



REVIEW ARTICLE

Electronic Laboratory Notebook-A Review

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ABSTRACT

Today's world demands new innovations. This is true even for laboratory environment. Whether R&D laboratory or GLP, paper based laboratory notebooks were the preferred choices for documenting day to day work. But, documentation of data manually in Paper laboratory notebook (PLN) is prone to error and hence they are being replaced by electronic laboratory notebook (ELN). ELN is system to create, retrieve and share fully electronic records in ways that meet all, regulatory, legal, scientific and technical requirements. Only authorized users access the ELN. This review describes various features and application of ELN. ELN are useful means of optimizing work and reducing costs as well as times. These are becoming an increasingly popular tool for research and routine laboratories. Future of ELN will eventually be used by all R&D scientists to record all their research and will become their central application.

KEYWORDS

Electronic Laboratory Notebook (ELN), Paper Laboratory Notebook (PLN)

INTRODUCTION

In today's technology predicated world, innovation drives performance. This is true for all the cases. In any good laboratory practice (GLP) environment some type of laboratory notebooks are found. A foretime the paper predicated laboratory notebook were preferred cull for documenting day to day work, whether it is a GLP or research and development (R&D)¹. But with the advent of new technologies paper laboratory notebook (PLN) are being replaced with electronic laboratory notebook (ELN). Documentation of data manually into a PLN is prone to errors and also in some cases it is not possible to transcribe the data into PLN, for example analytical data like spectra, chromatogram, and photographs.

According to collaborative electronic notebook system association (CENSA) ELN is defined as, an electronic laboratory notebook is system to engender, retrieve and apportion planarity electronic records in ways that meet all, licit, regulatory, technical and scientific requisites². There are two types of ELN, specific and nonspecific or cross disciplinary ELN. Specific ELN contain features to work with specific application, scientific instruments or data types. They are made for one department with specific needs related to its research subjects. Nonspecific ELN are design to support access to all data and information that needs to be recorded in a lab notebook. They are developed for whole company and its domain³.

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The concept of an electronic version of laboratory notebook is given by Dr. Keith Caserta. The laboratory notebook in an electronic format was in full swing in the early 1990's. In

2000 the true legal implication of a fully electronic lab notebook would have on the industry. In 2006, MEDRAD's Electronic Lab Notebook Project Final Report identified an "ELN market of 28 different vendors". Today, "there are over 30 supplier of ELN technology, year over year growth is still above 20 Per cent, making ELN one of the fastest growing informatics technologies⁴.

Why Electronic Laboratory Notebook?

There are two types of laboratory notebook may be used, loose leaves or bound notebooks. Bound notebook has fine-tuned page sequence therefore preferred method is bound notebook. Good method for capturing printout from instrument is loose leaves notebook. Bound notebooks have been utilized for experimental observation was recorded manually. However, with the advent of advanced and robotization instrumentation, in every department of pharmaceutical R&D, PLN became anachronism. Scientific data fall into raw data that are engendered by an instrument, recorded by data amassment software, and organized by data analysis software. The processed data represent the conclusion of an experiment⁵.

A common experience today is to handwrite the procedure and object in the paper laboratory notebook, act the experiment, raw data analyse using computer software, print the processed facts and paste it on to the notebook next to the opinions by reasoning. This process has several limiting conditions that act on amount produced: data in PLN cannot be readily made way in, looked for, reanalysed, cut and paste is tiresome, and paper records are hard to put in force.

ELNs accommodate the purport of daily record keeping and as a result, provide "Analyst Diary" functionally for laboratory scientist. Notebook data manage electronically would abstract the inhibitions of bound notebooks.

Basic Requirements

ELNs affect the record keeping workflow it must assemble the business requirement; following are some consequential aspects to be given in order

to be ELNs, to be practical supersession of paper bound notebooks

- Electronic laboratory notebook should provide a reliable environment to bulwark the integrity of both data and process, whilst additionally affording the flexibility to adopt incipient processes or changes to subsisting processes without recourse to further software development.
- The package design should be a portable design, so as to provide the benefit of minimizing validation costs of any successive changes that you may want to make in the future as your desiderata change.
- Follow key information like compound registration number, project number, author, experimental method, data and other keywords.
- Connect all pages in regard to a compound for easy recovery of chemical synthesis, structure, chromatograms, stoichiometry, and analysis and spectra information.
- All data inside the system should be save in a database (e.g. MS-SQL, MySQL, Oracle) and hence be completely searchable.
- Subject particular templates in case the users do not have to type in everything from scratch.
- Long lasting and transportable data entry device to refuse data entry at the laboratory bench top.
- Handwriting apperception and content storage as both image and text.
- The application should prevent secure forms to be generated that accept laboratory data input through PCs and/or laptops / palmtops, and should be directly connected to electronic devices such as pH meters, laboratory balances etc.
- It should involve configurable qualification requisites to automatically verify that instruments have been cleaned and calibrated within a designated duration that reagents have been quality-checked and have not

expired, and that workers are trained and sanctioned to utilize the equipment and perform the procedures.^{5,6}

Regulatory and Legal Aspects

There are many requisites for implementing a prosperous ELN. Meeting licit requisite is most critical, because laboratory notebooks utilized for scientific revelation. It is withal utilized for development or research in regulatory industries, such as medical contrivances or pharmaceuticals, are conventional to approve with FDA regulations cognate to software validation. The basis of the regulations is to protect the integrity of the ingressions in expression of time, authorship, and content. Dissimilar ELNs for patent auspice, FDA is not disturbed with patent interference proceedings, but is disturbed with avoidance of falsification. Typical provisions cognate to software validation are included in the medical contrivance regulations at 21 CFR 820 and Designation 21 CFR Part 11. Essentially, the requisites are that the software has been designed and implemented to be congruous for its intended purposes.

The FDA was set up in 1937 under code of federal regulation Title 21, conventionally abbreviated 21CFR. FDA has extensive regulation guidance to electronic records and electronic submission. It is pellucid that electronic records are acceptable proof for manages the data is placed under control.⁶

21 CFR part11

The regulations in this component set forth the criteria under which the firm considers handwritten signatures, electronic signature and electronic records, executed to electronic records to be trustworthy, reliable, and generally identically tantamount to paper records and handwritten signatures executed on paper⁷. Part 11 of 21CFR in 1997 was integrated to cover the maintenance, engenderment and preservation of electronic records and electronic signatures⁵.

A period of 2005, 21 CFR part 11 assent became a conventional requisite for ELNs, even while almost all ELN facility are not covered via that regulation. It is now mundane to visually

perceive claims that a product is 'GMP compliant' or '21 CFR part11 compliant'. These assert are false, however, because exclusive a consummate system, containing standard operating procedures and all cognate software at a firm, can be compliant. An ELN that assemble technical requisites can avail and firm become aquiescent⁸.

Components of ELN

- Experiments are recorded in electronic documents
- Experiment acceptance use computer-driven analytical equipment
- Computerization of laboratory
- Software systems
- Experiment acquisition uses robots /Manual
- Computer literacy of the scientists⁹

ELN as an Integral Part of Electronic Laboratory

ELNs are the combined with different computerized system. To maintain the approved processes, a typical laboratory utilizes a number of systems, like, ELNs, laboratory information management systems (LIMSs), Chromatography Data Systems, Chemical Registration Systems, Data and Document reservoir that give help for laboratory activity, are segregate across the firm. Being most intermittently used by the laboratory scientists, the ELN can be naturally converted into a tool that merges data from multiple systems. Therefore, the ELN can act as a portal, which can probably bring in a difference of data mining applications.

Data format standardization is an important aspect of integration. In the chemical registration area, the SD File format from Elsevier, although extensible mark-up language (XML) based standards are being developed recently, MDL remains the de facto industry standard. SD File is used for transferring a huge number of chemical structures in databases. Vendors with chemistry-enabled ELN products, like Cambridge Soft, support the SD File format. Because SD File format is in American Standard Code for

Information Interchange (ASCII) text, custom incorporation may be developed with relative ease.

One of the intricate aspects of instrument-ELN integration is various data standards that negatively influence information exchanges between systems. Pharmaceutical industry needs a prevalent format for long-term data repositories, which are vendor independent in reviewing or processing of analytical instrument data. Analytical Information Mark-up Language, for the storage of analytical instrument data AnIML may use. AnIML can withal be acclimated to record data from everyday experimental workflows in a laboratory environment. However, AnIML is yet to be adopted by most ELN vendors.

At the database level, most ELN products support relational databases, such as structured query language (SQL) Server and Oracle. As a result, incorporation between ELNs and other systems can be achieved data access implements or utilizing standard SQL available in most software development environments.⁵

Important Features of ELN

Ease of use: Ease of avail and wide acceptance of the electronic notebook is to not deviate too far from the functionality of the fundamental paper notebook. The basic goal will be to repeat standard practice in an electronic format. Engender an interface that provides intuitive ingress of information. Electronic notebook without having to read a utilize manual should be figure out by a researcher. The information that requires to be input into a notebook varies from researcher to researcher and project to project. The want to have any type of information facile to enter requires that the input interface be expandable.

Notebook Security: Access to a particular electronic notebook, authentication of ingressions and its contents in a notebook are fundamental security issues that any notebook must address. Every notebook has a list of sanctioned users. To provide non-tamper ability of ingressions, the design of the notebook should automatically date,

and digitally sign each ingression, then append the ingression to the last page of the notebook. Pages of notebook can be authenticating at the press of a button.

Witnessing is often mentioned as a more paramount feature than notarization. This is where an expert in the field habituated with the author reads the notebook pages and dates and signs them as being true and authentic. Design of notebook needs to provide a way of integrating such interpretation to a notebook page.

Interoperability and Expandability: Scientists will be accessing and updating electronic notebooks from many variants of computers from laptops to supercomputers. Software of electronic notebook should be designed to operate across Mac, PC, and Unit platforms. It is withal desirable from a software engineering standpoint to engender a single software package that is portable to a wide range of computer platforms rather than engender several packages each targeted to individual platforms.

The aim is to engender an interoperable, expandable electronic notebook that engineers and scientists will find more utilizable than their present paper notebooks.¹⁰

Electronic Signature and Electronic Archiving and Hybrid ELN Approach

Electronic archiving and Electronic signature provide a licit parity to their paper counterparts. ELN system must ascertain integrity, authenticity, non-repudiation, identity for each ELN record¹¹. This must be demonstrated over the lifetime of the record, from engenderment through to final disposition.

ELNs provide advantage to the sign-and-witness workflows that are acclimated to fortify due diligence during reduction to practice. A physical laboratory notebook, even ephemerally, so that a record can be signed is an inefficient and inconvenient process: consequently, it is often not carried out in the required timely pattern. Records should be signed at time that the research is conducted, but signing is often carried out 3 to 6 months later at a 'mass signing party'.

Corporate patent attorneys have been resistant to the conception of becoming 'fully electronic' in their work practice that is, employing electronic archiving and signatures information as electronic records. This resistance stems from the lack of case law in the area of patents, despite the fact that the Federal Rules of Evidence do not omit electronic documents, and that the decision in a number of high-profile cases has relied on email evidence.

The hybrid ELN approach: If a company has a manufacturing operation, then the US Food and Drug Administration (FDA) will hearten that company to submit the required regulatory information electronically, and the company will require introducing an electronic records management system. Such systems are extravagant to license and maintain: thus, minute companies, and concretely start-ups, are unlikely to become completely electronic. A hybrid approach, in which all data are entered electronically and are searchable, but the licit record constitutes a printout with 'wet signatures', will remain popular until electronic record systems become cost-efficient⁸.

Benefits of ELN

There are many benefits in utilizing ELN as an implement to record scientific information, including ease of access to research data, incremented quality in record keeping, better compliance to IP and regulatory policy, and operational consistency.

ELN incremented information sharing evades dispensable reiterates of a foretime failed experiments and optimizes equipment and resource utilization. Data can be effortlessly retrieved utilizing multiple criteria, such as compound ID, dates, and designations. Time spent in probing for definitions manually could be reduced due to ELNs' linked acronym database, which may provide the definition necessarily. With ELNs, a majority of perpetual steps can be eschewed while maintaining a compliant process. For example, there is no desideratum to fill in the "continued from" and "continued to" fields that are located on each page of a paper notebook. Many ELNs provide a

wide range of capabilities to import pictures (indirectly, as a scanned object, or directly, via an interface to another application) in a multiplicity of formats, which can be facilely resized when obligatory. ELNs detect typographical errors afore an e-signature is entered, preserving the time of initialing, dating, and rectifying minor typos. If only electronic records are maintained, the utilization of ELNs will eliminate the time and money needed for engendering and maintaining the paper and microfilmed records.

Typical Return on Investment (ROI): 100 scientists using ELN Savings ~\$850k per year because, less time for planning, recording and reporting, less time collecting information for IP protection and regulatory compliance, Eliminate duplicate experiment.⁵

Drawbacks of ELN

The flip side of information sharing is the potential misunderstanding and erroneous conclusions drawn by scientists who are not intimately acclimated with the data. Time should be sanctioned for cultural changes, cognate to treating notebook data as corporate asset rather than personal property, to take place. Ameliorated data annotation is essential to minimize the possibility of misinterpretation, and hearten communication between users when the designation of data needs to be demystified.

Computers are fragile and less portable than bound notebooks, which can be carried around the lab. Albeit portable contrivances such as tablet PCs are now available, they are more extravagant to maintain and may not be compatible with all commercially available software.

The efficiency gain in data ingress utilizing ELNs may not be as sizably voluminous as one would expect. Other time may be necessary to capture data in the ELNs than by handwriting it in a bound notebook, because keyboard data ingress is more cumbersome than handwriting in a laboratory environment. Albeit optical character apperception technology has become widely available in recent years, the precision rate may not be high enough for a laboratory

environment, where one does not have much time to redress software errors while performing an experiment.

Drawing a chemical structure is another quandary. Current drawing implements require the utilization of an implement kit of structural elements, such as bonds and atoms, an experience that can be amended dramatically if hand-drawn chemical structures can be interpreted into a computer representation. Such an implement has been developed by Brown University and it would be intriguing to visually perceive when such technology will be commercialized. Because electronic format and archiving media technology change rapidly, managing electronic records in a readable format for a long period of time is a challenge. The mainly long lifetime of a patent, requires ELN data be saved for decades.

To data preserve for a long term, care must be taken to ascertain that felicitous standard archiving formats such as PDF/A7 is utilized for data archiving. In the event of standard formats transmuting, one must be yare to convert data to the incipient format. The cost of implementing an incipient record-keeping process in the utilizer groups could be paramount. In integration to software and hardware cost, costs associated with utilizer workflow changes cannot be underestimated. Maintaining and implementing integration between ELNs and other computer systems can withal be of high cost.

Electronic security is another quandary that must be addressed. Procedures must be enforced to obviate password sharing, a typical problem in some utilizer areas. Felicitous infrastructure must be put in place to reduce exposure to malignant hacking and computer virus.⁵

ELNs Available in Market Today

Table 1: ELNs Available in Market Today¹⁴

Supplier	Comment	Supplier	Comment
Accelrys	Multiple (Symyx Notebook, ConturELN)	LabCollector	Non-specific (LabCollector ELN)
Agilent	Non-specific with add-on modules (OpenLAB ELN)	Laboratory Data Solutions	GxP-focused ELN (Labnotes)
Amphora Research	Non-specific (PatentSafe)	LABTrack	Non-specific (LABTrack)
Arxspan	Chem and Bio (ArxLab)	LabVantage	LabVantage LIMS-based (LabvantageeNotebook)
Asseco	SharePoint-based (shareSignELN)	LabWare	Labware LIMS-based (LabWare ELN)
Cheminnovation	Biology and chemistry-specific	Neudesic	SharePoint-based (Neudesic ELN)
Cognium Systems	Semantic non-specific (iPad ELN)	NoteBookMaker	Non-specific (NoteBookMaker)

Supplier	Comment	Supplier	Comment
Dotmatics	Chemistry-specific (Studies Notebook)	Quattro Research	Non-specific (Quattro/LJ)
DeltaSoft	Chemistry-specific (DeltaBook)	PerkinElmer	Multiple: Cambridge Soft E-Notebook, ArtusLabs, Labtronics
Enso Software	Chemistry(Ensochemlab)	RuRo	Non-specific (Sciency ELN)
Edge Software Consultancy	Biology data management with ELN (BioRails)	Rescentris	Biology and non-specific (CERF)
EZQuant	Biology (EZQuant)	Scilligence	Non-specific (OLN – Open Lab Notebook)
Formulator Software	Formulations (Formulator)	Siemens	MES-based (SIMATIC IT R&D Suite)
iAdvantage	Pre-clinical study management (eStudy)	STARLIMS	STARLIMS LIMS-based (STARLIMS E Notebook)
IDBS	Multiple (BioBook, ChemBook, E-WorkBook)	Studylog	Animal study management (Studylog)
Kinematik	Non-specific ECM-based with Project Mgt (eNovator)	Textco	Sequence analysis (Gene Inspector)
LabArchives	Non-specific (LabArchives)	VelQuest	Procedure Execution, GxP-specific (SmartLabgmpELN)

Some Industry who have Adopted ELN

Many of the industrial organization like Pfizer, AstraZeneca, Elan, Millenium, Kalexsyn Eli Lilly has adopted ELN. ELN has helped organization in many ways; some of the usefulness of ELN is enlisted here,

Experience, Aggregate data, and context to fuel insights and gain predictive control over key processes

Facilitate collaboration between analytical, medicinal, and process chemists and with outsourced partners

Eliminate paper-predicated workflows in validated environments and preserve 50% on documentation time

Preserve 25% off time spent documenting experiments. Preserve thousands of dollars per year -

Leverage prior work by cloning 50% of experiments. Amend IP utility and quality.¹²

Application

ELN helps accelerate the discovery and development for organizations of all sizes and within the fields of science in almost all branches of pharmaceutical R&D, QA/QC, Biology, Drug development, Formulation, Analytical chemistry, Pre-clinical studies.

ELN in general are utilized by technicians and scientists to document research, procedures and experiments performed in a laboratory. It is often maintained to be a licit document and may be utilized in a court of law as evidence. Akin to an inventor's notebook, the lab notebook is withal often referred to in patent prosecution. ELNs streamline the documentation and protection of intellectual property.

Pro and Cons between ELN and PLN

Table 2: Pro and Cons between ELN and PLN¹³

CRITERIA	PLN	ELN
Organization impact	Easy	Difficult

Job impact (learning curve)	Middle	High
Training	Minimum	Long
Use(writing)	Manual	Semi-automatic
Data research	Slow	Instantly
Storage(back up)	Risky	Secured
Data availability	Minimum	Permanent and parallel
Follow-up (witness, manager)	On the spot	24h/7d
Cost	Less expensive short term	Less expensive long term

CONCLUSION

Electronic laboratory notebook is a software program designed to replace paper notebook. ELN rapidly becoming a core part of every laboratory operation in industries from pharmaceutical, to chemicals, to consumer goods and more.

ELNs streamline the protection and documentation of intellectual property, help scientists collaborate in increasingly global and networked research & development activities, and make scientific data and observations associated with experimentation easier to search, find and use.

It has its application in all fields of research.

Fully paperless notebooks ELN reduce the time spent by 50% looking for data like PLN, eliminate repeat experiments lower cost by 25%.

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