06-07T09:44:03	LCMS
5	Run 5	Sample Analysis	chris	2011-06-06T15:01:42	LCMS
6	Mouse Plasma EDTA 05	Sample Analysis template	chris	2011-06-06T14:59:04	LCMS
7	Run 3 June 6	Sample Analysis	chris	2011-06-06T14:41:25	LCMS
8	Run 2 June 6	Sample Analysis	chris	2011-06-06T11:10:02	LCMS
9	Run 1 June 6	Sample Analysis	chris	2011-06-06T11:05:16	LCMS
10	Run 18	Sample Analysis	chris	2011-06-06T11:03:29	LCMS
11	Mouse Plasma EDTA 04	Sample Analysis template	chris	2011-06-06T10:49:58	LCMS
12	Run 17	Sample Analysis	EN1104	2011-06-03T12:39:16	LCMS
13	Run 16	Sample Analysis	cstrassel	2011-06-02T15:35:27	LCMS
14	Run 15.2	Sample Analysis	cstrassel	2011-06-02T15:33:08	LCMS
15	run b	Sample Analysis	EN1104	2011-05-25T04:55:36	LCMS
16	Run a	Sample Analysis	EN1104	2011-05-25T04:54:52	LCMS
17	Run 15	Sample Analysis	cstrassel	2011-05-16T12:30:58	LCMS
18	MV Run 12	Sample Analysis	jbond	2010-08-26T10:18:00	LCMS
19	MV Run 11	Sample Analysis	jbond	2010-08-23T09:27:37	LCMS

Figure 4: Log showing all Methods and Runs which have used a particular instrument.

Automating Recipes and Solutions

When defining a sample analysis method, the scientist must also define the specific recipe(s). E-Notebook offers time-savings for defining the specific recipe to be used when creating the reagents necessary for a run. A set of recipe forms serve as the starting point for creating a new recipe. These templates include:

- Stock Standard
- Buffers, including buffers from pre-measured components such as pouches or tablets
- Serial dilutions
- Liquid mixtures (for example, a solution of 50% Methanol with 50% water)

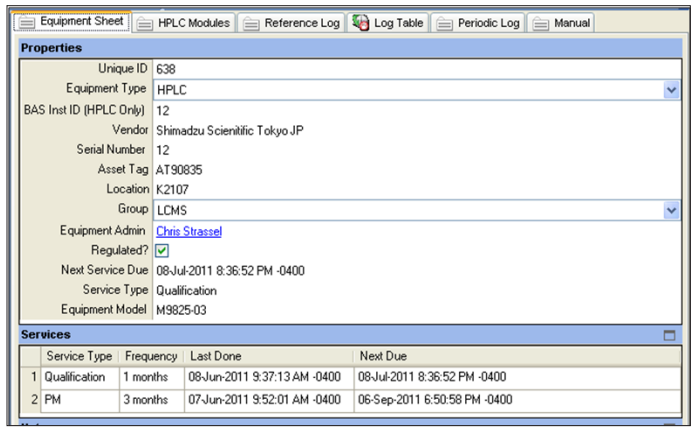
Each of these recipe templates includes a form specific to the preparation involved. In the Stock Standard recipe, the necessary amount of compound is calculated based on the desired volume, concentration and purity of the compound. For efficiency, new recipes may be created from an existing recipe. The existing recipe can be duplicated and any necessary changes are made to the copy.

When scientists are ready to prepare a solution, they select the recipe to be used. E-Notebook presents the appropriate forms to follow and fill out to prepare the solution. Barcodes may be printed for any solution in the system for later use in identifying and associating solutions with experimental work.

Tracking Equipment and Supplies

BioAnalytical E-Notebook maintains an inventory of all equipment and supplies used in the laboratory. Generic forms for equipment allow the user to enter standard information, such as name, model, vendor, serial number and more. Where appropriate, more specialized forms capture detailed information for any software associated with an instrument or sub-components such as HPLC modules. Balance forms bear special mention, as they include the necessary information to allow E-Notebook to read data directly from the balances. A scientist can simply press a button on the balance and the mass value is transferred directly into E-Notebook form. This reduces the need for data transcription and eliminates inevitable errors.

E-Notebook monitors all maintenance and service activities and provides an overview of the required maintenance and calibration activities over a period of time. Any item which may be past due for an activity can be removed from service until the necessary work is complete.



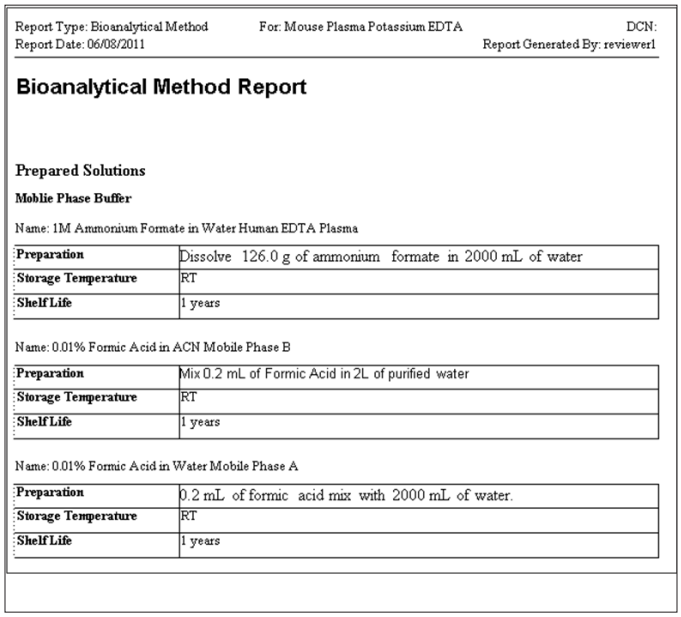
	Service Type	Frequency	Last Done	Next Due
1	Qualification	1 months	08-Jun-2011 9:37:13 AM -0400	08-Jul-2011 8:36:52 PM -0400
2	PM	3 months	07-Jun-2011 9:52:01 AM -0400	06-Sep-2011 6:50:58 PM -0400

Figure 5: The Equipment Management sheet. Note the services table, showing the activities which must be performed to maintain the instrument.

Documents, including PDFs and Microsoft® Word and Excel, may be attached to the equipment in E-Notebook, allowing a consistent means of storing manuals for each instrument. Maintenance reports provided by the vendor after service can also be archived with the instrument. As with solutions, barcodes can be generated for equipment items in E-Notebook and later scanned to identify a particular instrument's involvement in an experiment. Likewise, supplies, such as columns, plates and other disposables, can be recorded and referenced in E-Notebook. Scientists can then specify which types of consumables were used in an experiment.

The Advantages of Reporting and Dashboards

E-Notebook helps scientists quickly and easily prepare reports and optimize use of existing information. Canned reports and dashboard come standard, and a graphical interface enables users to modify or create new reports. For example, once a method is established, scientists may create a concise, formatted method report that collates data from the method and tracks all components, including equipment, recipes, solutions, protocols and so on.



Report Type: Bioanalytical Method For: Mouse Plasma Potassium EDTA DCN:
Report Date: 06/08/2011 Report Generated By: reviewer1

Bioanalytical Method Report

Prepared Solutions

Moblie Phase Buffer

Name: 1M Ammonium Formate in Water Human EDTA Plasma

Preparation	Dissolve 126.0 g of ammonium formate in 2000 mL of water
Storage Temperature	RT
Shelf Life	1 years

Name: 0.01% Formic Acid in ACN Mobile Phase B

Preparation	Mix 0.2 mL of Formic Acid in 2L of purified water
Storage Temperature	RT
Shelf Life	1 years

Name: 0.01% Formic Acid in Water Mobile Phase A

Preparation	0.2 mL of formic acid mix with 2000 mL of water.
Storage Temperature	RT
Shelf Life	1 years

Figure 6: The first page of a Method Report generated by the BioAnalytical E-Notebook, based on an approved Method Template

Several standard dashboards are available in E-Notebook. Dashboards provide users with a tabular summary of information, including views that display:

- "Items to Review" list
- Reviewed work requiring follow-up
- All items in a certain group (appropriate for lab managers)

Any of the standard dashboard views may be copied and personalized by the user. A scientist might copy the "Group Work" view and modify it to include only items of a certain type, such as solutions. The scientist could further limit the list to include only those solutions that are still available for use. Customizing the dashboard view enables users to find exactly the information they need -- in this case, available solutions in the lab.

Additional Features

BioAnalytical E-Notebook offers abundant functionality that streamlines workflows while ensuring compliance. Among the highlights:

- Email capture -- capture Microsoft Outlook email messages as part of a project or study. Simply drag emails from the user's Inbox into the email section of E-Notebook. A preview is generated and any attachments are preserved for later access and use.
- Integration with Microsoft Office -- users can incorporate Microsoft Word, Excel and PowerPoint documents directly with their experimental records.
- Generate PDFs -- experimental data may be exported from E-Notebook as a PDF for archiving, sharing and other purposes.
- Electronic signatures -- E-Notebook accepts electronic signatures. Scientist must provide, for example, an electronic signature when submitting a sample analysis run for review, to document that they performed certain work and to generate data according to the protocol as documented in E-Notebook.

BioAnalytical E-Notebook Documentation

BioAnalytical E-Notebook was developed in close collaboration with a pharmaceutical Bioanalytical group for use in a GLP-regulated environment. As such, all features are captured in an extensive Requirements Specification and are verified using a library of test scripts. Traceability is maintained and documented between requirements and test scripts. This documentation, as well as any necessary Professional Services work to deliver all or part of the installation and validation work, may be included as part of the BioAnalytical E-Notebook deployment.

Faster Turnarounds with Fewer Costly Exceptions

BioAnalytical E-Notebook, a solution by PerkinElmer, provides a complete set of functionality to support both scientists and management in GLP-regulated bioanalytical laboratories:

- Solution preparation forms with recipe management
- Barcode printing and scanning
- Balance integration
- Equipment management and maintenance logs
- Watson LIMS integration
- Calculations
- Expiration date checking with annotation
- Change logging with annotation
- "Sticky note" annotation
- Configurable review process
- "Before and after" audit trail view

With BioAnalytical E-Notebook, scientists can more efficiently and accurately design and execute experiments and more easily perform the analyses required. Lab managers and QA reviewers far more efficiently review experiments and account for exceptions. Built-in checks ensure that E-Notebook flags and prevents exceptions, and, for those that are unavoidable, audit reports keep exceptions visible and well-documented. Bioanalytical workflows are streamlines and fully compliant. E-Notebook provides all bioanalytical teams with the tools needed to achieve faster turnaround with fewer costly exceptions.

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