The Paperless Lab

Some scientists keep experimental records on sticky notes. Some groups maintain ordering information in the head of a single technician. But for researchers looking for more stable, searchable, and sharable records, digital options such as electronic laboratory notebooks (ELNs) and laboratory information management systems (LIMS) are readily available. Scientists can start with a simple online notebook or choose a complete lab management package to track the entire lifecycle of their projects. By Chris Tachibana

A paper notebook seems like it should last forever. After all, Gutenberg Bibles have survived since the 1400s. Still, paper is not perfect. Consider these true stories: At an Australian university, 30 years of notebooks became a pile of loose pages after the bindings crumbled during relocation. In the United States, a postdoc spent days combing through three-ring binders for experimental details requested by reviewers. In a positive example of going paperless, a Swiss contract manufacturing organization wowed clients with real-time, online chromatography runs of their samples. Electronic laboratory tools have definite advantages, but scientists have been reluctant adopters. The major barriers for going digital are cost, the activation energy required to change work habits, and the daunting number of options.

Where to Start

LIMSwiki is an excellent starting point for laboratory informatics newbies. The online resource is a community service from the Laboratory Informatics Institute, a trade organization founded in 2006 by **LabLynx**, a vendor of browser-based research management software. LabLynx emphasizes transparency, for example in pricing, and LIMSwiki provides prices when possible in its up-to-date vendor descriptions. "We've tried to maintain neutrality throughout," says Shawn Douglas, LIMSwiki curator, "avoiding marketing and self-promotion. The wiki is an evolving tool, and we're always looking for quality contributors."

LIMSwiki provides definitions for terms such as ELN (electronic laboratory notebook, generally used to document experiments) and LIMS (laboratory information management systems, traditionally used for tracking standardized processes such as production). But the distinction between informatics products is blurring, says Markus Dathe, good manufacturing practice and computer system validation coordinator at **Roche**, because "convergence is happening." ELNs, LIMS, and equipment software are expanding functions, interconnecting, and overlapping. Informatics packages increasingly aim to cover the entire lifecycle of an R&D project including reagent inventories, regulatory forms, and work requests in addition to experimental details. Most researchers start small, though, with a homegrown ELN with protocols in text documents and electronic data files.

"Everyone sees the value of ELNs, from scientists to principal investigators to lab managers," says Erik Alsmyr, senior director of software development for the **Accelrys** Notebook (previously Contur's iLabber) for small-to-medium-sized research groups. Alsmyr says most labs start with all-purpose organizing and sharing software such as Evernote or SharePoint, then realize they need more storage capacity or intellectual property (IP) protection. Electronic systems provide 24/7 global access to your records, says Alsmyr, and most commercial ELNs are compliant with regulatory requirements for electronic records, for example Part 11 of the Code of Federal Regulations Title 21, which covers the U.S. Food and Drug Administration, and European Union Annex 11 for the European market.

Researchers are still slow adopters, though, particularly at universities. That's why **LabArchives** offers a free ELN in addition to a subscription-based version with more storage and features. "Our research says that in academia, about 95% of scientists still use a paper notebook," says Earl Beutler, LabArchives' chief executive officer. Beutler, whose entire family are scientists (including a Nobel Prize winner), thinks it's time for labs to go digital. "I've worked around smart, technologically proficient scientists my entire life," he says, "and I'm amazed that their state-of-the-art is still taking a photo of a gel, printing it out, and gluing it into a paper notebook."

Realizing that adhesives disintegrate and notes on laptops don't have the strongest IP protection, universities are buying informatics site licenses that cover entire departments, says Beutler. This removes the cost barrier for scientists and ensures proper archiving of potentially patentable results. LabArchives also targets an audience that doesn't have paper nostalgia: students. "Many of our users are academic researchers who teach, so we created our classroom ELN at their request," says Beutler. "It lets instructors provide background information and give and grade assignments electronically. The largest class it's

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In this [nearly sci-fi] vision of the future laboratory, scientists simply do their work while an automated tracking system simultaneously keeps records.

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been used in was more than 2,000 students."

Tammy Morrish is an academic researcher who went digital from day one, setting up her laboratory with **Labguru**, a web-based research management system. As a postdoc, Morrish kept a homemade database of project resources but wanted an advanced, sharable system when she started as an assistant professor at the **University of Toledo** Biochemistry and Cancer Biology Department. That's a great time to set up a new system, she says, because you know all the mice, cell lines, and plasmids you have available for projects.

Morrish praises Labguru's customer service and says the system is a huge timesaver. It streamlines ordering by putting product numbers, vendors, and current orders in one place, she says. Labguru holds her laboratory's mouse records with full genotypes, and plasmid information including maps. Morrish says the system is particularly helpful for locating items. "Think how much time we waste looking for things," she says. "Now when I need something, even if other people aren't around to ask, I can type it into the database and find it. Of course," she adds, "people have to put things back where they found them." Her lab has a technician who checks inventories against the database weekly.

At a higher level, the system facilitates group interactions, for example by making data sharing easy. It also teaches best practices. "It helps students learn that with any database," says Morrish, "you have to enter information correctly and consistently or you won't be able to find it."

Going Digital But Maintaining Control

Science-based businesses also appreciate the efficiency of digital research management, but long-term stability is a high priority, too. "The challenge is assuring the accessibility and usability of data 20 years from now," says Dathe. Choosing a major informatics supplier such as IDBS, PerkinElmer, or Accelrys might give some assurance of permanence, but the market is so dynamic that any vendor will likely undergo changes. In the past decades, Thermo Fisher Scientific acquired InnaPhase; PerkinElmer purchased Labtronics, CambridgeSoft and ArtusLabs; Accelrys, which has its own lengthy merger and acquisition history, was recently acquired by the French software company Dassault. Still, after consolidating, companies strive to retain users. "We still carry software developed in the 1990s and we've always shown customers a path forward," says Leif Pedersen, senior vice president at Accelrys.

Nonetheless, industries are not uniformly adopting laboratory informatics. Although agencies such as the Food and Drug Administration encourage electronic documentation, Dathe says, "The pharmaceutical industry is generally conservative, and it's often easier and cheaper to stay with a paper system that is known to be accepted by regulatory agencies."

At **LEO Pharma** in Denmark, head of discovery informatics and data management Ulrik Nicolai de Lichtenberg developed a model for committing to a commercial informatics system. Start with in-depth stakeholder analyses, he says. Define your needs and goals and "how much pain you can put up with," meaning the money, time, and effort available for implementing a new system. Realize that your ELN or LIMS is just a part of an information ecosystem. LEO Pharma chose the Accelrys ELN for its Medicinal Chemistry R&D Department, but the ELN is just one element in a comprehensive infrastructure designed by de Lichtenberg's team. Their system will capture, validate, and permanently store records so they are accessible, searchable, and legally defensible in case of IP disputes. It's a complex project and de Lichtenberg recommends seeking advice from independent consultants who understand the ever-changing informatics market.

Looking to the Cloud And Beyond

Michael Elliott, chief executive officer of **Atrium Research & Consulting**, advised de Lichtenberg and endorses his approach. "Don't get enamored with a demo," he says. "Look under the hood and check out the capabilities of an informatics system." Clients dream of a single system that streamlines process management and securely and permanently stores data while rapidly retrieving needed information. An ideal system would even find "dark data"—previous work that could answer current research questions but is buried in disorganized files. Clients want scalability, a user-friendly interface, and outstanding global support. However, products vary in these capabilities, says Elliott. "Don't choose based on a presentation or brand name. Think carefully about your needs now and in the future."

If expandability and ease of use are priorities, a cloud-based system, for example from Core Informatics, might be the answer. In principle, the cloud can house unlimited amounts of data and has a familiar interface since accessed is through a web browser. Brower-based systems don't require specialized software, so they're easy to upgrade. Informatics vendors are also creating user-friendly modular packages. Similar to choosing mobile phone apps, users select only the components they need.

Also on the horizon is greater mobility and compatibility. Researchers are taking smartphones and tablets into the laboratory so informatics developers are making products compatible with handheld devices. Increasingly, data needs to be compiled across different instruments and informatics platforms, so Pedersen says he is personally pushing for increased standardization to facilitate information sharing. Ever the continued>

realist, though, Elliott says progress in standardization is slow because even within a single department, users might employ different terminology and definitions. The force that could drive both standardization of scientific informatics and better data integration, says Elliott, "is the move toward more collaborative work."

To the wish list of informatics improvements, Dathe adds features that give data context: when and where they were collected and for what project. Data should be linked to relevant molecular and clinical information and the entire data-generating process, including the type and status of equipment used. "Without context," says Dathe, "the mountain of data we can collect is meaningless."

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Atrium Research & Consulting
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www.limswiki.org

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Additional Resources

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Being Open-Minded

Scaling the data mountain is Britt Piehler's job. Piehler is president of **LabKey Software**, which develops tools for data management and integration. The trend toward globalization and multisite collaboration, he says, means project managers must coordinate data collected at far-flung sites under diverse conditions with a variety of instruments. "That's where LabKey comes in," says Piehler. "We build tools for specific tasks, usually data integration for multisite collaborative projects that need to standardize heterogeneous data." An unusual feature of LabKey Software is that its product is open source.

"We grew out of the academic community," says LabKey's Science Outreach Director Elizabeth Nelson, "so we believe it's an advantage for the software platform to be freely available." Open source code allows researchers to tailor their systems, says Piehler, and building and sharing LabKey tools creates a community.

If the code is free, what does LabKey offer? "Customization," says Piehler. LabKey Software experts can create tools that directly address Dathe's call for giving context to data, for example by adding demographic information. And in August 2013, open source and open access came together via LabKey to promote scientific transparency and reproducibility. For a clinical trial of a vasculitis therapy published in the *New England Journal of Medicine,* the LabKey open source platform was used to create a web portal with free public access to participant-level data, stripped of identifying information.

Researchers who are committed to transparency and are also do-it-yourselfers have a choice of open source workflow management tools. Carl Boettiger, an ecology and evolution postdoctoral researcher at the **University of California, Santa Cruz** has traveled the entire DIY lab notebook journey. Boettiger started keeping publicly accessible lab records in the OpenWetWare platform. "It's a bit radical," says Boettiger. "Anyone can go in and edit other peoples' notes, although that rarely happens." After OpenWetWare, Boettiger moved to platforms that give him increasing control over his research records, starting with WordPress, which is usually used for blogging. Boettiger now uses the online software development site GitHub as his notebook and Jekyll website-generating software to publish his notebook online.

A blog-type ELN creates a robust, cached history of your research, says Boettiger. It discourages fraud because any changes leave records. You choose what is public, private, and password protected. And think of the advantages when talking to people at conferences or answering reviewer requests, he says. You can just pull up records on a handheld device to see what you tried and when, and how it worked out.

What's Next

"The trends in laboratory records," says Boettiger, "are toward more open and collaborative, more secure, and more automated." Although Boettiger and Dathe should have different perspectives as an ecology researcher in Santa Cruz and a pharma development and information technology specialist in Basel, respectively, they share a nearly sci-fi vision of the future laboratory. In this vision, scientists simply do their work while an automated tracking system simultaneously keeps records. Barcoding will note reagents, samples, and instruments used, providing context to the data for subsequent analysis. The entire process will be recorded, showing the provenance of every byte and definitively establishing IP claims. "It will give a much more extensive record that can be transparent or shared if you want," says Boettiger. A fully automated system would simplify research by capturing experimental details with no manual data entry. Then, all we'd need is a robot to return reagents to the right shelves.

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