Laboratory Information Systems

Signed, Sealed and *Indelible*

Electronic lab notebooks help a worldwide biopharmaceutical research firm protect intellectual property while reducing paperwork.

By Dr. Nicole Vaughan-Spickers

For any company competing in the healthcare, biotechnology and pharmaceutical industry, the ability to bring products to market more quickly increases opportunity for revenue and company growth. However, streamlining processes means implementing lab automation technologies that let scientists reduce the time they spend documenting their work and spend more time actually producing work. In addition, it is critically important to ensure that records can withstand litigious scrutiny and compliance pressures.

Ferring Pharmaceuticals is a family-owned, research-driven biopharmaceutical company devoted to identifying, developing and marketing innovative products in the fields of urology, gynecology and fertility, gastroenterology and endocrinology. In recent years, Ferring has expanded beyond its traditional European base with 2,500 employees in offices spread over 40 countries with treatments available in more than 70 countries.

In addition to the ever-present commitment to patients and stakeholders, the company faces an increasingly competitive landscape, adding to the difficulty of maintaining this international growth. To meet this commitment and remain ahead of industry competition, Ferring executives identified the need to reduce the product development and market introduction lifecycle and cost.

The Paper Trail of Discovery

When kept properly, lab notebooks create the "trail of evidence" that is essential in protecting valuable intellectual property. The information contained in lab notebooks is often the best record as to when an invention was conceived and reduced to practice. Conception and reduction to practice can be used to prove "priority" (i.e., an earlier invention date) in the event a second inventor of the same "thing" is also seeking patent protection. It can also be used as a defense in the face of an accusation of patent infringement. Furthermore, this information can establish the identity of the inventors and their respective contributions to the invention.

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Despite the vast sums invested by the major healthcare and pharmaceutical companies on research and development, most of these companies still rely on the same antiquated method of paper lab notebooks used by their counterparts years ago to protect their scientific intellectual property (IP). As most lab and process development chemists will tell you, issues with lab notebooks are nothing new in the pharmaceutical and biotechnology industries. Paper lab notebooks are often illegible, incomplete or include other errors that would render the experiment incapable of duplication.

Finding information in a team member's lab notebook proved to be a nearly impossible task, all but eliminating the prospect of knowledge-sharing or team collaboration. With dozens upon dozens of lab notebooks in any given lab at one time, scientists with R&D responsibilities spent more and more time looking for information in these lab notebooks than analyzing it or coming up with new experiments that would lead to new product discovery or development.

Where similar digital solutions like digital signatures expire over time, digital timestamps are persistent and can be stored for as long as necessary to meet regulations.

From Paper Trail to Electronic Pathway

With the inefficiencies so easy to note, one might wonder why companies have stayed true to the paper notebook method. The strongest justification for this continued usage of an outdated technology is the perception that IP protection cannot be managed by electronic systems. Until recently, companies still relied on the traditional "signed and witnessed" practice for paper lab notebooks in order to prove IP ownership.

Ferring's R&D process was no different. A vast majority of experiment-related documents were printed out by the scientist, pasted into a notebook and signed

and dated by a witness to verify its authenticity. The physical space required to store every scientist's notebook was enormous. The time scientists spent compiling their paper notebooks was considerable, meaning their companies lost additional R&D time and its associated revenue. With rising demand to meet regulations and provide value to the stakeholder, this process was deemed unnecessarily time-consuming and ultimately counterproductive.

To expedite the documentation and data-entry process, Ferring decided to migrate from paper lab notebooks to an Electronic Lab Notebook (ELN). In doing so, we believed it could provide a means of faster and easier information retrieval, collaboration and knowledge sharing among its more than 100 scientists and across its two R&D sites - one in the United Kingdom and one in the United States.

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Creating an Electronic Map

Ferring embarked on an exploration to seek out the best methodology to fulfill its demands. We needed to make information sharing easier, to ensure its documents met legal and regulatory standards and to more expediently bring drugs to market. The move to ELN would instantaneously reduce the physical storage previously required for paper lab notebooks, increase their legibility and encourage knowledge sharing and collaboration in Ferring's labs.

However, the critical component of a successful transition would be the assurance of maintaining legally credible documents. We still required a solution that would enable our new electronic records to stand up to the most stringent legal evaluations. Without such a solution, the company would expose itself to lost IP claims and rejected patent requests.

Based on this, our legal department required that the selected ELN technology ensure that any proprietary lab document pass legal muster, meet their need to verify the integrity of each document and prove origination for patent purposes. Ferring saw four available options:

1. Print out electronic records and paste the laser printer-generated sheets into bound notebooks, continuing the signing/witnessing process. While this option introduced the speed and convenience of electronic data entry, it retained a time-consuming manual paper process.
2. Print out the electronic records using a loose-leaf paper-based system. Although notebooks are laser printed by scientists, the integrity of each laser notebook would be demonstrably verifiable as each sheet would be numbered, certified and registered by hand by a Registrar. Compared to the first option, this system would generate paper records more rapidly, as no pasting was required.
3. Go fully electronic and use a secure digital timestamp service that is independently verifiable by a third party. This option allowed the exact content of every record and its creation time to be proved independently of Ferring.
4. Go fully electronic and use electronic signatures with no digital timestamp. While this was the least expensive option, the Ferring legal team determined that it did not provide the protection necessary to withstand legal scrutiny.

After considering the legal implications as well as the strategic direction of Ferring, the option of using digital time-stamp technology embedded in the ELN was approved by the legal department.

After careful review of available options, we decided to implement Surety's AbsoluteProof technology. Surety's technology allows for a unique timestamp token or Seal containing the document hash, timestamp and traceability information to be generated from every electronic document produced in Ferring's ELNs. This timestamp token or Seal is then stored offsite in a data center and is fully accessible, searchable and verifiable.

Each week, these compiled tokens are widely witnessed through publication in the *New York Times'* public notice section. Using a commonly accepted cryptography, any third party can compare the hashes of a document in storage with those published in the *New York Times* to determine the date and time on which the document was created and if it has changed since. The exact content of any document can be cryptographically verified, removing human trust from the equation.

Because Ferring's records, as with most pharmaceutical or medical and health-related records, need to be stored for lengthy periods of time, the time-stamps also proved to be the appropriate solution for the ELN. Where similar digital solutions like digital signatures expire over time, digital timestamps are persistent and can be stored for as long as necessary to meet regulations.

Making the Switch

Although the migration to ELN required one half-day of specialized training for the scientists, there was no complex user process for Ferring's scientists to implement the digital time-stamping solution. Our scientists also had a one- to two-week timeframe to experiment with a test

ELN system prior to the official changeover. The ELN technology embedded with the digital time-stamping was deployed in less than 30 days including making the appropriate IT software, hardware and system configuration changes.

The previously lengthy process of signing and witnessing was effectively replaced overnight once the ELN was fully implemented. The user acceptance of the ELN is high and the research scientists are able to concentrate on their experiments and studies rather than administrative work.

This digital time-stamping solution embedded in an ELN has numerous applications across health management. Any number or type of records can be enhanced through a trusted timestamp. A hospital pharmacy can verify prescriptions, or a hospital manager can verify any patient's medical records for indefinite periods of time. One can prove that no document enabled with a digital timestamp has been tampered with or otherwise manipulated. With particular regard to patents or medical records, which are heavily regulated, the assurance that documents are inextricably linked with a unique hash that can be interpreted by any cryptographer provides value, both to the organization and the stakeholder.

At the End of an Electronic Trail

Soon after using this trusted time-stamping capability, Ferring began to see the inherent benefits and extended its application to areas other than signing and witnessing lab experiments. Beyond empowering the ELN, we applied timestamping to standard methods, risk assessments and test reports.

Now, scientists are able to increase their efficiency without getting bogged down in record keeping and witnessing. Countless hours have been saved by forgoing the labor-intensive process of printing and pasting documents relating to experiments, then having each one signed and witnessed. With an ease of search and a more collaborative process among researchers, Ferring is expediting the R&D process without sacrificing due diligence or appropriate record keeping.

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