January 2010 Volume 5 • Number 1

The Online Lab Manager

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The Economic Realities of Lab Automation

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- Ultra-High-Throughput Screening
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10

52

MAGAZINE

The Online Lab Manager

With increased demand to do more with less, lab managers now have a host of online tools at their disposal to help with everything from hiring staff, benchmarking efficiencies, purchasing equipment and collaborating with off-site colleagues. While not the solution to all issues, these new tools can provide a bit of relief from management overload.

John K. Borchardt

Perspective On: A Pharmaceutical Research Lab

Precision Anitibody, part of A&G Pharmaceutical, Inc., is a contract company that creates custom antibodies for pharmaceutical and biotechnology companies and federal and academic research labs. Lab manager Joe Corvera shares how he and his staff of nine successfully manage hundreds of projects each year in their 8,000-square-foot lab.

Sara Goudarzi



LEADERSHIP & STAFFING

I Told You!

"There's nothing particularly special about 360-degree feedback. It's just a tool and, like any tool, is only useful if you know how to use it and if it's the right tool for the job." 360-degree feedback done right requires that people are given the information they need to change and provided with a rationale for that change.

Stephen Balzac

20 **Conflict Management**

As unpleasant as it seems, conflict can be one of a lab manager's best ways of discovering where problems exist among his or her staff and where values, goals, roles, statuses and perceptions are causing problems that need to be dealt with. Resolving such conflict can only happen when managers are first willing to confront it.

Ron Pickett

TECHNOLOGY & OPERATIONS

26 The Paperless Lab

Two different laboratory software projects illustrate the tasks and issues involved in "going paperless." Key to success is mapping processes and deciding how to proceed. In both projects, the labs went paperless because the paper pieces of the process were standing in the way of their productivity or operational goals.

Gloria Metrick

LAB DESIGN & FURNISHINGS

Scanning the Scene

Three-dimensional laser scanning allow designers and builders to get the full perspective of the lab site, including electrical outlets, casework, wall devices and equipment in the room. This kind of information is invaluable especially during the planning and design phases of a renovation project.

Thomas Walsh, PE, and Chris Zmijewski

BUSINESS MANAGEMENT

The Economic Realities of Lab Automation

Imagine a lab without any automated equipment. How would your productivity be affected? Automated equipment provides a significant economic benefit to lab operations. However, the real benefits, both economic and functional, come when people change their thinking about how to plan for, choose, and apply the technologies.

Joe Liscouski



SURVEY SAYS: In our recent Lab Manager Magazine Pittcon 2010 Attendance Survey, we asked our readers, "What is your main purpose for going to Pittcon?" The majority, 69 percent, said to visit vendors and learn about new technologies; 13 percent said they go to attend the short courses and technology sessions; 9 percent go to network with attendees; 3 percent go in search of employment; and the others, 6 percent, were exhibitors. Turn to page 14 for more survey results.



Dr. Michael Hopkins talks about his experiences and involvement in designing the Searle Chemistry Building, located in the University of Chicago campus, which has received a LEED Gold certification for its "green" features.















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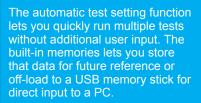




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CONTENTS

Free Agency Rich Pennock	24
PRODUCT FOCUS Ultra-High-Throughput Screening Automated Liquid Handling Biological Shakers Microplate Handlers	36
LAB SAFETY Burn Notice Tips and guidelines for safe storage of flammables in the lab Vince McLeod	42
EVOLUTION OF Microplate Readers	46
TECHNOLOGY NEWS The latest equipment, instrument and system introductions to the laboratory market	59
HOW IT WORKS Transfecting B-cell lymphomas with siRNA Nucleic Acid Contamination Solved with ExitusPlus™ Technology Using Cryogenic Liquid Argon Dewars Cost-Effectively Benchtop Flow Cytometry	64
MARKETPLACE	73
ADVERTISERS INDEX	72
PARTING POINTS	74

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EDITOR'S NOTE



Managing Online

For those of us who did the bulk of our Christmas shopping last month online, reports of the Internet's usefulness in saving time and money won't come as big news. However, online applications for improving the work lives of lab managers might. In this month's cover story, John Borchardt identifies tools that can increase lab productivity and reduce costs by taking tasks such as interviewing and training staff, collaborating with off-site colleagues, and benchmarking productivity and efficiencies online. Of note is the Lawrence Berkeley National Laboratory tool that allows managers to benchmark their energy use by comparing it to that of similar facilities, with the goal of identifying cost-saving opportunities and reducing energy consumption.

Both of this month's Leadership & Staffing articles deal with the often dreaded management tasks of providing feedback to employees — both positive and negative — and resolving workplace conflict. In "I Told You!" (page 16), author Stephen Balzac presents techniques to get the most out of a 360-degree feedback exercise. An important point he makes is, "If you expect employees to make changes in their behavior, or continue a behavior that you like, the trick is to make the feedback specific."

In "Conflict Management" (page 20), author Ron Pickett tells us that "the first step in resolving conflict is to gain an understanding of the sources of the conflict. The second is to have the courage to confront the conflict." He then offers an easy-to-follow model to help get beyond the fear that often comes with getting involved in a conflict. To learn more about Ron, check out last month's Meet the Author video at www.qorpak.com/labmanager.

With a nod to LabAutomation2010 taking place at the end of this month in Palm Springs, Joe Liscouski weighs in with "The Economic Realities of Lab Automation" (page 48). In the article he asks whether laboratory automation is a realistic way to increase productivity under the constraints of tightening budgets and scrutinized spending. His answer provides practical tips for successful lab automation implementation. And speaking of LabAutomation2010, if you're planning to attend, please stop by the Lab Manager Magazine booth and say hello.

And finally, as I've been discussing both online and in previous editor's notes, we are happy to introduce here our new "Ask the Expert" feature. Please turn to page 34 for a one-on-one Q&A with Dr. Michael Hopkins, Professor of Chemistry at the University of Chicago, who shares his knowledge in designing an eco-friendly lab. Next month's expert will discuss the ins and outs of creating a high-throughput screening lab. Please visit www.labmanager. com to submit any and all questions on this and future topics.

Next month is our Pittcon issue, in which we provide a sneak peek of what you'll be seeing on the show floor. The cover story, "Coloring Outside the Lines," is by Jeff Tobe, who will also be the presenter at this year's Lab Manager Magazine Boot Camp on Wednesday at the Orlando Convention Center. I hope to see you there.

Pamela Ahlberg Editor-in-Chief

In the December 2009 Product Focus on laboratory freezers, we neglected to include Marvel Scientific. Please visit www.marvelscientific.com to see Marvel Scientific's complete lab freezer offerings.

In the Lab Freezer Purchasing Guide in December, the three LABREPCO freezers in the left-hand column were misidentified. Those should have been: LABREPCO Arctic Series, LABW-20 FM, 20.1 cu.ft., -20 Manual Defrost Enzyme Freezer; LABREPCO Futura Series, LABN-24/33/52/80-FA, -25 Laboratory Freezer; and LABREPCO Arctic Series, TSLAB-23/35/49/72F, -20 Stainless Steel Laboratory Freezer.



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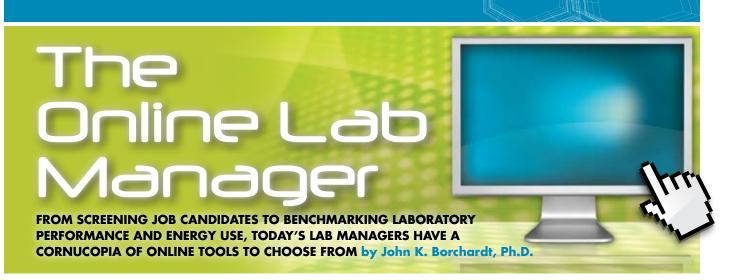
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In an era in which corporate management is requiring lab managers to do more with less, a new generation of Internet-based services provides a means for them to accomplish this. There are many online applications available besides online open innovation services that enable lab managers to access ideas of others outside their companies.¹ Often referred to as "Web 2.0," these applications include tools that let people collaborate and share information online in ways that enable managers to increase lab productivity, reduce costs, and do things such as train, share information, and hire in new and different ways. Corporate intranets offer a means of collaborating and sharing proprietary information. For example, proprietary wikis can be developed and maintained on a corporate intranet to store and share laboratory reports, meeting minutes, company safety manuals, and other documents.

"Lab managers can use new Web 2.0 technologies to interview and compare job candidates."

Finding and screening employment candidates

Lab managers now have an increasing number of online options to post job openings and solicit résumés from job candidates. "Traditional" methods include large job boards such as www.monster.com and www.hotjobs.com. There are also specialized laboratory job boards such as that operated by the American Chemical Society (ACS) on its website at www.acs.org and www.sciencejobs.com. For cash-strapped lab managers interested in hiring staff locally if they can, there is craigslist. Many companies post job openings on their own websites and job hunters can apply online.

Lab managers can use new Web 2.0 technologies to interview and compare job candidates. For example, virtual career fairs held online eliminate the cost and time required for business travel while allowing participation on the individual schedules of hiring managers and job hunters.² Just as with a traditional career fair, employers can post a list of available positions, search a database of submitted résumés, and schedule interviews with employment candidates. Last June, the ACS held a virtual career fair online.

Virtual interviews can be conducted in real time, with managers and job hunters using webcams to talk to and see each other. Alternatively, the hiring manager submits a list of questions to which job candidates record answers, with the hiring manager viewing the video at a later time.

Using services such as InterviewStream (www.interviewstream.com), lab managers can post a predetermined set of questions for job candidates for a particular job opening. Using webcams, candidates can record and post their responses. InterviewStream and similar services are intended to serve as screening interviews and not to replace on-site interviews that are the final step in the hiring process.

However, Web 2.0 wizardry can have limitations and even pitfalls compared to old-fashioned methods of screening employment candidates. For example, human resources consultant John Sullivan has noted that hiring managers can rapidly scan traditional résumés, whether on paper or displayed on a computer screen; time-pressed managers cannot do the same with video résumés.³ One cannot highlight key points on a video résumé for others to see nor make notes directly on the video. One can't place video résumés side by side to compare them. Video résumés, by providing a video recording of the candidate, enable employers to identify an applicant's race, sex, age,

disability status, and other characteristics that are typically omitted from traditional résumés for EEOC reasons.

Lab managers are beginning to use social media, including LinkedIn, Facebook, and even Twitter, to search for job candidates. They can also use these social media and search engines to search for information on specific job candidates.

Online purchasing

Many vendors of laboratory instruments and supplies offer purchasing services on their websites. For example, lab managers can browse various product descriptions and specifications, and purchase products online using the Thermo Fisher Scientific website.

"...a benchmarking tool [enables] laboratory managers to benchmark their energy use by comparing it to that of similar facilities."

Rather than going to the websites of several different providers of a particular type of lab instrument or lab supplies, one can go to an "emporium" website such as LabX.com to save time and view instruments available from many vendors. (In the interest of full disclosure, LabX is the owner and publisher of *Lab Manager Magazine*.) LabX.com also offers refurbished instruments. If prospective buyers cannot find the refurbished instrument they want, they can post a "wanted" advertisement.

There are many websites from which one can order computers, printers, monitors, calculators, and a wide variety of office supplies. Comparison shopping is less time-consuming than paging through catalogs and less damaging to the environment as well.

Benchmarking

Wayne Collins has discussed benchmarking laboratory performance at length in the pages of *Lab Manager Magazine*.⁴ Online benchmarking tools are usually customized for use by specific industries and for specific functions. Information technology costs is a popular category for benchmarking. For example, Aupec is customized for firms in the oil and gas industry to benchmark their information costs against competitors (www.aupec.com/benchmarking/online.htm). Aupec services of interest to lab managers include benchmarking product development time and employee retention.

Because they are closely regulated, clinical laboratory managers are strongly interested in benchmarking their labs' performance against both that of similar laboratories and regulatory standards. A review summarizes an extensive study of clinical laboratory benchmarking.⁵ Chi Solutions (www.chisolutionsinc.com) is among the online providers of benchmarking services tailored for clinical laboratories.

Working for the U.S. Environmental Protection Agency, Lawrence Berkeley National Laboratory developed a benchmarking tool to enable laboratory managers to benchmark their energy use by comparing it to that of similar facilities, with the goal of identifying cost-saving opportunities and reducing energy consumption (www. labs21century.gov/toolkit/benchmarking.htm). The current database is comprised of more than 170 laboratories against

which lab managers can benchmark their own laboratories.

Using their own databases of laboratories, commercial services such as Management Insight (www.management-insight. us.com/benchmarking.htm) offer bench-

marking services to lab managers. These services enable managers to assess their laboratories' performance in a variety of categories.

Online alternatives to business travel

Business travel is both expensive and time-consuming. An increasing number of companies are using economical alternatives such as online meetings, web seminars (webinars), and videoconferences using PCs and webcams combined with high-speed broadband Internet connections and voice over Internet protocol (VoIP) systems.⁶ Such online meetings are also more environmentally friendly than traditional conferences.

Companies such as Cisco, which bought WebEx in 2007, and Adobe, which acquired Macromedia in 2005, make it possible for firms to connect multiple sites around the globe for internal meetings and meetings with customers and suppliers. Costs have dropped dramatically from those of videoconferences of a decade ago. For example, Thermo Fisher Scientific traditionally has flown scientists, engineers, and support staff all over the world to help customers install instruments and solve problems. More than 1,600 Thermo Fisher Scientific employees now use Adobe's virtual meeting Connect Pro service to perform R&D, conduct training, provide customer technical support, and make sales and marketing calls. Thermo Fisher Scientific uses other web conferencing applications as well but may make Adobe Connect Pro a corporate standard, according to web specialist Dudley Torres.6

Using services such as GoToMeeting (www.gotomeet-

ing.com), users can speak to each other over conventional telephone lines or using VoIP while sharing computer screens. Versions for small meetings of up to fifteen people and large corporate or professional conferences of up to 1,000 attendees are available. It is also useful for conducting small or large meetings and online training. For example, last November this writer, *Lab Manager Magazine* editor Pam Ahlberg, LabX Media Group general manager Ken Piech, and LabX's Peter Ferris—located in three different offices separated by hundreds of miles—met for online training in blogging. Lab personnel located many miles apart can also edit documents and presentations on shared computer screens.

For companies that want to experiment with online meeting services, some vendors offer free trials. There is also DimDim, which offers a free version based on open source software that can accommodate as many as twenty users in a virtual meeting room.

One can display PowerPoint slides as well as conduct discussions.

The drawback of these online meetings is the near-total absence of unplanned discussions and interactions between attendees in informal settings. An important part of conventional meetings and conferences, these informal discussions can spark great ideas,

eventually leading to new products and services. Perhaps as scientists, engineers, and lab managers become more comfortable with using online social media such as Facebook and Twitter this disadvantage will be overcome.

LIMS

Four articles on laboratory information management systems (LIMS) have been published in *Lab Manager Magazine* in the past year.⁷⁻¹⁰ LIMS are increasingly web based and continue to become more sophisticated and useful. Using online software based on remote servers decreases demands on the memory capacity of desktop personal computers.⁷ Since the desktop computer interacts with the remote server using a web browser, any desktop or laptop PC operating system such as a version of Windows, Apple's Snow Leopard, or Linux may be used. With the LIMS software located on a remote server, there is less disruption of laboratory operations when the software is updated. Lab personnel save the time required to install new software on their computers themselves. All

users always have the most up-to-date software.

One concern that some users may have with web-based LIMS is data security. However, Robert Pavlis, president of Labtronics, Inc., (www.labtronics.com) notes that users typically have to log in to systems using their names, their companies' names, and passwords. This restricts their access to only the data for their companies. Pavlis notes that his firm's integrated LIMS product, Nexxis iLAB, may also be used to store information on users' intranet systems. One can e-mail Nexxis iLAB reports to others who need to see the results. One can also import the results into a Word or PDF document that includes additional results generated by other laboratories.

Nexxis iLAB can also be set to accept only data generated using chemicals and formulations whose use dates haven't expired and results were determined using properly calibrated instruments. "The lab manager knows the

work is being done right because the system won't let you do it wrong," notes Pavlis.

LIMS are also becoming more specialized, increasing their usefulness. For example, lab managers can tailor the modules of LabVantage Solutions' SAPPHIRETM software to the unique requirements of their laboratories (www.labvantage.com/solutions/researchdevelopment/index.

html). Conformia Software, recently acquired by Oracle Corporation, offers customized software

designed to manage drug development from initial candidate selection through clinical trials to commercial manufacture (www.oracle.com/conformia/index.html). Orchard Software Corporation's Orchard® HarvestTM LIS offers a number of modules designed for clinical laboratories (www.orchardsoft.com).

A recent trend in LIMS is greater integration, making information from all laboratory applications available to any other application in real time. Laboratory managers can have online access to all the information they need to run the lab, while many of the necessary daily workflow management decisions can be automated.

Online training

"A recent trend in LIMS...

[makes] information from

all laboratory applications

application in real time."

available to any other

Many organizations, including universities, offer online courses in a wide variety of subjects. For example, the ACS offers forty-two Harvard University online business-skills short courses. These include budgeting, coaching, developing employees, managing meetings, and many



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other business-related subjects (https://acs.learn.com/learncenter.asp?sessionid=3-7673499A-3D4B-42F9-A663-64294F8510C8&id=178419&page=47). In addition, some ACS technical short courses are available in webcast versions.

These examples suggest that online services will continue to become increasingly useful tools for lab managers.

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WHO'S GOING TO PITTCON AND WHY?

The 60-year-old U.S. laboratory science exposition, The Pittsburgh Conference, is fast approaching. (February 28 — March 5, 2010. Orange County Convention Center, Orlando, Florida) With that in mind, last month we conducted a *Lab Manager Magazine* Pittcon 2010 Attendance Survey in which we asked our readers to weigh in on their experience with the show and their expectations for 2010. More than 200 of you shared your attendance history, reasons for going and overall satisfaction with this important event which, according to the Pittcon website, attracts nearly 20,000 attendees from industry, academia and government from 90 countries worldwide.

BASED ON THE SURVEY, THIS IS WHAT WE LEARNED:

For those attending Pittcon to shop for equipment, 78 percent come prepared, having researched vendors and equipment well in advance of hitting the show floor. Seventy four percent said they conduct that research via the Internet, 18 percent learn about new technologies from trade magazines and ads, 12 percent from talking to colleagues or vendor representatives, 7 percent rely on product literature, and 9 percent from a combination of all of these.

When asked how they decide which vendors to visit, 43 percent of readers said it was based on product offerings. After that, vendors to visit were chosen by reputation (10%), discussions with vendor representatives (8.7%), a vendor's website (8%), known/familiar vendor (7%), recommendation by colleagues (6%), vendor promotion (4%), and other (13%).

WHO ARE YOU GOING TO TALK TO?

Thirty two percent of readers told us they set up appointments with vendors in advance of the show and when visiting those vendors, 61 percent preferred speaking with product managers. Seventeen percent said they wanted to speak with a sales representative, 11 percent with marketing managers, and the balance with technical specialists, service representatives, application scientists, and others.

When asked how, if any, the value of Pittcon has changed over the past 5 to 10 years, nearly 33 percent reported no change, 29 percent said they didn't know, 22 percent said they thought the show has decreased in value, and nearly 16 percent believe it has increased in value.



When asked to explain their answers to the above question, verbatim responses ranged from, "I like being able to talk to vendors and scientists rather than getting all my info from the Internet" to "vendors I would like to talk to are no longer exhibiting."

Obviously, trade shows in general have been negatively impacted in recent years by both the economic downturn and online alternatives for researching new equipment and technologies. We'll know just how much of an impact that has had come next February in Orlando.

For complete survey results, visit www.labmanager.com

14 Lab Manager January 2010 labmanager.com



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I TOLD YOU!

360-DEGREE FEEDBACK DONE RIGHT by Stephen Balzac

"We were thinking of doing a 360-degree feedback to help him understand what other people think."

This very frustrated comment was made to me recently regarding efforts to explain to a very senior manager that his style of leadership wasn't working for his team. At that point, all efforts to convince him to change were foundering on the manager's simple perception that things were working just fine.

Such being the case, it's hard to imagine how a 360 can help. Sure, he might find that his subordinates don't like him very much, but he might also feel that his job isn't to be liked, but to get people to perform.

More broadly, it's important to recognize that there's

nothing particularly special about 360-degree feedback. It's just a tool and, like any tool, is only useful if you know how to use it and if it's the right tool for the job. Before you can tell if it's the right tool, you have to understand what the job is.

In this situation, the job is getting someone to accept feedback and then make use of that feedback to alter his or her behavior. At a very fundamental level, feedback is only useful if it gives people the information they need to change, and provides them with a rationale for the change. It helps considerably if the feedback also increases an employee's sense of competence and commitment to the goals of the team and the company.

I've certainly known of many managers who had the attitude that their subordinates were either going to change or find employment elsewhere. This attitude

is not particularly useful for either the employee or the team. It doesn't benefit anyone to have a disgruntled employee quit at a critical time in the life of a project, or an employee not learn how to improve his or her performance in a meaningful way. In this situation, the team never really achieves the level of performance it's capable of achieving. If we were talking about sports, it would be

like being the evil sensei in *The Karate Kid*.

Before you can provide feedback to the manager, you need to decide what the feedback is going to be about.

In other words, clear goals must be established well in advance of any

feedback session. As obvious as this may sound, I had someone at one company tell me just the other day that he had no idea when he was going to get a performance review, but that was okay because he also had no idea on

what criteria he was going to be evaluated. As a result, this employee figured he'd simply do his best and hope that things worked out in the end.

Without goals, feedback is often arbitrary and comes across as little more than criticism and argument.

Assuming that you have clear goals defined, feedback needs to be timely. The idea of giving feedback at six-month or oneyear intervals is convenient, but of limited effectiveness. Few things are more infuriating to an employee than to be criticized about something that happened months before. Half the time, employees don't even remember the incident in question; it's even worse when the criticism is about a behavior the employee's been repeating because he or she didn't know not to. There are a number of ways that people can get timely feedback that doesn't involve a formal feedback session with a manager. It is well worth the time and effort to set that up.

One of the big criticisms I've heard from employees is that they feel powerless

when they get reviews. Making people feel powerless is one of the best ways to get them to ignore what you are telling them or argue every step of the way in an effort to reassert themselves. Fortunately, it's relatively easy to avoid this. I always invite the employee to pick the time and date of the feedback session. It's best to provide some choices and let your employees make the decision.

"Without goals, feedback is often arbitrary and becomes little more than criticism and argument."



That simple act of giving them some power dramatically increases the probability that they will be receptive during the feedback session itself.

Another problem that I've run into repeatedly is feedback that is so vague it's useless. Telling someone that he or she is "too aggressive," or "not aggressive enough," is basically meaningless. Your definition of "aggressive" and your employee's definition may be completely different. In one company I worked with, the same employee was told by two different managers that he was "too passive" because "he wouldn't argue for his position with the team," and "a good team player," because he was willing to "put his ego aside and work for the good of the team." In this case, the feedback said more about the people giving it than about the person receiving it!

"It's important to create an atmosphere conducive to presenting the information."

If you expect employees to make changes in their behavior, or continue a behavior that you like, the trick is to make the feedback specific: "In the meeting the other day, I felt you had some very valid points and were too quick to give up on them," is far more useful than, "You were too passive." What's more, "I noticed the other day that you requested input from the rest of the team and used that input to modify your suggestion; I really appreciated you setting an example of collaboration instead of competition on the team," is far better than, "You're a good team player."

A question I frequently get asked is how to provide negative feedback. The key thing to recognize is that while you might see negative feedback as helping employees improve their performance, they probably see it a bit differently. They may feel that their jobs are being threatened. Someone who feels threatened will not be receptive, so it's important to create an atmosphere conducive to presenting the information. It must be clear that you are trying to build the employees up, not tear them down. The stronger the relationship you have with your employees, the easier that will be.

Many managers like to deal with negative feedback by using the sandwich technique: they slip the negative comments in between two positive comments. There's nothing wrong with that, but you still have to make the feedback precise. In this case, it's even more critical to focus on specific behaviors in specific situations. As MIT's Ed Schein

advises, avoid making generalizations about someone's motivation or personality. As soon as you tell someone that they "clearly don't want to do well," or "clearly don't have what it takes," or that they "have a difficult personality," you are moving into the realm of criticizing unchangeable aspects of the person. That's neither useful nor productive and will only generate resistance. Instead, just as with any feedback, focus on exactly what the employee did and when they did it. Explain to them how you feel that their actions sent the wrong message. Focus on your perceptions and feelings; don't try to tell them what they were feeling. Take the time to understand exactly what the problem is; don't make assumptions.

In one situation, a lab manager had an employee who wasn't producing results. He first told her that she wasn't working hard enough and quickly moved to haranguing her to work harder. She quit and was replaced by another scientist. He also failed to get results and the process repeated until that employee quit. The manager went through another two employees before he accidentally discovered that there was an error in a protocol the scientists were required to follow. Each one had tried to discuss the possibility with him, but he consistently refused to listen, adopting the attitude that any problems were purely a result of their lack of dedication. This cost the lab four excellent employees and set them back more than a year on one of their projects.

"If an employee is worth keeping, there is always something to praise."

Paradoxical as it may seem, the best way to improve the performance of someone who is not performing as well as desired is to find things to praise, not things to criticize. You still need to convey the problems, but you should also take the time to build the person up. For example, "What is wrong with you? That experiment had nothing to do with our goals. Why did you waste your time and energy on that instead of working on something productive?" is not particularly useful or effective. At best, it will decrease, if not destroy, the employee's motivation.



To build the employee up and increase his or her motivation, the situation needs to be approached a little differently:

"I am concerned that you are not producing results at the rate we expected. I need to understand what is going on. Can you fill me in on what obstacles you are facing?"

Give employees the chance to present their perception of what is going on. Like the manager in the example above, you might hear something unexpected, or they might have

misunderstood their goals. This is not uncommon among newer employees, especially those fresh out of graduate school. The trick is to focus them where you want them and give them the confidence to

"If you want someone to change, focus on the things that are changeable."

If necessary, conduct the conversation over coffee or lunch; changing the venue and adding a relaxed note helps stimulate creativity. Inviting them to help you help them increases their sense of personal control and their level of

personal commitment to success. Transforming a negative into a positive is one of the most powerful techniques for increasing an employee's productivity, motivation, and commitment.

Remember, if you want someone to change, focus on the things that are changeable. It's easier for all concerned, and far more productive. No one likes to be changed, but most people will eagerly embrace change when they see the benefits of the change.

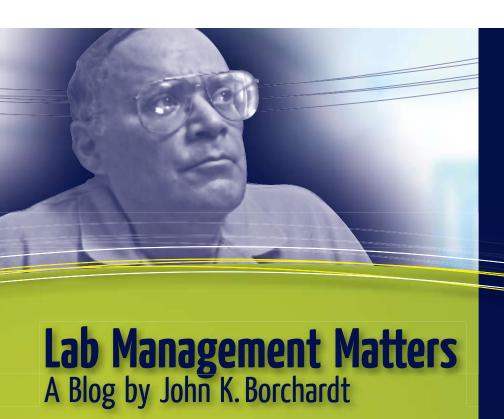
What sort of feedback are you providing?

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succeed. Like the coach of a star athlete, you should make it your goal to send them out ready to move mountains. Try saying something such as:

"While that experiment wasn't really appropriate to our goals, I really liked the way you approached it. You put an incredible amount of effort into it. You researched the information you needed, you spent the time necessary to carry it out. I have rarely seen that level of focus. How can I help you apply it to..."

If an employee is worth keeping, there is always something to praise. Make it specific and tie it to the behaviors you want to see repeated. Invite employees to participate in brainstorming with you to improve their performance.



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CONFLICT MANAGEMENT

UNCOVER THE SOURCES, SUMMON YOUR COURAGE AND CONFRONT THE PROBLEM by Ron Pickett

Conflicts happen! They are all around us, and the fact that you manage a bright and well-educated staff makes managing conflict more difficult in some ways. Why don't they see it my way? Why can't they just work it out? They just need more data. Or, in the words of Reginald Denny, "Why can't we all just get along?" The only reasons for the legal profession, it seems to me, are avoiding, managing and resolving conflict. As a manager, it is vital to understand why conflict exists and to have the tools available to confront and resolve conflict.

Personal Application Exercise I — Think about an issue — current or recent — involving conflict in your work group. Describe the facts as you know them in some detail: who is involved, what the major issues are, how long this has been going on, etc.

The sources of conflict

The first step in managing conflict is to understand the sources of conflict in organizations in order to discover the cause of *your* conflict.

Value differences

While we share the vast majority of personal and cultural values, minor differences in values and the importance of different values can lead to conflict. For example, if I hold fairness as one of my most important values and you hold freedom as more important, conflict may emerge when your desire for loose workplace rules leads to the perception of unequal assignment of responsibilities. The values that tend to be problematic in the lab are not high-order values such as quality and accuracy but rather "lower level" values that are more akin to preferences, such as acknowledgment and composure.¹

Role pressures

20

Our various roles at work, the hats we wear, may be quite clear (however, usually they are not), but the pressures from outside the workplace can be a serious source of conflict. The demands of a multigenerational family can be daunting, and fitting it all together leads to tension and fatigue and is the source of much of the conflict that arises. Staying late to finish an important project or proposal can be in direct conflict with attending a soccer game or a dance recital or with getting an aging parent to an appointment with a physician. Role pressures also come from poorly trained and poorly prepared staff and from an environment that is not open to discussion and dissent.

Goals

"Okay, boss, what is more important to you, accuracy or meeting a deadline?" "Both!" While the overall goals for your lab may be clear to everyone, individual, divisional or departmental goals can be widely divergent. There are always tensions between cost and quality, accuracy and timeliness, and relationships and efficiency associated with specific goals that can bring staff into conflict.

Perception differences

What do you see in this image? A human skull or a woman at her dressing table? All of us see things from the reference of our experience, our emotions and our values. Our mood impacts our reaction to a situation, and that is particularly true when we are angry or excited or our ego is involved. Assume that people will have a different reaction to a situation based on their perception. The '70s mantra "the perception is the reality"



is true. (http://www.moillusions.com/2006/04/what-do-you-see-illusion.html)

Status conflict

Our status in society is very important, and people who are not aware of different status symbols can get into trouble quickly. The differences between a technician and a technologist may not be important to outsiders, but in some laboratory settings they can be crucial distinctions.

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Status comes from several sources and is closely tied to the values of the organization. Any threats to our status are seen as attacks on the values we have accepted. This is particularly true when a large percentage of the staff is at the same level on the organization chart or receives substantially the same salary.

A couple of years ago I was on a tour in Turkey. One of my companions was the director of a large university lab. He had numerous telephone conversations with his staff during the tour, dealing with the names to be included in an article that was being finalized for publication. This was a clear attempt to reduce status conflict.

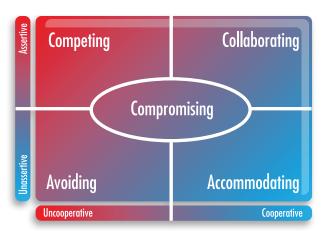
Personal Application Exercise II — Think about the conflict you identified in the first step in the Personal Application Exercise. Can you identify the possible sources that are coming into play? What about your own position?

Resolving conflict

The first step in resolving conflict is to gain an understanding of the sources of the conflict. The second is to have the courage to confront the conflict. Courage comes from commitment and the knowledge that you possess the requisite skills.

In the following model, from the Thomas-Kilmann Conflict Mode Instrument, "assertiveness is defined as the extent to which the individual attempts to satisfy his or her own concerns, and cooperativeness is the extent to which the individual attempts to satisfy the other person's concerns."

So, someone who is being Assertive and Cooperative would be using a Collaborating mode. As you read the following descriptions, you probably will find one or two



Adapted from Thomas-Kilmann Conflict Mode Instrument

modes that you use most frequently. That's normal; skillful conflict managers have developed a wide repertoire of responses and select the approach that best fits the situation.

Competing

This combination of Assertive and Uncooperative is appropriate when quick decisions and actions are imperative. You may not face many such situations except in emergencies. This is also an approach that may be appropriate when implementing unpopular but necessary changes in organizational procedures or in processes such as downsizing. Another use is when you are certain you are right but do not have the time to present a detailed explanation of your reasons and the background information.

Collaborating

When you combine Assertiveness with Cooperation, you have the basis for a mode that, given enough time and a sufficiently important issue, may be the most valuable approach to solving conflict. This is the method to use when the issues, are too important for Compromise. You

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will learn about the interests of the others involved. This is the mode that will help you work through hard feelings that have been interfering with interpersonal relationships. Perhaps most important about this approach is that it will lead to strong commitment to the decisions that emerge. However, be cautious about moving into a Collaborative mode when other techniques are better suited to the realities of the situation.

Compromising

Being midway between Cooperative and Uncooperative and midway between Assertive and Unassertive leads to a Compromising approach to conflict management. It works best when goals are important but not overwhelmingly so. Compromise may be necessary when the people involved have equal power and are strongly committed to mutually exclusive goals. Compromise is also a good technique when you need a short-term solution to a complex problem or when you need to reach a quick solution on a deadline. This is also useful when other modes have failed. However, remember that in Compromise, no one is fully satisfied, so it should not be used in the case of vital issues with ethical implications.

"Conflict can be...one of the best ways to discover where problems exist."

Avoiding

When you take a stance that is both Unassertive and Uncooperative, you are Avoiding, and this mode does have legitimate uses. For example, it can be helpful when an issue is insignificant or of transient interest, or when spending time to resolve the conflict would interfere with more important issues. Avoiding is also a reasonable mode when there seems to be little chance of satisfying your concerns and when the potential damage from confronting a conflict outweighs the benefits from resolving it. This is a valuable approach when people need to cool down and return to a rational emotional state. Avoiding makes sense when you need to gather additional information and when others are better positioned to resolve the issues than you are.

Accommodating

Being Unassertive and Accommodating is the best combination when the issue is much more important to the other person than it is to you or when you need to build up "points" to use later for more important issues. This mode is best if your long-term goals are to foster harmony and to avoid disruption when you realize that you are wrong. This is a great technique to employ when your primary interest is the development of your staff.*

Each mode has advantages and disadvantages; a right time and place even for Avoiding and Compromise is not always the best approach! These are covered well in the information that accompanies the Instrument.²

Personal Application Exercise III — Review the conflict and your assessment of the underlying causes. Which conflict-handling mode seems to have the best fit and seems most likely to be successful?

Conflict resolution model

After uncovering the sources of conflict and considering the options available to get on with solving the problem, all you need is courage! There are two ways to build up your courage (forget about the kind that comes in a bottle). The first is to have successful experiences, and the second is to have a plan or a model to use. Here is a simple model to help you get beyond the fear that often comes with getting involved in a conflict.

- 1. Make sure that the issues are clear.
- 2. Use active listening, restatement and paraphrasing.
- 3. Understand the underlying causes of the differences:
 - Values Roles Goals Perception Status
- 4. Select the best Conflict-Handling Mode:
 - Competing Collaborating Accommodating Compromising
 - Avoiding
- 5. Schedule a meeting.
- 6. Consider having a third or fourth party involved.
- 7. Get agreement.
- 8. Follow up.

Personal Application Exercise IV — Use the model above and add your judgment about the causes and the best technique to use. Then just do it!

We have no conflict here

What bliss! Wrong—having no conflict means one of the following things: People are fearful about raising their concerns; they are convinced that management is impotent; or they are not being pushed enough. In fact, conflict can be one of a manager's best temperature sensors, one of the best ways to discover where problems exist, and where values, goals, roles, statuses and perceptions are causing problems that need to be dealt with. Conflict is good! That's what some of my colleagues pronounce, but it's not good for me (and I think they are trying to drum up business!). The idea of conflict causes my stomach to twist into knots and my hands to sweat. I know that my favorite conflict-handling mode is Avoiding, so I try to convince myself that this conflict is ideally suited to Avoidance.

SUMMARY

KEY POINTS FOR MANAGERS:

- 1. Unresolved conflict can cause great disruption in a work group.
- 2. Active conflict resolution can surface and resolve a variety of issues.
- 3. Learn to recognize the causes of conflict.
- 4. Remember your own predisposed conflict mode.
- 5. Expand your repertoire of responses.
- 6. Deal with conflict don't deny it.
- 7. Acknowledge your contribution to the conflict.
- 8. Deal with the anger and then take action to change the underlying causes.
- Learn from conflict and make changes based on your learning.

References

- 1. Steve Pavlina lists 374 values that people hold, and he provides an interesting way to assess your most important values. Visit his Web site at http://www.stevepavlina.com/articles/list-of-values.htm. For more information, read the entry on values in Wikipedia.
- For more information on the Thomas-Kilmann Conflict Mode Instrument and to order a copy of the Instrument with a detailed explanatory booklet, see https://www.cpp.com/products/tki/ index.aspx.

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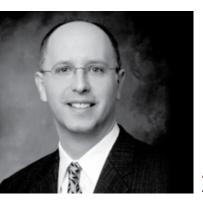
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SCIENCE MATTERS

LATEST TRENDS SHAPING THE SCIENTIFIC WORKFORCE By Rich Pennock



FREE AGENCY

During the past few years, there has been a steady increase in the number of self-employed "free agents" in the United States. According to a survey conducted by Kelly Services, Inc., a workforce staffing solutions company, 26 percent of the nation's working population is freelancing, up from 19 percent a few years ago.

While company downsizing leads many individuals to consider freelancing, others have worked as freelancers for most of their lives, despite having never been laid off from an organization. So, what leads individuals to pursue a career in freelancing? What do they find most appealing about free-agent work in the scientific industry? In order to better understand the positives of contract scientific employment, I interviewed four former and current freelance scientists.

Each freelance employee found project work through Kelly Scientific Resources (KSR), a specialty service of Kelly Services, which has provided staffing and placement services for science professionals since 1995.

Summer Watterson, a molecular biologist from Cleveland, has worked with KSR in the past to find short-term contract positions. Amanda Michaelis, a recent college graduate from Lees Summit, Missouri, has begun her scientific career as a lab technician, an assignment she obtained with the help of a KSR recruiter.

Karen Demby, a current resident of Las Vegas, has typically worked in the pharmaceutical industry and has used KSR to find freelance work in the past, while Clare Gerstein, of Libertyville, Illinois, is currently working in the biotechnology and medical device industries.

Rich Pennock: First, what led you to pursue a career as a free agent—a freelance worker with or without the support of a temporary staffing agency? Is this a planned career track or one that you "stumbled" upon?

Summer Watterson: This is a career track that I chose because I was interested in pursuing a position with a certain company. The company worked only with staffing firms at the time. Because of that first experience, I was willing to freelance again.

Amanda Michaelis: I had just graduated from college and was looking for lab employment, with no particular field in mind. I was willing to pursue positions on my own, but I greatly appreciated the help that a staffing agency provided.

Karen Demby: While I have always preferred having a full-time, salaried position, Kelly Scientific Resources helped me find contract assignments with wellrespected companies, which at times led to direct employment after my contract assignments were completed.

Clare Gerstein: After graduating with a B.S. from the University of Iowa, I desired a position in a lab on a temporary basis in order to have the greatest flexibility for my eventual return to the Chicago area.

After arriving back home, I worked on a contract basis at a major pharmaceutical company before finding full-time employment as a general lab aide at a major academic research center.

At first I was pleased with this turn of events, thinking that a direct position was the best choice for me. With time, though, I found myself dissatisfied with the breadth and scope of my work. Working through staffing firms such as KSR has afforded me the chance to explore different fields and environments, diversifying my skill set and broadening my ability to contribute to the design and optimization of experimental planning.

Rich Pennock: What are some typical roles that you have had as a KSR contract employee?

Summer Watterson: My roles were primarily in laboratory-based bench work. One was temporary for only a predetermined amount of time and the other was temp-to-hire.

Amanda Michaelis: I have had only one—as a lab technician. My job duties include running samples through a number of instruments that test for fuel, viscosity, metals, and water. Some computer work and data entry were also required.

Karen Demby: My roles with KSR were all laboratory and pharmaceutical based. I have a B.S. in microbiology and I am passionate about either working in the laboratory or performing research. When I lived in California, pharmaceutical companies were plentiful and the opportunities were excellent. While living there, I worked as a process development scientist and a production associate with KSR.

Clare Gerstein: I have had just one assignment through KSR, as a research associate in an exploratory group with a major biotechnology and medical device company. It has proven to be such a successful match that the assignment has been ex-

tended twice and will likely continue for some time.

Rich Pennock: What are the benefits of a freelance career?

Summer Watterson: I think the best reason to freelance is that you have the ability to check out different career tracks. It is great to freelance when you are in a transition period with your career. It can really help give you direction. If you find work that you love, you can continue to pursue those types of positions. Meanwhile, if you find work that you never want to do again, just fulfill your contract and move on.

Amanda Michaelis: Freelancing provides some freedom to explore many career options. For example, if one place is not suitable for you, staffing firms may be able to find another position that might fit better. This kind of work definitely has the potential to offer individuals both variety and experience in different types of career fields.

Karen Demby: Generally, benefits of freelance work is higher pay.

Clare Gerstein: Most freelancers have more flexibility than typical full-time employees have. This flexibility is particularly good for people who are entering or returning to the workforce, or who are interested in working part-time or on a project basis. Contract work also creates an opportunity for employees to provide specific skills or services to various companies around the country and the world.

Rich Pennock: Finally, how do you view the future of free-agent work?

Summer Watterson: I will definitely do free-agent work again during the next transitional phase of my life. Free-agent work is especially useful when you are moving, searching for a short-term position, or looking for new or different types

of work opportunities in your life.

Amanda Michaelis: I think it has serious potential, especially for new graduates. With contract work, both well-experienced and inexperienced employees alike have freedom to explore many opportunities in the work force. Contract work also helps new employees ease into the career world. Through contract work, recent graduates have a mediator to help guide them through the unsure and new "real world" experiences such as interviews, resumes, and company policies.

Karen Demby: I think people will continue to look for help from staffing firms such as KSR as the economy continuously shifts. The opportunities that KSR provides can be the edge that people need in order to begin employment with different companies.

Clare Gerstein: I think that for many people freelance work can make a lot of sense, especially during transitional phases of life, when people desire a high degree of flexibility.

Free agency has positively impacted the lives and careers of scientists during the past few decades. As individuals continuously pursue new career interests, they may want to consider freelance work. Free agents not only have opportunities to work with some of the most well-known organizations in the world, but they are also able to expand their skill sets in order to become more marketable as they pursue future careers. Now more than ever before it seems that free agency will help many scientists obtain success well into the future.

Rich Pennock is vice president of Kelly Services, Inc., a world leader in workforce management services and human resources solutions. For more information, visit www.kellyservices. com. Rich can also be followed on Twitter at http://twitter.com/richpennock.

Qorpak* DIG DEEPER

This month Lab Manager Magazine introduces a new editorial feature called "Ask the Expert" (page 34). Each month author Tanuja Koppal will interview industry experts to discuss a range of topics important to lab professionals. This month she spoke with Dr. Michael D. Hopkins, Professor of Chemistry at the University of Chicago, who helped renovate the Searle Chemistry Building, which received a LEED Gold certification for its "green" attributes.

If you want to learn more about this month's expert, Dr. Michael Hopkins, visit www.qorpak.com/labmanager to see his video interview.

Next month's expert will answer questions concerning setting up a high-throughput screening lab. To submit your questions to future experts, visit www.labmanager.com and click on the "Ask the Expert" link below Laboratory News.

Look for more "Dig Deeper" video links in upcoming issues of *Lab Manager Magazine*. This new online feature is designed to offer a more in-depth exploration of the ideas behind particular articles and unique information that only the authors and "experts" themselves can provide.





THE PAPERLESS LAB

FOCUS FIRST ON BUSINESS OPERATIONS AND ROI AND SECOND ON "GOING PAPERLESS" By Gloria Metrick

We talk a good deal about "the paperless lab," but how do real labs become "paperless"? This article highlights two different laboratory software projects that illustrate the tasks and issues that came up based on specific projects and situations. The idea is to help you think about your own situation if you're considering moving toward a paperless lab. These examples are given by two members of the upcoming LRIG (Laboratory Robotics Interest Group) and LIMS (Laboratory Information Management System)/Laboratory Informatics ELN (Electronic Laboratory Notebook) expert panel being held in Boston, Massachusetts, on February 10, 2010, where these examples will be more fully explored.

QC (Quality Control) Project: Major Pharmaceutical

This example comes from a discussion with Mike Stroz, Global Operations IS - Global QC Systems program manager at a major pharmaceutical company.¹

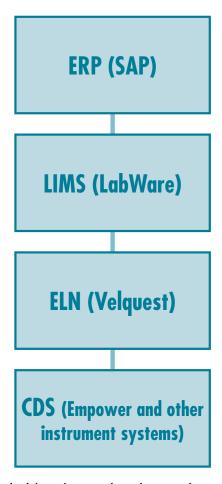
The goal: To harmonize all of the company's QC labs around the world

Project details: The project began in 2006, when the company defined a strategy for data and sample management in the labs. A key task was to integrate the systems. At the end of 2009, the company was halfway through its worldwide rollout.

Early in the project, the team worked out a global process to follow. This process was designed to apply to the greatest proportion of the company's operations and products. The occasional product or process that did not fit into this process model was left alone. The model was not "bent" to accommodate each exception, and the exception cases were not forced into the model. The team also prioritized products by starting with those that would carry the highest return if made paperless, i.e., the most common products that require and create the largest amount of data. The team made these highestpriority products paperless first and then kept working on the rest of the products from there. Additionally, where there were variations in methods, the team's priority was to convert the most common methods first. So the team had several layers of prioritization in order to convert most quickly those items that the laboratories used most often.

Once an area begins its rollout, it faces a variety of situations; at any given time some products will be paperless, some will be hybrid and some will be entirely on paper. It could take several years to get everything converted, depending on the size of the area and the number of products involved. But the priority remains to convert the products with the highest volume or impact the soonest.

The company also defined a model for the layers of information it would have. The model looks like this:



For the labs to be paperless, the team determined that these were the systems that must be integrated into the model. The LIMS layer is used by QC management for scheduling and COAs (certificates of analysis). The execution layer is the ELN, where the analysts do all their work.



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The instrument data layer is the CDS, which is linked to the ELN layer to make all the data easily searchable.

In this model, each system interacts only with those immediately adjacent to it in the drawing. For example, the ERP interacts only with the LIMS. The LIMS interacts only with the ERP and the ELN, but not with the CDS or other instrument systems. Therefore the ELN collects instrument data so users can access that data in their electronic laboratory notebooks. Then the data required by the LIMS is sent to the LIMS from the ELN. Also, a critical feature in this model is its design that keeps people from having to switch systems. Thus, the processes around these "levels" are designed to keep the roles working within that particular system level.

"The team...prioritized products by starting with those that would carry the highest return if made paperless."

Some detail at each level looks at things appropriate to that level. For example, the team defined where their samples were coming from: some came from SAP, others were ad hoc and still others came from other sources. The team also considered what review people needed to do within a level or who needed to see what information. Within a level, one department might need specific information or the laboratory might need to schedule samples. The team designed each system to accommodate these low-level differences.

However, their goal was to keep each system as usable right out of the box as possible. They did not want to spend much time customizing systems or trying to make systems do things they weren't intended to do, so the team refused to accept from software vendors new system pieces that were immature or meant to extend what each layer would do. Also, they used one system for each level to set the standard.

ROI (return on investment): Mike claims that the company realized a 30 to 40 percent gain in resources as a result of being paperless. It saves time because employees no longer print documents to review, for example. Along the way, the team considered the company's KPI (key performance indicators) and measured them.

Specific points: Mike makes the point that you must consider how much time and effort you will spend going paperless versus the benefit you'll get from it or the money

you'll save. To do this, analyze how you run your business and identify where and how the benefits will occur.

Legal: The company's legal department did not find the proposed paperless process to be an issue in and of itself. There were a variety of issues that came up along the way, but a technical solution was always found to address them.

Research Project: Millennium Pharmaceuticals

The second example comes from a discussion with Craig Tulig, associate director of R&D systems at Millennium Pharmaceuticals.² Millennium has two ELNs, one already implemented for chemistry and a second that is in its pilot phase for biology. The latter is the subject of this example.

The goal: To make scientists more productive by allowing them to easily search their data electronically and to give them quicker and more reliable access to their data.

Project details: The Millennium team wanted to make sure that they could input data so that it was highly searchable. This was especially important because this data is unstructured. Thus the team decided to be somewhat cautious and carefully addressed their data needs. They wanted to make sure that their data was captured in a high-quality manner.

"[The] goal was to keep each system as usable right out of the box as possible."

A number of systems such as the reagents database and other related systems make up the overall Millennium strategy. However, the scientists see only their e-notebooks. For example, Craig said that they will be linking a homegrown LIMS into this strategy. Millennium's ELN product is from the Symyx family of products. Even though they are not doing the same thing for biology that they did for their chemistry project, the team thought that it was important to have a single e-notebook platform for Millennium and they made their selection through a rigorous evaluation process. Thus, both chemistry and biology are using solutions from the Symyx platform.

In the biology area, the lab notebook is the last paperbased system, as everything else is already paperless. At this time, the Millennium team has put much thought into what they want in a system and is now running the initial pilot to test their concept. That phase is expected to take three to six months. The purposes of this pilot are to verify that their solution is effective and that the data integration is fully realized.

Once the pilot phase is over, the first phase of rollout is expected to take place in the subsequent three-month period, followed by another phase of rollout in which labs have been prioritized into phases.

"They went paperless because the paper pieces of the process were standing in the way of their productivity."

ROI: Because this is a research environment, Craig's team believes that the "soft" benefits are the most important. However, he said that there is a noticeable difference between the time it took people to dig through paper notebooks and documents and the time it takes when they do an electronic search to get their data. This is important to the research area, and the value is not easily calculable.

Specific points: Craig's advice is to establish your goals up front so that you can measure your project against them. He tells us to make sure that we define not just our goals but also the exact efficiencies we hope to gain, which will help direct the project.

Legal: In 2004, when the Millennium team began the chemistry project, they worked with their legal department to determine how to take precautions with the IP (intellectual property) within their strategy. They briefly had a hybrid system as the details were worked out but did not have to run in hybrid mode for long.

Final points

Notice that neither company had the specific goal of becoming paperless. Rather, in each case they wanted to improve productivity or harmonize operations. To do so, they mapped their processes and made decisions on how to proceed. They went paperless because the paper pieces of the process were standing in the way of their productivity or operational goals. Keeping this in mind is key to maintaining perspective on your true goals and finding how to achieve them.

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- 1. Telephone discussion with Mike Stroz on Friday, November 6, 2009.
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Gloria Metrick is the owner of GeoMetrick Enterprises (http://www.geometrick.com/), which provides consulting services for laboratory informatics projects. She is the author of "Out on a LIMSTM: The Newsletter for People Who Risk Life and LIMSTM on a Daily Basis" and "Out on a LIMSTM: The Blog for People Who Risk Life and LIMSTM on a Daily Basis" as well as being a contributor to theintegratedlab.com. For projects, speeches or writing, Gloria can be contacted at GeoMetrick Enterprises, +1.781.365.0180, Gloria@GeoMetrick.com.



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SCANNING THE SCENE

3-D LASER SCANNING HELPS FACILITIES WORK THROUGH THE RENOVATION AND BUILDING PROCESS FASTER by Thomas Walsh, PE, and Chris Zmijewski

Building renovations can be a nightmare for laboratory facilities. From biocontainment and contamination issues to finding the space and time for proper surveying and construction, the entire process is daunting, and it is often so difficult to negotiate around lab operations that the drawbacks seem to outweigh the benefits. However, three-dimensional laser scanning, a new tool in the construction and development world, is helping facilities work through the renovation and building process in a much faster, less disruptive manner.

"The entire facility can be 'measured' much more quickly...allowing the crew to get in and out as fast and cleanly as possible."

The way it works is the so

The way it works is the scanning equipment pulses the scene repeatedly with a laser, collecting the spatial data for each of the hundreds of thousands of points it sees, and then reproduces that data to form a series of images. The resulting views look much like digital photographs but have all the three-dimensional angles

and their equipment must repeatedly enter and exit the

space, compromising the sterility or continued operation

of labs that require such conditions. With laser scanning, however, the entire facility can be "measured" much

more quickly and with much less equipment, allowing

the crew to get in and out as fast and cleanly as possible.

and perspectives of the real thing. These 3-D images allow designers and builders to get the full perspective of the site, down to the window heights, sprinkler systems, piping, electrical outlets, casework, wall devices, and equipment in the room.

A single laser scanning unit can scan an entire lab in a fraction of the time it takes to use traditional survey methods.

This kind of information is invaluable especially during the planning and design phases of a renovation project, for the scan images show not only every detail of the site but also the exact dimensions from the interior to the exterior of the building, which makes designing the floor plans and the wiring,

fireproofing, HVAC, and other building systems much easier and more accurate. For lab facilities, in particular, the benefits of laser scanning go beyond its usefulness for design purposes. There are a number of efficiency and safety benefits as well:

The hands-on tradition

During a building or renovation project, traditional survey crews set up their equipment at various points in a space to measure

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at various points in a space to me the angles, alignment, footings, foundation, and other spatial dimensions that inform the final design and construction details of the renovation. This process requires setting up equipment, measuring from point to point, taking it down, and repeating the process until enough information has been collected on the entire space. This data is then literally handwritten onto the building plans of the space in question.

The problems with this method, especially for sensitive environments such as labs, are many. Hand-measuring all the spaces is time-consuming, which can seriously impact a facility conducting time-sensitive research. The process is also quite invasive; meaning the crew



▲ Labs with little extra room can use laser scanning to help fit in new equipment and make the most efficient use of their space.

Time. As mentioned, the speed of laser scanning is one of its most significant advantages. Depending on the complexity of the space, scanning an average-sized research laboratory, for example, could be completed within hours. This same process could take the better part of a day if done using conventional methods. Again, for facilities undergoing time-sensitive or continuous research, the less time the process takes, the faster lab technicians can resume their work. What's more, the data collected is processed within minutes and quickly converted to working CAD files, making it available to designers almost right away.



◆ Scanning data can be converted to CAD files, which lab managers can use in their own facility planning software programs and documentation.

Space. The speed of the laser scanning process isn't the only factor that minimizes disturbances to the work in a lab; its relatively simple equipment avoids conflicts as well. Laser scanning requires only the laser scanner and one operator to collect the field measurements. There is no need for extra people, tools, ladders, and other equip-

ment to crowd the space and pose the risks of damage to a lab's equipment.

The streamlined process also helps a survey crew get into spaces that would otherwise be difficult. The scanner can be elevated on a post to reach high spots or mounted over ductwork or inside the ceiling to measure interstitial spaces and other areas. This does require moving the scanner a few times, but it allows access to these types of spaces that traditional survey operations can't provide.



◆ Scanning equipment can document hard-to-reach spaces such as behind ductwork or above the ceiling.

Safety. The versatility of the scanners means survey staff are much less likely to need to climb ladders or balance on lifts to reach out-of-the-way spaces. And for biocontainment or sterile labs, crews can simply set up the equipment and walk away, allowing the scanner to do all the work and avoiding any need for protective suits, respirators, and the like.

Accuracy. The amount and detail of the data collected by laser scanners is staggering. Rather than measure from several point A's to point B's as in conventional survey operations, the scanner measures literally millions of data points within the same geospatial coordinate system, providing extremely accurate measurements and nearly photo-quality images. This level of detail also means the likelihood of needing to make return field visits is very low, which reduces costs and, again, disruption to the lab and its operations.

The accuracy of this data also helps designers better plan a lab's space, which is especially useful for small labs or labs with a lot of large or complex equipment to accommodate. The 3-D images that result from laser scanning allow designers to examine the room from all angles and create precise models of how the many pieces can fit together. In other words, they can take all the components of the room as if they were pieces of a puzzle and continue putting them together in the model until they find a solution that works. With such accurate measurements, the model is extremely reliable and allows crews to begin construction quickly and with confidence. This same idea can be used to model how material, people, and processes flow through a space, helping identify bottlenecks, the potential for cross contamination, and other issues.

Validation. Similarly, laser scanning can be a particularly valuable tool for facilities with legacy systems or others that need validation from such authorities as the FDA. Laser scanning provides real coordinates and as-built data within a tenth of an inch, fully documenting each pipe, valve, and vent—the entire system. This is especially helpful for a lab that is planning to change its process or system, as the documentation can prove that all components are in place before the new system is implemented.

Compatibility. One of the more useful benefits in the long term is the ability of laser scanning data to provide a comprehensive, consistent, and compatible record of not only a specific lab or room, but also its relationship to the entire building, campus, or surroundings. As the data can be converted into other building modeling software programs such as CAD, it is easily integrated with other parts of the building. That means, for example, that the building team could develop a full model of an entire research campus, including all the interiors and exteriors, the streets, the infrastructure under them, etc. Each of those components would be labeled accordingly, creating a comprehensive, accurate foundation for any future renovations or changes, as well as a flexible plan that can accommodate those additions.

Planning for the future

While the use of laser scanning is just getting its start in the laboratory and research world, its potential to streamline the building and construction process for these facilities is immense. For starters, facilities with limited existing documentation, with plans for significant changes, or with especially critical environments are well-suited to take advantage of this technology.

The visual images it creates can also help a facility get approvals and the budget to move forward on renovation projects as they help visually communicate not only the current state of a space but also the benefits and possibilities for its growth and improvement.



▲ Laser scanners connect directly to a laptop, allowing users to see the results of the scans almost instantly.

As the technology continues to develop, this communication will become even more sophisticated, allowing facility managers to have access to all the measurements and geospatial data right from their desks. The hope is that ultimately these systems will allow users to highlight a building or space on their computer screens and pull up all the related building information, including photo data, walk-through animations, dimensions, and other details. This information can then be used to forecast what the facility could look like in 5 or 10 years and project the costs of making those changes.

With the many complications the lab environment can pose for construction and renovation projects, 3-D laser scanning is a sophisticated tool that can provide some simple solutions for keeping a lab, its staff, and its research up and running.

Thomas Walsh, PE, is a senior principal and practice leader of the biopharmaceutical engineering division of Stantec, and Chris Zmijewski is a principal and leader of the company's 3-D digital imaging and mapping practice. They can be reached at tom.walsh@stantec.com and chris.zmijewski@stantec.com, respectively.

All photos courtesy of Stantec



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had extensive experience leading space planning, design, and construction projects for the Chemistry Department and the Physical Sciences Division (PSD). He was a member of the committee that developed the Space

Master Plan for the PSD; led the faculty team that designed the synthetic chemistry laboratories for the Gordon Center for Integrative Science, a \$220M building completed in 2006; led the Jones Laboratory renovation project in 2005-2006; and led the Searle Chemistry Laboratory renovation from its inception, including selection of the architects, programming of the project, and the design and construction phases.

ASK THE EXPERT

DESIGNING AN ECO-FRIENDLY LAB

WANT MORE INFO? DIG DEEPER **Qorpak** Dr. Michael D. Hopkins talks to Tanuja Koppal, contributing editor to Lab Manager Magazine, about his experiences and involvement in renovating the Searle

Chemistry Building at the University of Chicago, which has now received a LEED Gold certification for its "green" attributes. The renovation was a multi-year project which began in 2002 with an internal proposal to get the University on board. Dr. Hopkins was involved with the project at every stage, right from planning and design to construction and occupancy.

Did the renovation of the Searle Building start out as a "green" project or did that happen over time?

That was something that was not planned from the outset. As we worked with the architects we realized that there were opportunities for cost savings and energy efficiencies that would prove beneficial in the long-term to both the University and the environment. It evolved into a green project over time and now we have been assigned the LFFD Gold Certification.

Can you elaborate on some of the green features of the building?

Buildings that are designed for synthetic chemistry need to have a lot of fume hoods and these hoods are notorious energy consumers. They constantly draw air from the laboratories and this air is released outside and cannot be recycled, in order to maintain the safety of the occupants. This happens 24/7 and according to some metrics a typical fume

hood consumes energy equivalent to that consumed by about 3.5 houses. So a building like ours that has over 100 fume hoods has the energy footprint of multiple city blocks with single family houses. We have now designed hoods that have proximity sensors where the unit lowers the sash if the hood



▲ A photograph showing the sensor-controlled fume hoods, low flow sink faucets and other energy efficient features in a laboratory at the recently renovated Searle Chemistry building. ©Wilson Architects, Anton Grassl / Esto.

is not being used for a certain period of time, hence reducing the volume of air that is drawn. Lowering the sash not only reduces the energy consumption but also makes the lab safer by providing a shield between the contents of the hood and the people walking by. There are also other features that may be transparent to the users but nonetheless have a big impact on the energy efficiency (see sidebar for additional details).

How can scientists get involved in the design of areen laboratories?

The amount of impact that you can have depends on the stage that you get involved in. Buildings are highly integrated systems and one decision may impact several others which can then affect the budget and performance criteria of the building, both of which are often set early in the project. So obviously the earlier you get involved, the bigger the impact you can have. The most important decision to be made early on is choosing an architect who knows how scientists think and what they need and has experience working with a green design. Hence, scientists must be willing to invest the time early in the project to help choose the right architect and set the design criteria.

Are there resources that can help one find the green options available for a laboratory?

The Lawrence Berkeley National Laboratory's high performance building design group has a website with information about many different aspects of building design. This website can provide information

34 Lab Manager January 2010 labmanager.com

THE "GREEN" SEARLE CHEMISTRY BUILDING

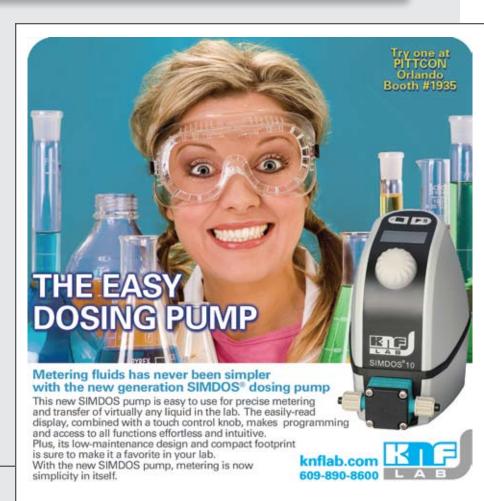
While the Indiana limestone framework of the original five-story building built in 1968 remains largely unchanged, the renovation of the Searle Building has completely refurbished and modernized its interiors. Estimated to cost \$49 million, the renovated space will allow the Department of Chemistry at the University of Chicago to expand from its current 21 to 25 faculty members and will house the latest state-of-the-art equipment. The third floor of the building will house the \$11 million Tri-Institutional Center for Chemical Methods and Library Development, while the lower level will accommodate clean rooms and next-generation scientific instruments.

The Searle Chemistry Building will be the first LEED (Gold) certified project on the University of Chicago campus. LEED, Leadership Excellence in Environmental Design, is a green building program developed by the U.S. Green Building Council (USGBC). The Council provides third-party review and certification of building design, construction and performance in five key areas of environmental and health concern: sustainable site development, water savings, energy efficiency, materials and resources selection, and indoor environmental quality. The LEED program points awarded to the Searle building are based on the following "green" attributes:

- At least 75% of building was reused (walls, roof, floors)
- Vegetative and reflective roofs to minimize heat island effect
- 33% water use reduction—lavatories have sensors; high efficiency toilets; low flow faucets with aerators on lab sinks and cup sinks; and low flow kitchen sinks, lavatories and shower
- 9% energy cost savings due to high performance envelope (insulation and glazing), improved lighting design, and improved heat exchanger efficiencies
- High indoor air quality. Entire building is supplied by 100% outside air so no air recirculation from chemical use and storage spaces
- Control of indoor chemical and pollutant sources. Refrigerants selected that minimize emissions that contribute to ozone depletion and global warming
- Exemplary management system for chemical handling and exhaust dispersion
- 21% recycled content in materials. 92% of construction waste diverted from landfills and recycled
- At least 90% of the walls, roof and floors were saved, minimizing the use of new materials while conserving resources, reducing waste and transportation costs

both at a broad and at a more specific level about the types of options that are available. There are also many trade conferences. But the scientist's time being limited, your architect is probably the single best source for information. In our case, our architects understood what was important to us and presented us with a set of thoughtful options that we could choose from and worked closely with us to refine the designs offered.

The Searle Building officially re-opened in June 2009 but few areas still remain under construction and labs are being occupied in stages. The laboratories are designed mainly to facilitate research in Synthetic Chemistry and Chemical Biology and to accommodate instruments that support those areas of research. The total renovation costs were estimated to be \$49 million but the project is now expected to finish under budget.



CRITICAL DRIVER FOR DRUG DISCOVERY by Angelo DePalma

Ultra-high-throughput screening (uHTS) is an automation-based methodology for conducting hundreds of thousands of biological or chemical screening tests per day. The cutoff between high-throughput screening (HTS) and ultra-high-throughput is somewhat arbitrary. "There is no fixed boundary," says Simon Sheard, Ph.D., business development manager at RTS Life Science (Manchester, UK), which supplies automated sample management equipment used in uHTS. The generally accepted crossover point today is 100,000 tests per day.

agitation, bar code reading and incubation are also possible.

uHTS achieves its speed through a combination of higher-density microtiter plates and multichannel (384 and higher) liquid dispensing. Equally important in achieving high throughput, however, is assay simplicity. Most ultrafast screens involve simple binding and rapid reading of results. For this reason, uHTS lends itself most readily to drug screening where, classically, tens of thousands or hundreds of thousands of wells are plated with

available is collected. Wells that "light up" are examined more closely, for example by purifying mixtures or plating components individually.

The pharmaceutical connection

Parallel screening methods have been used for decades in the pharmaceutical industry. The advent of automated plate-handling and reading instrumentation, and the replacement of radiolabeling assays with luminescence- and fluorescence-based screens, created the opportunity for the several-hundredfold improvement in throughput represented by uHTS. Original equipment was expensive, but over the past decade instrumentation prices have fallen in terms of cost per assay per day, to the point where uHTS is now accessible to small drug discovery firms and academic groups. Numerous service providers also conduct uHTS services for organizations that lack this capability or whose own systems are overcommitted.

Wei Zheng, Ph.D., a group leader at the NIH Chemical Genomics Center (Rockville, Md.) learned the HTS and uHTS trades while screening drug candidates at Merck and Amgen. One of the instruments in use at the NIH Center is a plate-handling robotic system, codeveloped by Zheng at Merck,

"Equipment for conducting uHTS is indistinguishable from a standard microplate handling system."

uHTS is conducted in microtiter plates. To provide numerical perspective, 100,000 tests per day require 1,450 96-well plates (by far the most commonly used type), 261 384-well plates, or 65 1536-well plates. uHTS programs that exceed 1 million screens per day use ten times as many plates.

Equipment for conducting uHTS is indistinguishable from a standard microplate handling system, consisting of a robotic microplate handler, a liquid dispenser, and a plate reader. Additional components for washing,

entries from a large compound library, and the assay reagents (protein, enzyme, cell, or receptor, plus reporting reagent) remain constant in every well. Depending on the nature of the detection event, the interaction between compound and target is read as fluorescence or luminescence.

It is possible to "cheat" in HTS/uHTS by utilizing unpurified compounds, mixtures of compounds, or even multiple targets, a technique known as high-content screening because a multiple of the information normally

that processes hundreds of thousands of wells per day and has 1,536-well capability. "It runs between half a million and a million screens per day, depending on the assay," Zheng told *Lab Manager Magazine*. The system uses plate readers from PerkinElmer and GE, and core robotics from Kalypsys Systems.

Recently, researchers from the Chemical Genomics Center, in collaboration with scientists at Trinity College (Dublin, Ireland) reported on a screen of 17,143 FDA-approved and experimental drugs. The biological target in this case was a panel of human liver enzymes that metabolize drugs, and hence are critical to a medicine's effectiveness.

"As assay strategies become more sophisticated and screens more numerous, the number of components increases."

Zheng's group uses 1,536-well plates almost exclusively, as do most pharmaceutical labs. "Miniaturization saves time and enables higher throughput at reduced cost," he notes. However, minuscule assay volumes sometimes create difficulties for cell-based assays. "It's often difficult to deliver the number of cells you need for an assay at such low volumes. In these circumstances the screens cannot be run at 1,536-well density."

uHTS received a bad reputation around the beginning of the decade, based on a perceived low success rate in identifying new drugs. The fault, says Zheng, was not with uHTS methods but with the drug companies' choice of screening targets.

Simon Sheard agrees. "We hear comments about the failure of the 'law of big numbers' regularly. That's a generalization, and the approach of cranking the handle faster has not completely

fallen out of use. Nevertheless, what we have seen during the last few years is a shift away from uHTS to automated screening of smaller compound sets through assays that provide more information per well, or higher-quality data."

HTS and uHTS systems don't differ much in terms of instrumentation. What changes is the trend towards modularity. "Both systems employ a collection of instruments linked by software and robotics," Sheard observes. As assay strategies become more sophisticated and screens more numerous, the number of components increases. uHTS is greatly facilitated, for example, by dedicated compound management systems that store compounds directly in readyto-test plates. At some point, Sheard notes, "It may not be sensible to have a single robot feeding plates to numerous instruments." And all this added functionality necessitates software products that tie everything together seamlessly.

Angelo DePalma holds a Ph.D. in organic chemistry and has worked in the pharmaceutical industry. You can reach him at angelo@adepalma.com.

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ENABLERS OF HIGHTHROUGHPUT ASSAYS by Angelo DePalma

Automated liquid handlers encompass a range of instruments and systems whose function is to dispense liquids rapidly, usually in very small quantities, at user-specified volumes, and with great accuracy, precision, and reproducibility.

Liquid handlers are sold in a variety of fluid-dispensing configurations, single-channel through eight (one row of a 96-well microtiter plate), 96, and 384 channels. As the successors to manual pipettes, automated liquid handlers are the principal enablers of rapid experiments and assays conducted in tubes, vials, or microtiter plates. Liquid handlers are often just one component of systems consisting of microplate handlers, washers, readers, stackers, shakers, and incubators. Automation became necessary as assays were miniaturized from vials to tubes, and finally to microplates, and as researchers switched from radionuclide-based assays to tests that used non-radioactive detection.

Biology, medical testing, and screening of development-stage drugs are the primary markets for automated liquid handling. The energy, environmental, and heavy industries also use liquid handlers when accuracy and reproducibility, but not necessarily high throughput, are desired. "Any time you work with many samples and small quantities of fluids, automating liquid handling with a workstation will provide good return on investment," says

38

Scott Eaton, director of robotics marketing at Hamilton (Reno, NV).

Assessing workflow requirements is essential when selecting an automation system. Liquid transfers take time, which adds up rapidly as dispensing and other operations increase. Users who work with labile or highly toxic samples or reagents may prefer to process a smaller number of plates per run in order to move them rapidly through the protocol.

"Assessing workflow requirements is essential when selecting an automation system."

Another factor to consider, Eaton says, is the effect of physical forces on very small liquid-dispensing volumes used in higher-density plates. "While 96-well plates remain the most common, 384- and even 1,586-well systems that employ sub-microliter volumes are gaining in popularity. At these volumes, evaporation and absorption onto the plastic plate surface become issues."

Automated liquid handlers have evolved from automated pipetting systems to workstations that employ liquid handling as one component, according to Nance Hall, vice president for automation and detection systems at PerkinElmer (Waltham, MA). Today's systems perform washing, incubation, and plate manipulation in addition to dispensing. "In the past, liquid handlers performed just one function; today, they are 'application solutions' in which liquid handling is part of a larger picture," Hall says.

Differentiators

Eaton believes a combination of ease-ofuse and flexibility in software is an important differentiator when selecting an automated liquid handler. "Some software is very easy to use, but it's locked into specific applications." The best of both worlds, he says, is a software package that presents operations graphically, provides "wizards" or templates for routine tasks, and that adapts to different assays.

Hall suggests that potential buyers analyze their liquid-handling needs the way a cook examines a recipe. "What are the 'ingredients'? What labware are we dispensing from and into? What do I expect from the automation component? What volumes are involved, and what sample-tip options are available?" Hall says. "Users who fail to optimize the liquid handler's fluidics design to desired volumes will be forced to compromise either on performance or throughput."

Users should weigh throughput considerations when considering a liquid-handler purchase, says Jason Greene, liquid-handling product manager at BioTek (Winooski, VT). "The cutoff point for automation versus a multi-channel handheld pipette is several strips [rows or columns on a microplate] per day," Greene says.

This seems like a small number of assays to justify the investment in automation, but as Greene notes, liquid handling is just one component of what may be a complex workflow. "Operating manually, users must work through the various reagent additions, incubations, washing, and reading steps," he says. "Nobody likes to wash microplates. It's pretty easy to get users to buy into the idea of automation on that function alone." Moreover, he says, even low-throughput labs come to value the reproducibility of automated systems.

For Nadine Gassner, associate director of the Chemical Screening Center at the University of California-Santa Cruz, experience with a particular vendor is a major factor in selecting a liquid-handling system. The center, which performs high-throughput screening on natural-product and newly synthesized drug candidates, has the capability of testing hundreds of thousands of compounds in one experiment using 96- and 384-well plates.

Gassner had already been using a PerkinElmer plate reader. During the start-up phase of the screening center, she visited the company and was impressed with the ability of its liquid handlers to service a variety of assays. "We were also looking for a strong industry track record and considered our experiences with PerkinElmer's excellent service."

Angelo DePalma holds a Ph.D. in organic chemistry and has worked in the pharmaceutical industry. You can reach him at angelo@adepalma.com.

Automated Liquid Handling

Agilent Technologies	Santa Clara, CA	877-424-4536	www.agilent.com
Apricot Designs	Covina, CA	626-966-3299	www.apricotdesigns.com
Aurora Biomed	Vancouver, BC	604-215-8700	www.aurorabiomed.com
Beckman Coulter	Brea, CA	800-526-3821	www.beckmancoulter.com
BioMicroLab	Concord, CA	925-689-1200	www.biomicrolab.com
Biosero	Monrovia, CA	661-284-6650	www.bioseroinc.com
Biotage	Charlottesville, VA	800-446-4752	www.biotage.com
BioTek Instruments	Winooski, VT	888-451-5171	www.biotek.com
BioTX Automation	Conroe, TX	877-275-2468	www.biotxautomation.com
Caliper Life Sciences	Mountain View, MA	650-623-0700	www.caliperls.com
CETAC	Omaha, NE	800-369-2822	www.cetac.com
Drummond Scientific	Broomall, PA	800-523-7480	www.drummondsci.com
Eppendorf North America	Westbury, NY	800-645-3050	www.eppendorfna.com
Essen Instruments	Ann Arbor, MI	734-769-1600	www.essen-instruments.com
Gilson	Middleton, WI	800-445-7661	www.gilson.com
Hamilton Robotics	Reno, NV	800-648-5950	www.hamiltonrobotics.com
Hudson Robotics	Springfield, NJ	973-376-7400	www.hudsoncontrol.com
Innovadyne Technologies	Rohnert Park, CA	707-588-2000	www.innovadyne.com
Jencons Scientific	Bridgeville, PA	800-846-9959	www.jenconsusa.com
Labcyte	Sunnyvale, CA	877-742-6548	www.labcyte.com
Labnet International	Woodbridge, NJ	888-522-6381	www.labnetlink.com
Molecular Devices	Sunnyvale, CA	800-635-5577	www.moleculardevices.com
PerkinElmer	Waltham, MA	617-225-0400	www.perkinelmer.com
Rainin Instrument Company	Oakland, CA	800-472-4646	www.rainin.com
Staubli	Duncan, SC	864-433-1980	www.staubli.com
TECAN	Durham, NC	800-338-3226	www.tecan-us.com
Thermo Scientific	Hudson, NH	800-345-0206	www.thermo.com/matrix
Tomtec	Hamden, CT	877-866-8323	www.tomtec.com
TriContinent Scientific	Grass Valley, CA	800-937-4738	www.tricontinent.com
Zinsser North America	Northridge, CA	818-341-2906	www.zinsserna.com







New Brunswick Scientific manufactures over two dozen models of biological shakers to suit a wide variety of applications and budgets. Models include open air, incubated or refrigerated systems in benchtop to space-saving stackable styles. Top-of-the-line Innova® Shakers feature our often

imitated but never duplicated Triple-Eccentric Drive for uniform motion and superb reliability. Innova shakers handle heavier workloads, provide precise setpoint control, and are offered with advanced programming capabilities. Optional features include photosynthetic lighting, gassing, humidity monitoring, and UV germicidal lights. Or, select from our economical Excella® Shaker line, featuring microprocessor controls (and one analog controlled model) with counterbalanced drives for accurate control and dependable operation. www.nbsc.com/LMF



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Heidolph products come with a 3 year warranty. Heidolph Brinkmann was formed as our North American headquarters and includes exclusive partnerships for Tuttnauer™ autoclave sterilizers, Radleys™ synthesis solutions, and AirClean™ laboratory ventilation solutions. Our Chicago area office provides National Customer Service, Product Repair, Technical Support, Warehousing, and Field Sales Management. www.heidolph.com



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For over 25 years, Labnet has proudly served the Life Science, Clinical and Industrial Laboratory
Markets. As a leader in Benchtop Shaking Equipment, Labnet has a wide array of models that includes
Vortexers, Orbital Shakers, 3D Mixers, Rockers, Reciprocal Shakers and Rotators. These instruments

incorporate the latest in motor drive and motor control technology for long term reliability and ease of use. Recent additions to the line include the EnduroTM MiniMix and the award winning Revolver Rotator. Contact Labnet's technical support department for help choosing a model that best suits your specific requirements. www.labnetlink.com

LAB SHAKERS are primarily used for culturing organisms in shake flasks or test tubes, and can also be used for mixing liquids. When choosing a Lab Shaker you should consider the type, quantity and size of your flasks and test tubes. Shakers range from small to mid-size benchtop models, larger-capacity console (floor standing) models, or space-saving stackable models. Heavier loads may also require a heavy-duty drive mechanism such as a triple-eccentric drive vs. a lighter-duty single-eccentric drive. Lab shakers are available in two different mixing actions: orbital and reciprocal. The next step in this guide will help you choose which is best for your needs. NOTE: Some manufacturers make a combination reciprocating/orbital shaker. These are shown in only one of the categories, so be sure to check both categories if this is what you are looking for ese are shown in only one of the categories, so be sure to check both categories if this is what you are looking for.

ORBITAL SHAKERS are ideal for culturing cells by imparting gentle to vigorous agitation in a smooth, circular motion, typically in a speed range of 40 to 500 rpm. Many models are offered with built-in temperature control (see incubating/refrigerating shakers at right), while others can be placed directly inside incubators or in cold or warm rooms. Most models can be used with interchangeable platforms to support a range of flasks, tubes, beakers or bottles. Different flasks and/or tubes can be accommodated on the same platform.

DIGITAL ORBITAL SHAKERS have a digital control panel, display and microprocessing unit which offers precise and reproducible management of agitation speed and running time.



















































LAB MANAGER'S INDEPENDENT GUIDE TO PURCHASING A LAB SHAKER, STIRRER OR MIXER

HEATED MAGNETIC LAB STIRRERS consist of a

hot plate and magnetic stirrer in one. They feature adjustments to control both the platform temperature and the mixing speed. These come in single-position or multi-position platform units.

SINGLE POSITION HEATED MAGNETIC LAB STIRRERS will heat and mix one beaker or flask at a time in one position on the platform.

1

There are many different factors to consider when making a lab shaker, stirrer or mixer purchase: Is the equipment going to be used to grow cultures or to mix chemicals and liquids? Is temperature control needed, and if so, do you need incubation only or refrigeration as well? Do you need digital controls to ensure precise and reproducible results, or will analog controls do? This guide wil look at 14 different types of equipment you might purchase to mix, shake or stir in your lab. Let's start by choosing either a shaker, incubating/refrigerating shaker, magnetic stirrer, overhead stirrer or mixer.

RECIPROCAL SHAKERS are typically used for mixing liquids and provide gentle to vigorous agitation in a reciprocal mixing motion that pushes the liquid from one side of the beaker to the other.

DIGITAL RECIPROCAL SHAKERS have an added digital control panel, display and micro-processing unit. With this function they are able to be programmed to operate at various lengths of time and speed settings.





California or





























































INCUBATING/REFRIGERATING SHAKERS should be considered if you require a shaker with temperature control. They can either cool down or heat up the shaking materials as required. A series of small fans inside the shaker's enclosure ensures uniform temperature dispersion. The size will range from a benchtop unit to a floor model as well as a stackable option, which can handle larger capacities in a smaller space. There are several choices of interchangeable platforms to accommodate any combination of lab needs. Different sized flasks and racks can be used on the same platform as well. Some models offer multi-step programming, allowing the user to incubate and/or refrigerate at predetermined time intervals.

DIGITAL INCUBATING/REFRIGERATING SHAKERS have a digital control panel, display and micro-processing unit. With this function they are able to be programmed to operate at various lengths of time and speed settings. For more advanced controls look for models which offer multi-step programming. With this function they can also be programmed, depending on the model, to perform functions ranging from simple programming of start/stop, temperature and speed; or capable of multi-step programs with auto-ramp up/down of speed, temperature and even photosynthetic lighting.















ANALOG RECIPROCAL SHAKERS are adjusted by mechanical dials on the front of the unit and are suitable for many common









































MULTI-POSITION HEATED MAGNETIC LAB STIRRERS will heat and mix multiple beakers or flasks at a time in more than one position on the platform.

MAGNETIC LAB STIRRERS mix liquids by moving a stir bar with a magnet, or series of electromagnets, to create a rotating magnetic field that spins the stir bar immersed in the liquid. Magnetic lab stirrers are available with a heated platform or a non-heated platform.





































OVERHEAD LAB STIRRERS are available in a variety of motor speeds measured in horsepower. If you are purchasing an overhead stirrer for general lab use make sure to invest in one with enough horsepower to mix the largest volume and thickest viscosity you anticipate.

MECHANICAL OVERHEAD STIRRERS often have two o more speed settings based on the viscosity of the materia to be mixed. A wide range of paddles, clamps, tube holder nd stands are available to suit your mixing needs.



ELECTRONIC OVERHEAD STIRRERS are very similar to mechanical overhead stirrers but have an added digital







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DIGITAL VORTEX SHAKING MIXERS have an add digital control panel, display and micro-processing u With this function they are able to be programmed operate at various time lengths and speed settings.























NON-HEATED MAGNETIC LAB STIRRERS do not contain a heating element in the platform. The speed at which they rotate the spin bar is adjustable. These come in single-position or multi-position platform units.

MULTI-POSITION NON-HEATED MAGNETIC LAB STIRRERS will mix multiple beakers or flasks at a time in more than one position on the platform.





























BASIC VORTEX SHAKING MIXERS are adjusted be mechanical dials on the front of the unit and are suitable for many common lab mixing needs.



VORTEX MIXERS are ideal for vigorous agitation from 200 to 3,200 rpm in a vortex mixing motion. On some models the platform can be interchanged to support a single tube for intermittent use or a platform for a range of capped or sealed containers. Most will operate in either touch mode or continuous operation.









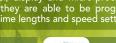
















































ESSENTIAL TOOLS AT MACRO SCALE; AUTOMATION FRIENDLY FOR MINIATURIZED ASSAYS

by Angelo DePalma

Biological shakers are instruments used to agitate a collection of biological samples simultaneously. Shakers consist of a motor attached to a flat surface, with fasteners for securing labware whose contents require mixing. All points on the surface move in the same fashion within the x-y plane, either back and forth (reciprocal shakers) or in a circular motion (orbital shakers).

The principal application of shakers is for growing yeast, bacteria, or mammalian cells in specialized containers known as shaker bottles. Shaking promotes the growth of cells and microorganisms by improving aeration and oxygen transfer and by promoting more efficient mixing of cells with food and nutrients. Biological shakers generally operate at temperatures between ambient and 37°C, but some models offer refrigeration, and high-temperature instruments operate at up to 100°C.

For years, shakers were instrumental in drug development and manufacture. Some important products are still produced in shaker bottles/flasks, as are most small-scale experimental cell cultures and fermentations. Shaker flasks are similar in design to Erlenmeyer flasks but may have a baffled bottom to promote mixing.

Orbital shakers were employed in the development of the antibiotic streptomycin in the 1950s and interferon in the

1980s. Today all new production-scale bioprocesses use much larger bioreactors, but chances are at some point they were first conceived using a shaker.

"Orbital shakers can accept vessels of almost any size or shape, from Erlenmeyer flasks to test tubes and vials, as well as trays for staining and destaining electrophoresis gels," notes Janet O'Bryan, product manager at Thermo Fisher Scientific (Vernon Hills, Ill.)

Differentiators

Biological shakers are distributed by dozens of vendors. Choosing a shaker comes down to such features as heating/cooling capability, capacity, shaking speed, orbital vs. reciprocating motion, ease of use, programmability, heating capability, and footprint. With research budgets tight and lab space even tighter, groups or departments are increasingly sharing shakers. "Customers frequently choose models based on how much space they require. It's highly desirable to be able to stack shakers, pizza oven style, and keep them in a shared equipment room," O'Bryan told Lab Manager Magazine.

Customers also value ease of use—the ability to utilize shakers fully, out of the box, with labware of any shape and size. Labware flexibility is particularly critical for shared instruments.

A start/stop mechanism is a feature

that anyone who uses cotton "stoppers" in Erlenmeyer flasks will appreciate. Shakers that start or stop abruptly will cause fluid to splash up into the cotton, creating opportunities for contamination and loss of material. The soft-start feature is typically found on shakers with digital controls. Users who can tolerate abrupt starts and wish to save money can settle on a less expensive analog shaker.

Microplate shakers

As biology experiments and assays become smaller, vendors must accommodate the need to provide simple manipulations on a micro- or nanoscale that lab workers take for granted in the macro world. One such operation is mixing through agitation. Not all microplate-based assays require shaking, but those that do can use dedicated plate shakers from Thermo Scientific, Orbis, Troemner Henry, ForteBio, VWR Scientific, and others.

In addition to performing simple fluid mixing, microplate shakers facilitate chemical and mechanical cell lysis and the homogenization of inert samples, cells, or cell components; they also help emulsify liquid-liquid and solid-liquid mixtures. An efficient shaker can also reduce the time by half for assays that depend on rapid agitation, for example, detection of biomolecules through the interactions of biotin-labeled proteins

Biological Shakers: Are you using a biological shaker in your lab? Are you considering purchasing a biological shaker soon? Lab Manager Magazine's online surveys help improve the purchasing process and provide you with greater confidence in your final purchasing decision. To take the survey, please visit www.labmanager.com/biological-shakers.

and microscale biosensors coated with streptavidin.

Like their large-scale counterparts, microplate shakers operate at variable, user-specified speeds and employ mechanical agitation—rocking or circular (orbital) movement—to mix components within microplate wells. A typical microplate shaker handles all common plate densities, rotates at up to 1,500 rpm, and accommodates sample volumes of up to 250 microliters.

Most units are small and robust enough to operate inside incubators and cold rooms for assays requiring temperature control.

For reasons of dimension, performance and reliability are somewhat more critical for microplate shakers than for full-scale shakers. Operators can easily determine if the mixing processes are proceeding normally in normal-sized labware. Visualizing on a microliter scale, particularly for high-throughput experiments on densely formatted microtiter plates, is impossible.

Engineering issues also come into play for mixing very small samples. As sample volume decreases, mixing efficiently becomes an engineering problem, as the fluid's low mass causes it to adhere to surfaces, says Sriram Kumaraswamy, Ph.D., product manager at ForteBio (Menlo Park, Calif.).

Plate shakers become the "slow step" in high-throughput workflows unless they are interoperable within a larger microtiter plate-handling environment, which generally includes a microplate handler. Essential integration features include a spring lock to retain the plate against the shaking surface and a robot-friendly lock/unlock mechanism. "Plate shakers, like other components in a microplate-handling system, should be automation-friendly," notes Dr. Kumaraswamv.

Angelo DePalma holds a Ph.D. in organic chemistry and has worked in the pharmaceutical industry. You can reach him at angelo@adepalma.com.

Biological Sh	akers, Stirrer	s and Ove	erhead Stirrers
Bel-Art Products	Pequannock, NJ	800-423-5278	www.belart.com
BioCold	Fenton, MO	636-349-0300	www.biocold.com
Boekel Scientific	Feasterville, PA	800-336-6929	www.boekelsci.com
Caframo	Wiarton, ON	519-534-1080	www.caframo.com
Dragon Medical	Berlin, CT	860-977-3588	www.dragonmedusa.com
Eberbach	Ann Arbor, MI	800-422-2558	www.eberbachlabtools.com
Eppendorf North America	Westbury, NY	800-645-3050	www.eppendorfna.com
ForteBio	Menlo Park, CA	650.322.1360	www.fortebio.com
Grant Instruments	Minotola, NJ	856-697-1257	www.grantsci.com
Heidolph	Elk Grove Village, IL	888-522-0966	www.heidolph.com
IKA Works	Wilmington, NC	800-733-3037	www.ika.net
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Kinematica	Bohemia, NY	631-750-6653	www.www.kinematica-inc.com
Labnet International	Woodbridge, NJ	888-522-6381	www.labnetlink.com
Labnics Equipment	Fremont, CA	925-271-4322	www.labnics.com
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Fremont, CA	925-271-4322	www.labnics.com
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Oxford, CT	203-267-4600	www.proscientific.com
Bohemia, NY	800-368-7178	www.sartorius-stedim.com
Bohemia, NY	888-850-6208	www.scientificindustries.com
East Longmeadow, MA	815-398-6860	www.silverson.com
Greensboro, NC	800-852-0102	www.slscience.com
Asheville, NC	866-984-3766	www.thermo.com
San Marcos, CA	866-573-9104	www.torreypinesscientific.com
Thorofare, NJ	856-686-4204	www.troemner.com
Fort Collins, CO	970-482-2060	www.udyone.com
Santa Clara, CA	800-292-6286	www.yamato-usa.com
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THE "GLUE" THAT BINDS MICROTITER PLATE-BASED ANALYSIS SYSTEMS

by Angelo DePalma

Microtiter plates have become common labware in life science and medicine. Automated systems employing microplates in biological and chemical assays may consist of liquid dispensers, plate washers, mixers, readers, sealers, labelers, shakers, incubators and storage. Tying these components together are microplate handlers, which feature a computer-controlled robotic arm. Once programmed with a specific workflow, microplate handlers move microplates and deliver them to locations on various instruments precisely when they are needed.

but any industry that uses microtiter plates and requires a high degree of automation and reproducibility in assays will also benefit.

"Microplate handler" is a somewhat ambiguous term. Integrated microplate analyzers usually include some mechanism, which may or may not be recognized as robotic, for manipulating plates. True robotic systems are distinguished by their programmability and interoperability with any instrument within physical reach.

Microplate handlers evolved from

"True robotic systems are distinguished by their programmability and interoperability with any instrument within physical reach."

Some handlers include built-in plate stackers. Those that do are usually limited to their original stacking and storage capacity. Users are able to add stacking units to systems without integrated stacking, as they would any other component.

Principal markets for microplate handlers are biology and medicine,

40

bulky industrial robots that were programmed and adapted to hold microplates—a task for which they were clearly not designed. "They were overkill for the weight of a plate," observes Todd Christian, who heads global marketing at Agilent in Palo Alto, Calif. Today's handlers are designed specifically for laboratories

and, with lab space at a premium, optimize the use of vertical space, thereby taking up less room on a benchtop. Pharmaceutical companies interested in eliminating human intervention in high-throughput drug screens were the earliest adopters. Soon biologists recognized that handlers permitted them to automate all aspects of any high-throughput experiment. Today robotics specifically designed for microplate handling are sold as either stand-alone instruments or bundled into a complete system.

Large laboratory equipment vendors may sell stand-alone robotic plate handlers, but most customers prefer purchasing the robotics already integrated with plate readers, stackers, and other instruments. For example, Agilent sells plate handlers by themselves but specializes in delivering complete workflow systems with user-specified components, some of which are sourced from third parties. Customers with dedicated automation groups may prefer to design their own systems from components they select, but they are the exception. "Our key strength is integrating components to meet a pro-

Lab Manager January 2010 labmanager.com

tocol or workflow that is unique to a customer," Christian says. High on the list of specifications are plate capacity, incubators, and specific plate readers. Another is the ability to handle the gamut of microplate formats, up to 1,536-well format, and deep-well and low-profile plates.

Ease of use is a top priority with most purchasers of microplate handling systems. Robots must be "smart" about the space around them, particularly with respect to collision avoidance, and capable of rapidly "learning" precise endpoint positions in three-dimensional space.

Most plate handlers must be "taught" key positions in space by manually moving the arm to the desired location and noting that in the control software. The path to the location does not matter—the robot automatically takes the shortest route. Maneuvering around objects requires creating and storing an intermediate location. Some advanced control software packages allow users to input set points in the software without actually moving the arm.

First-time users approach robotics with a combination of awe and suspicion. "They are especially nervous that the handler will drop the plate or improperly position it," Christian notes.

Moreover, user requirements and expectations of automation differ widely. Many organizations, such as medical testing laboratories, purchase microplate handlers to carry out one or several specific tasks 24 hours a day.

Others, such as academic institutions, expect flexibility, versatility, and programmability, particularly for acquiring new plate readers or workflow changes. These users are better off investing in plate-handling capabilities based on anticipated needs; for example, rapid swapping in of components, particularly readers.

"Robotics specifically designed for microplate handling are sold as either standalone instruments or bundled into a complete system."

Understanding the customer's work-flow—the science behind the ro-

botics—and being willing to source third-party instruments for specific microplate operations are traits that customers seek among vendors of microplate handlers.

"The ability to understand the experiment and to help customers select the right solution based on the right components is highly valued," says Mary Duseau, VP of global sales for molecular medicine at PerkinElmer in Waltham, Mass. She adds that due to the complexity of microplate handling systems and the general lack of experience with robotics, purchasers of the systems require more "handholding" than do those who buy other instruments. "It's important to serve both expert and novice customers," Duseau told *Lab Manager Magazine*.

Angelo DePalma holds a Ph.D. in organic chemistry and has worked in the pharmaceutical industry. You can reach him at angelo@adepalma.com.

Microplate Handlers

Agilent	Santa Clara, CA	877-424-4536	www.agilent.com
Biotage	Charlottesville, VA	800-446-4752	www.biotage.com
BioTek Instruments	Winooski, VT	888-451-5171	www.biotek.com
Caliper Life Sciences	Mountain View, MA	650-623-0700	www.caliperls.com
Molecular Devices	Sunnyvale, CA	800-635-5577	www.moleculardevices.com
PerkinElmer	Waltham, MA	800-762-4000	www.perkinelmer.com
Phenix Research Products	Candler, NC	828-418-1060	www.phenixresearch.com
Staubli	Duncan, SC	864-433-1980	www.staubli.com
Thermo Scientific	Asheville, NC	866-984-3766	www.thermo.com
Tomtec	Hamden, CT	877-866-8323	www.tomtec.com

BURN NOTICE

SOME TIPS AND RULES OF THUMB FOR SAFE STORAGE OF FLAMMABLES IN THE LAB By Vince McLeod

Now that most of us are experiencing the heart of winter, it is an especially good time to review our use and storage of flammable materials in the lab. Why now? Read further to find the answer; hopefully you will pick up some useful information in the process.

"The most common fire hazard in the typical research lab is a flammable liquid or the vapor produced by one."

Flammable substances are those that can easily catch fire and burn in air. They may be solid, liquid or gaseous, but this article will focus on liquids for two reasons. First, according to *Prudent Practices in the Laboratory: Handling and Disposal of Chemicals*, the most common fire hazard in the typical research lab is a flammable liquid or the vapor produced by one. Second, for a majority of laboratories, flammable liquids are the most commonly stored materials and make up the largest volume of hazardous materials.

A quick review of basic fire safety is in order. We are all familiar with the "fire triangle"—the three conditions that must exist

simultaneously for a fire to occur: an oxidizing atmosphere (usually air); a source of ignition; and a concentration of flammable gas or vapor within its flammability limits. If any one of these is absent, a fire cannot occur. Since air is nearly always present, controlling flammable vapors and gases and eliminating potential ignition sources are the best ways to reduce fire hazards. As flammables are used in most laboratories, strict control of all ignition sources is the primary approach to preventing fires.

Important physical concepts of flammable and combustible substances

The National Fire Protection Associa-

tion's (NFPA's) NFPA 30: Flammable and Combustible Liquids Code is an excellent resource and introduction to the hazards of these materials.² Without getting too bogged down in technical details, there are a few concepts that need to be mentioned and understood at the outset. The first is flash point temperature. Flash point temperature is the lowest temperature at which sufficient

vapor is given off

to form an ignit-

able mixture in air. The flammable range is between the upper flammable limit (UFL) and the lower flammable limit (LFL). Flammable limits are expressed in percent volume in air. Concentrations above the UFL are too rich to burn and concentrations below the LFL are too lean to burn. The most dangerous materials are those with the lowest flash point and widest flammable ranges.

The next important concept is the difference between flammable and combustible liquids. Flammable liquids are more dangerous. These are liquids that have flash points below 100°F (37.8°C). Combustible liquids have flash points between 100°F and 200°F (93°C). NFPA 30 further classifies flammables as Class I, and divides them into Class IA, Class IB and Class IC. Class IA and IB both have flash points below 73°F (22.8°C), with IA liquids having boiling points below 100°F and IB liquids having boiling points above 100°F. Materials with flash points between 73°F and 100°F are classified as IC. Combustible materials are classified as Class II, Class IIIA and

Class IIIB, based on flash points as well. Class II materials have flash points between 100°F and 140°F (60°C), Class IIIA between 140°F and 200°F and Class IIIB above 200°F.

The maximum quantity of flammable and combustible materials that can be stored in the lab is set in *NFPA 45: Standard on Fire Protection for Laboratories Using Chemicals* and determines the hazard classification of the laboratory³, as we shall see shortly.

One more thing: NFPA 30 rates the fire hazard of flammable and combustible materials on a scale of 0 to 4, based on flash point. This rating helps you to quickly assess the potential danger of a substance. A 0 is the least hazardous rating; it indicates the material will not burn. A rating of 1 is given to materials with flash points above 200°F; this rating indicates the material needs to be preheated to burn. A 2 rating is for materials with flash points between 100°F and 200°F and indicates that these materials

will ignite with moderate heat. Materials with flash points below 100°F and above 73°F are rated a 3 and will burn at normal temperatures. Flammables with flash points below 73°F are rated a 4 and

Important guidelines for storage of flammable and combustible materials

Now that we understand some basic concepts regarding flammable and combustible liquids, it is time to discuss

"Strict control of all ignition sources is the primary approach to preventing fires."

are extremely flammable and the most dangerous. The fire hazard rating and flash point data are readily available on the container label and material safety data sheets.

Quick, what is the fire hazard rating of a Class II combustible liquid? OK, good work, it is a 2.

proper storage of these hazardous materials. *NFPA 45* is the first reference we turn to, as it provides universal guidelines for safe storage.³ Chapter 4 of *NFPA 45* classifies laboratories into four fire hazard categories, based on the amount of flammable and combustible material in the lab. These are Class A (high fire hazard), Class B (moderate),

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Class C (low) and Class D (minimal). Educational laboratories (high school or through 12th grade) are Class D and are limited to 50 percent of the Class C quantities. Instructional labs are basically college-level undergraduate labs and are limited to Class C or Class D amounts. All others, including graduate, research and development labs, can fall into any of the four classes.

The heart of NFPA 45 is chapter 10 (specifically, table 10.1.1), which lists the maximum quantities of flammable and combustible liquids that can be stored in laboratories. The most lenient in terms of total amount is the highest fire hazard, Class A; it allows up to 10 gallons (38L) of Class I flammable liquid per 100 square feet, or 20 gallons (76L) of Class I, II and III flammable and combustible liquids combined. These quantities can be doubled to 20 gallons of Class I liquid and 40 gallons (150L) of Class I, II and III liquids if safety cans or storage cabinets are used. The total quantities drop to 5 gallons (20L) and 10 gallons for Class B, 2 gallons (7.5L) and 4 gallons (15L) for Class C and one gallon for Class D, with the same doubling rules in effect.

Also addressed in chapter 10 are the maximum capacities for different container types. For example, for Class IA flammable liquids, the largest allowed container is one pint (500ml) for glass, one gallon (4L) for metal and approved plastic or polyethylene, and 2.6 gallons (10L) for safety cans. These maximum capacities are listed for each class of flammable (Class IA, Class IB and Class IC) and combustible (Class II and Class III) liquids. So it is important to maintain awareness of both total quantities and your largest (in terms of size) containers.

Safely storing flammable and combustible liquids in laboratories or stockrooms is risky business. However, by paying attention to the hazard class of the material, the largest container size and the total quantities, we can minimize that risk. In addition, here are some general guidelines for safe flammable and combustible storage:

- Do not store large, heavy containers of liquids on high shelves or in high cabinets. A good rule of thumb is to store them at shoulder level or below.
- Do not store bottles on the floor unless they are in some type of secondary containment.
- Do not store flammable or combustible solvents near heat sources or in direct sunlight.
- **Do** substitute nonflammable materials whenever possible.
- Do post the work area with appropriate signs, e.g., "No Smoking" and "No Open Flames."
- Do store flammable liquids in approved storage cabinets, explosion-proof refrigerators and safety cans.
- **Do** clear the area of all ignition sources.
- **Do** transfer flammable liquids with extreme caution.

A few final words on ignition sources

We mentioned at the beginning the best way to prevent laboratory fires is to control ignition sources. The open-flame Bunsen burner is an obvious one we can easily focus on. But do not overlook the not-soobvious ones, such as refrigerators, stirring motors, electric hot plates, heat guns and microwave ovens. Check all things electrical and anything else that generates heat. For those who want to know, the dry winter air is perfect for generating, you guessed it, static electricity. And when static electricity arcs to the ground, you have an excellent ignition source. This is just one more reason to spend a few minutes going through your lab with this information fresh in mind. We hope this helps avoid any major incidents with flammable and combustible storage. As always, "Safety First" is an excellent motto.

Comments or questions are always welcome. Contact thesafetyguys@labx.com.

Vince McLeod is an American Board of Industrial Hygiene—certified industrial hygienist and the senior industrial hygienist with the University of Florida's Environmental Health and Safety division. He has 22 years of occupational health and safety experience at the University of Florida, and he specializes in conducting exposure assessments and health hazard evaluations for the university's 2,200-plus research laboratories.

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EVOLUTION OF MICROPLATE TECHNOLOGY BY JOHN BUIE

Enter any clinical diagnostic or research lab today and you will see the intricate dance of microplates being filled with samples, transported into various diagnostic and analytical instruments, washed, and then begin the process all over again. The microplate has

1951 — Dr. Gyula Takatsy created the first

microplate by constructing 6 rows of 12 wells

His goal was to increase the throughput and

reliability of influenza virus identification tests

During the same time frame, Dr. Takatsy also

tion tool, a loop that mixed and transferred a

pre-defined volume from one well to another.

This was used in serial dilution testing.

developed the first form of a microplate automa-

needed to address an epidemic in his home

of test tubes.

country of Hungary.

into a block of acrylic, which were used in place

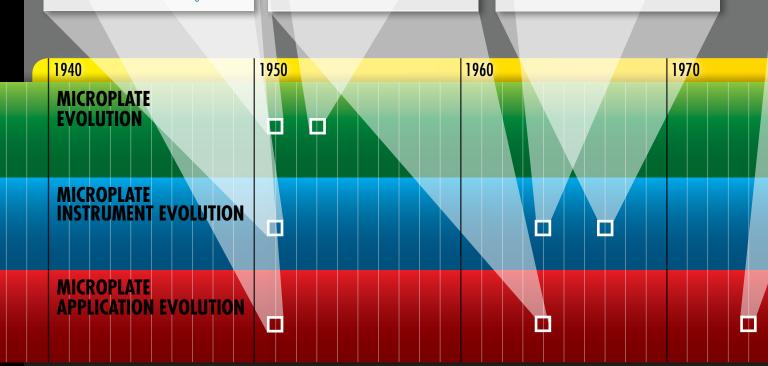
evolved over the past 60 years into an indispensable piece of equipment used in many labs today. This guide will take a look at the evolution of three main areas of microplate technology — instrumentation, applications and the plates themselves.

1953 — The use of microplates caught on enough that the first manufacturer, the American Linbro Company, began mass producing the molded 96-well microplates. This led to a substantial gain in momentum for the platform.

1964 — While working at NIH (National Institutes of Health) Dr. John Sever saw the need to mechanize the loop system being used for serial dilution in order to keep up with the demands of the Rubella vaccine program being launched by NIH.

1964 — Dr. Sever teamed up with Cooke Engineering to begin manufacturing a more automated loop system. With the help of Frank Cooke, they introduced the first manufactured screw machines loops and droppers called the Microtiter[®]. Lab technicians held between 8 and 12 loops in their hands while twirling them and moving them from row to row in a plate. While this was still a manual process, it provided a vast improvement in throughput and accuracy.

1967 — Seeing the need for a fully automated serial dilution instrument, Tom Astle at Astec (now TomTec) produced the Autotiter. After being deployed at Smith Kline & French to perform thousands of Hemagglutination inhibition tests for the trial of their Rubella vaccine, the Autotiter earned its stripes and became a popular instrument in the clinical lab.



1974 — Perhaps one of the most common applications for microplates started to take form when the Centers for Disease Control (CDC) in London began using microplates for ELISA (Enzyme-Linked Immunosorbent Assay) diagnostics and quality control techniques.

1976 - The demand for advanced instruments to perform ELISAs prompted the manufacturer Lab Systems, now part of Thermo Fisher Scientific, to evolve the early microplate readers into the Multiskan photometer. This is the earliest version of the common day microplate reader.

1986 - Wallac (now PerkinElmer) developed the first automated microplatebased instrument for scintillation counting, the Wallac Betaplate.

1990 - Tom Astle at TomTec continued to drive innovation and meet the needs of drug discovery labs by adding harvesting and automated pipetting functionality to the popular Wallac Betaplate. This resulted in the production of the Harvestor2 and Quadra 3 automated pipettors.

1991 - Helix Diagnostics, now Bio-Rad, produced the first 864-well microplate. This made it possible for a single machine to increase its throughput to over 10,000 samples per day.

1992 — Continuing advancements in various sized microplates to find the right combination of thermal mass and capacity, led to Genetix producing the first 384-well plate.

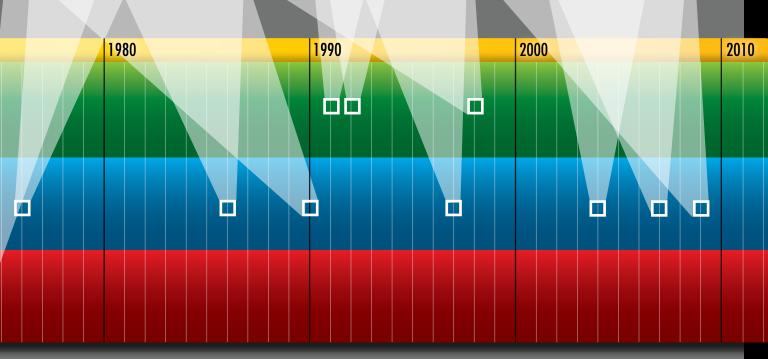
1997 - BMG LABTECH, which has a continued history of firsts in microplate technology, introduced the first multi-detection microplate reader that included fluorescence polarization with the BMG POLARstar.

1998 - One of the most important evolutions of the microplate was led by the SBS (Society for Bimolecular Screening) and a key group of manufacturers who set out to establish standards that all microplates would meet going forward. The standardization led to an increased ability to develop automation equipment to move, sort and wash plates in future instruments. All microplate manufacturers at this time modified their production equipment to the exact specifications of the new microplate standards.

2004 — With BioTek's introduction of the Synergy™ 4 with Hybrid Technology, scientists had a multi-detection system capable of performing an unlimited number of microplatebased assays.

2007 – BMG LABTECH evolved its offering to the POLARstar Omega, delivering the first multi-detection microplate reader on the market with UV/VIS Spectrometer absorbance.

2009 - BioTek continues to evolve microplate automation with the release of the EL406, which combines both a microplate washer and reagent dispenser in one instrument, eliminating the need to maintain and purchase separate instruments.



THE ECONOMIC REALITIES OF LAB AUTOMATION

SUCCESSFUL IMPLEMENTATION WILL RELY ON STANDARDS DEVELOPMENT, EDUCATION, AND CAREFUL PLANNING by Joe Liscouski

Budgets are tightening and expenses are being carefully watched. Is laboratory automation a realistic way to increase productivity under those constraints?

Take a look around your laboratory. Now imagine it without any automated equipment. What would your productivity be like in a facility where all the work was done manually, without the benefits of any automation?

- The recording spectrophotometer is an example of automation. The non-automated process requires manually selecting the wavelength, reading dark currents, reading the intensity with and without the sample present, and repeating as needed.
- The strip chart on your chromatograph is an automated recording of detector output, as is the data system that captures and processes analytical data. How productive would your lab be if peak parameters were measured by hand from charts?
- No hyphenated techniques, liquid-handling systems, high-throughput screening, microplate-based assay techniques, or automated sample preparation would be available without automation.
- Your lab would be back to double-pan balances for weighing. There is a long list of automated equipment that we take for granted.
- What samples need to be worked on? ... Flip through the sample log book.

The introduction of automated instrumentation, equipment, and software has had a major impact on a lab's ability to carry out work, whether in an analytical testing lab, a materials lab, or a lab focused on primary research. Automation in the form of Web applications has sped up the process of placing orders, searching, finding products and contact information, and so on. We really wouldn't want to go back to ordering products by phone with endless phone menus and holding.

Automated equipment has provided a significant economic benefit to lab operations, but many of us have just scratched the surface. The real benefits, both economic and functional, will come when we change our thinking about how to plan for, choose, and apply the technologies. Interest in the topic is increasing. A 2008 survey¹ shows that automation is part of the lab's future planning: 88 percent of those surveyed said that they would be more reliant on lab automation in the future and 12 percent planned on staying at the same level of automation.

The reasons are demonstrated by two questions, one from the survey noted above, and the second from the 2006 survey.²

From the 2006 survey: What reasons do people give for their interest in lab automation?

Reason Rating	(0-5, 5 is high)
Increased Productivity	4.7
Improved Data Quality	3.8
Reduced Operating Cost	3.5
Improved Safety	2.4
Improved Working Conditions	2.8

The 2008 survey looked at the factors driving labs to consider automation technologies.

% Reporting Factor's Importance As: Decreasing Factor Increasing Workload 90 Staff 45 12 7 Budget 38 Outsourcing 5 14 Complex Science 50

In addition, the 2008 survey found that 74 percent of those responding wanted to use lab automation to streamline operations, and 71 percent wanted to add new capabilities. If you change "Improve Data Quality" to "Improve Product Quality" (in many labs, the data and information produced is part of the product), you'll find yourself with a set of management pressures and re-

Lab Manager January 2010

quirements that are common to any production facility. And in many cases, automation is a practical means of meeting those demands. But does it work in laboratories? One good example shows it can work.

"The introduction of automated instrumentation, equipment, and software has had a major impact on a lab's ability to carry out work."

Clinical laboratories have a lot in common with testing and analytical labs in other industries. Samples are submitted, tests are scheduled, the analysis is performed and the results are reported. There are three major differences. The first is that their samples are drawn from us in the form of fluids, tissues, etc., that are evaluated according to standardized methods. Secondly, their charge rates are set by contract or the federal government and they have to operate within that limit. The third point we get to later. The response of clinical labs to increasing sample loads with a fixed cost structure—not dissimilar from the points noted above—was to automate their protocols. The results are impressive.³ The following bullets are quoted from the article's abstract:

- Between 1965 and 2000, the Consumer Price Index increased by a factor of 5.5 in the United States.
- During the same 36 years, at our institution's chemistry department [Mt. Sinai Medical Center], the productivity (indicated as the number of reported test results/employee/year) increased from 10,600 to 104,558 (9.3-fold).
- When expressed in constant 1965 dollars, the total cost per test decreased from \$0.79 to \$0.15.

Another report,⁴ from The Ohio State University, gave an overall productivity labor increase of 26 percent with an increase of 72 percent in the number of specimens processed per Full Time Equivalent Person. These improvements are due in large measure to an industry shift to the concept of "Total Laboratory Automation." An article⁶ by George Streitberg discusses the impact that the concept has had at the Monash Medical Centre in Melbourne, Australia. The article covers the technology, changes in personnel duties, training, etc. *The bottom line is this: Properly done, automation works in the laboratory environment.*

"Properly done" is the key element. In the clinical lab-

oratory industry the needed work was done to establish a framework for communication that allowed systems, including instrument-data-to-laboratory-information systems, to exchange information. That standard "glue" holds things together and makes them work; that is the third key difference between the clinical lab environment and the environments we commonly encounter in analytical, testing, pharmaceutical, biotech, materials characterization, and other labs.

If you'd like more evidence, look at the ease of microplate-based assays. Samples are processed and read using a variety of devices from a mix of vendors that work on a standardized sample format.

And for the rest of us...

For those not working in a clinical lab setting, how does this apply? The work on clinical laboratory and hospital information standards goes back to 1987 with the initiation of the HL7 program (www.HL7.org), which continues its work today. In addition, three ASTM standards were designed for clinical laboratories:

"The real benefits [of lab automation]...will come when we change our thinking about how to plan for, choose, and apply the technologies."

- ASTM E1238 Standard Specification for Transferring Clinical Observations Between Independent Computer Systems
- ASTM E1381 Specification for Low-Level Protocol to Transfer Messages Between Clinical Laboratory Instruments and Computer Systems
- ASTM E1394 Standard Specification for Transferring Information Between Clinical Instruments and Computer Systems

These ASTM standards provided the initial basis for standardizing instrument-to-LIS communication." (Note: Clinical people use LIS where industrial people use LIMS.) The successful implementation of lab automation in clinical labs provides a model for what could be done in your lab (the ASTM 1394 standard carries the note that it "does not necessarily apply to general analytical instruments in an industrial analytical or R&D setting.") These ASTM standards have been replaced with work by the Clinical Standards and

Laboratory Institute (CSLI - www.clsi.org) in the form of the "Laboratory Automation: Communications with Automated Clinical Laboratory Systems, Instruments, Devices, and Information Systems" electronic document. This approved standard is in its second edition. From this author's point of view, the structure of the standards is an appropriate model, although the specific language and terminology will differ.

"The successful implementation of lab automation in clinical labs provides a model for what could be done in your lab."

Three issues have to be addressed:

- · Standards development
- Education
- · Planning for automation

Standards Development

First we'll look at the long-term consideration of standards development. The need for standards is addressed along with several other points in the web article "Integration in Laboratory Automation & Informatics." If we are going to bring the maturity to lab automation necessary to allow products to exchange information without the need for custom coding, we have to move toward standards, and we must do so rapidly. Since the operational structure of clinical labs is similar to those of other testing and analytical labs, it may be possible to jump-start a standards development program by building on the HL7 and ASTM / CSLI work; this should be explored, and those interested in pursuing this should contact the author. Consider the following quote: "These individuals also believed that the total market for automation systems and equipment would be significantly greater with standards than without standards, especially if customers were not forced to purchase everything from one vendor, and that there might be competitive pricing and new technology fostered via the standards."8 Sound like something you might believe? That was part of the rationale for developing the data interchange standards at the lab level for the HL7 program, which includes the same instruments as LIMS, and LIMS to management databases [note: the ASTM standards noted above are frequently referenced as a data interchange

methodology]. Developing a similar standards program would dramatically improve the economics of lab automation. This isn't wishful thinking—it has been done successfully in one significant area of work.

The alternative is to continue developing programs that may forge a connection between an instrument or data system and a LIMS or Electronic Laboratory Notebook (ELN) that works, possibly at considerable expense, but ties you not only to a specific product but to a specific version of that product as well, since upgrades may obviate that work and require that it be re-implemented. While the idea of instrument-to-LIMS/ELN communication is nice, doing it outside the facilities provided by the vendor (vendor-supported instrument interfaces) is both risky, in terms of project failure, and expensive.

Education

Education is a major differentiator between successful lab automation programs and those that fail. Education includes user-level material (working with lab automation systems, what does a LIMS/ELN do, etc.) as well as management-level material that looks at how to plan for automation, implementation considerations (including project management), product life cycle management and its impact, regulatory issues, and so on.

The cost of projects can be severely impacted by failing to fully understand the ramifications of decisions such as linking instruments to LIMS/ELNs outside the capabilities provided by the vendor, by not properly defining the scope of a project or missing key requirements, and by not fully evaluating the range of technology options. For example, in the LIMS/ELN environment, implementations can be the traditional system on site or perhaps the increasingly popular software-as-aservice model in which the application is run on external equipment. Both implementations are viable options, but corporate considerations may make one more appropriate than the other.

If we use the clinical environment as a potential model for what an automated lab can be, then we need to look at how it changed the nature of lab work, and how that change could be reflected in your lab. Much of laboratory work consists of carrying out tests and experiments. In a fully automated lab—including a research lab—much of that effort will be done by systems. We can see elements of this today in fully automated microplate-based assays. The tasks will change from manually conducting the work to planning work to be done, making sure

systems are performing properly, doing data analysis, and doing what laboratory people do best: thinking, developing, and being innovative. This was the promise held out all along by lab-automation advocates.

An investment in education will pay for itself many times over in more-effective lab personnel, betterplanned programs, improvements in lab operations, and better science.

Planning for Automation

There are several ways of approaching lab automation. One is the gradual introduction of automated equipment into the lab, replacing manual tasks, such as liquid handling, with more-efficient automated components. This equipment can speed up aspects of lab work, but people still make the process work.

Another is to make a commitment to automation and reevaluate the procedures you are using: Are they suitable for automation? Are there steps in the procedure that, due to materials handling or the nature of the processing, prevent the use of automation, and if so, are there alternative methods that may lend themselves to automated systems? Within your industry, is it possible for several companies to evaluate and standardize procedures for automation (this is a role that ASTM fills for some applications)? This latter point is one of the elements that has led to automation successes in the clinical lab and can guide your own developments.

Laboratory economics is not just about saving money. It is about the efficient and effective use of resources, especially those working in the lab.

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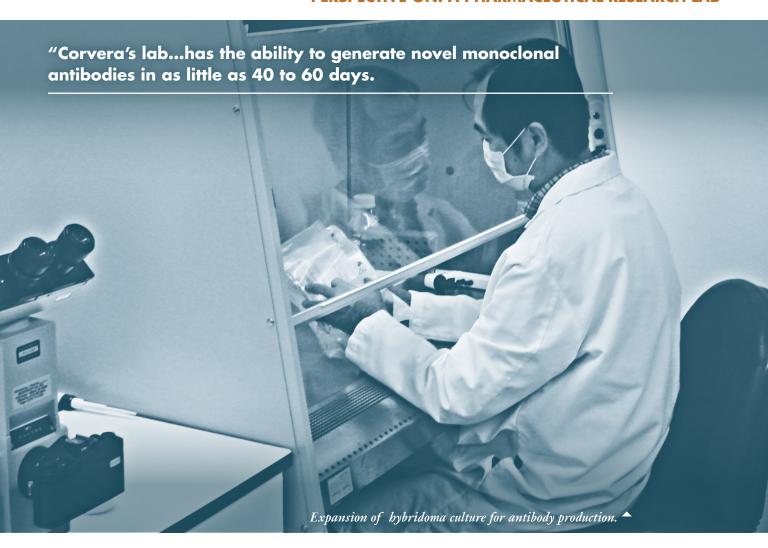
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FOR LAB MANAGER JOE CORVERA, TEAMWORK IS KEY TO REACHING BOTH COMPANY AND CLIENT GOALS by Sara Goudarzi

Lab Manager January 2010 labmanager.com

52



hen foreign objectssuch as viruses, fungi, parasites, and bacteria-attack our bodies, gamma globulin proteins in our blood and other fluids identify and neutralize these invaders. These antibodies are the immune system's strongest line of defense. For this reason, many researchers and pharmaceutical companies are interested in developing antibodies in the laboratory. For example, in cancer therapy, engineered antibodies mimic the natural antibodies the body produces and are directed to mark specific parts of cells that the immune system needs to detect and destroy.

Precision Antibody, a wholly owned service division of A&G Pharma-

ceutical, Inc., is a contract antibody development company located in Columbia, Md., that engineers thousands of novel, customized antibodies for pharmaceutical and biotechnology companies as well as for federal and academic research laboratories.

"Our division is responsible for the development of monoclonal antibodies that can be used for basic research, for diagnostics, and in some cases as a basis for early-stage therapeutic candidate development," says Joe Corvera, the lab director of Precision Antibody. "The division uses our proprietary technology as a means to develop tailored immunoreagents for our company's research as well as rare immunoreagents for our clients' research programs.

"Some of the antibodies we have

developed throughout the years have targeted cancer-specific biomarkers, disease-specific antigens, transmembrane receptors, small molecules, epitopes targeting single amino acid substitutions or modifications, neoepitopes from cleavage sites, phosphorylation site-specific epitopes, methylation sites, and anti-idiotypic antibodies for pharmakinetic studies," he adds.

Corvera's lab rapidly and successfully produces antibodies against various antigen types—antigens being foreign substances that promote the generation of antibodies—and targets, and has the ability to generate novel monoclonal antibodies in as little as 40 to 60 days. Monoclonal antibodies are those that are identical because they are produced by one



← GE AKTA purification system for purification of antibodies and proteins.

type of immune cell and are therefore clones of one parent cell.

"Our team has developed custom monoclonal antibodies to targets including parasites, cancer-specific surface antigens, GPCRs, hormones, growth factors and their receptors, glycoproteins, peptides, proteins and their modification sites (mutation site specific, phosphorylation site specific, cleavage site specific, single amino acid substitution/modification, etc.), and other antigens such as smallmolecule compounds and DNA," Corvera explains.

provides comprehensive mammalian cell banking services to generate and store cell-bank lots for its clients' research programs.

Structure and clientele

With a staff of 20, Precision Antibody completes hundreds of projects each year in an 8,000-square-foot laboratory. Corvera, whose background is in immunology, manages a team of nine. The team members specialize in immunology, cell culture, protein purification, molecular biology, and biochemistry, and serve clients ranging from large pharmaceutical and biotechnology companies to federal research and academic laboratories.

"We have several contracts with pharmaceutical companies for antibody development and production," Corvera explains. "We teamed as a subcontractor with a large research company under a prime National Institutes of Health contract to provide antibody development and production, and assay support services for a

"We have been able to provide antibodies that many of our clients have not been able to generate internally."

The capabilities of Corvera and his team also include mouse polyclonal antibody development, antibody production and purification, affinity determination, and mammalian cell banking.

"Our polyclonal antibodies have a titer range of 1:10,000 to 1:50,000. This service can be useful in prioritizing potential targets and for initial immunoassay development," Corvera says. "We offer an array of other antibody characterization services as well [and] are capable of small-scale as well as bulk production of antibodies."

Additionally, Precision Antibody

malaria vaccine program. The agreement was renewed and extended for seven more years in 2007."

Precision Antibody was also recently selected as an antibody developer for a component of the National Cancer Institute's Clinical Proteomic Technologies for Cancer (CPTC)—focused on improving the number and standardizing the quality of monoclonal antibody reagents available for clinical cancer proteomics research.

"The contract award is the result of a third solicitation for contract proposals from custom antibody suppliers as part of the Clinical Proteomic Reagents Resources component of the CPTC, whose mission is to develop high-quality, standardized, renewable reagents that are needed for effective proteomic analysis," Corvera explains.

To keep up with all these contracts and the high volume of work, Corvera and his colleagues have automated several steps of their processes—such as completing various immunoassays, culturing and screening large numbers of hybridoma cell lines, and producing and purifying the final product—to increase throughput.

Some of the instruments they use most are automated plate wash-



← Cell culturing of hybridoma clones targeting specific antigens.

ers (Molecular Devices, Beckman Coulter), spectrophotometers (Bio-Rad, Molecular Devices), plate readers (colorimetric, luminescence, fluorescence; Molecular Devices, Anthos), GE AKTA Primeplus for purification, and HPLC systems for low-pressure affinity chromatography.

Inventory, maintenance, and hiring

Each week, Corvera and his staff go through their supplies and take inventory using a list of commonly ordered supplies for which they maintain a predetermined stock. The

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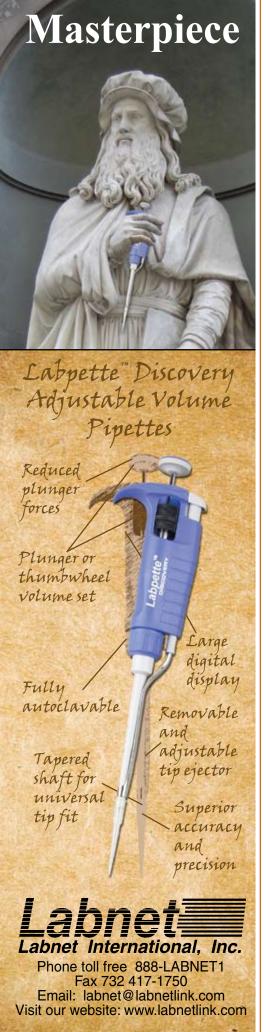


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purchasing agent will then place the orders accordingly. Specific items that are not purchased regularly can be requested on an as-needed basis. Additionally, there is a list of critical reagents whose inventory is checked by an individual designated for this task. These items are ordered through specific prescreened vendors whose products Corvera's team uses regularly.

"Each week our group meets to discuss general information regarding projects, inventory, shipments, future projects, and general billing [and]

accounts payable issues," Corvera explains. "If necessary, we'll discuss other work-related items such as training and safety."

Maintenance on lab equipment is dependent entirely on each case. With major equipment, the company has

scheduled preventive maintenance. Typically, those contracts run on an annual or semiannual basis. For smaller items and regularly used items, the staff takes care of the upkeep and repairs in-house.

The staff manages the workload quite well. However, if an employee leaves or if the team is looking for another member to join them, Corvera and other company managers will start to look for suitable fits.

"The interviewing process will include Jun Hayashi—vice president of Precision Antibody—and me, as well as at least one other person in a management role," Corvera says. "Typically, the initial interview is

a phone interview. The next step would be an interview at the facility to discuss the position and the candidate's qualifications, in person and in more detail." This allows the individual to see the facility, meet the staff, and see if the position is a right fit for him or her.

Management roles and challenges

As manager, Corvera has responsibilities that revolve around making sure each of the working jobs is on the right track and the staff has

the required resources to complete the work. Additionally, he is responsible for maintaining contact with new and current clients concerning their projects.



sues with individual projects to broad strategies for collaborations with clients," Corvera explains.

Each project the lab faces is unique. This fact, while one of the most exciting parts of the job for Corvera and his colleagues, is also a challenge. For this reason, careful strategic planning, coupled with years of experience and dedication from his staff, is necessary to execute the work with precision and deliver projects on time.

"We have been able to provide antibodies that many of our clients have not been able to generate internally, so we accept projects that we know are very difficult," Corvera explains.



▲ BioRad Spectrophotometer for protein & DNA quantitation, Beckman Coulter and Molecular Devices 96-well plate washers.

PERSPECTIVE ON: A PHARMACEUTICAL RESEARCH LAB

"We have a talented and dedicated group of researchers who work very diligently and relentlessly to tackle each new challenge."

"Each year we redefine and stretch our abilities. This keeps the work dynamic but also very challenging," he adds. "A significant challenge is keeping a balance of completing gspecific goals, planning for future growth, and bridging the gap in between."

Because the goals themselves are dynamic, Corvera believes that it is important to be able to show flexibility. "The path is never as straight as you would like it to be. I think all labs face these types of challenges on small and large scales," he says.

Although the dynamic goals make work life challenging for Corvera and his colleagues, it's precisely the freshness of each day and each job that the team looks forward to.

"My role allows me to see various perspectives of the industry," Corvera says. "The spectrum of the work is wide, so each day brings something new. There is always something to look forward to. As is the case for all pharmaceutical researchers and managers, there are a lot of challenges; but our job is to determine how to face and resolve them."

Synergy and teamwork

Teamwork is an essential part of reaching the goals of the company and its clients. To achieve this, Corvera depends on everyone on his team to complete projects. The work needs to be well coordinated from the initial idea through the delivery of the final product, and each individual's contribution is critical to the success of each project.

"It is critical to everything we do that

we are able to work together," Corvera says. "Although everyone has his own individual responsibilities, we are interdependent. With large projects, we work together to manage the workload. Without everyone's effort and cooperation, we would not see the same level of success."

"The spectrum of the work is wide, so each day brings something new."

There is also a level of trust amongst Corvera's workers and colleagues that allows them to lean on each other when a large and challenging project comes their way.

"We'll discuss many things as a group, sharing opinions and perspectives, but this is based on comprehensive individual training," he says. "Our group has a good foundation from the training we provide."

The requirement for teamwork extends to the company's clients as well, since the customer needs to be able to clearly communicate his or her specific goals and essentially be able to work with the researchers.

"It is crucial to define the goals to very specific details in order to reach an end that will be acceptable and applicable," Corvera says.

In order to provide a friendly environment and an atmosphere of cohesiveness within the company, Corvera and the rest of management plan company events for the employees.

"We have an end-of-the-year holiday party and a lunch party for our company birthday, and we also celebrate



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when we reach certain milestones," he says. "The end-of-the-year party is a time to get together and discuss our achievements and our goals for the upcoming year, as well as just relax and enjoy time with coworkers."

Corvera also likes to update everyone on the progress of each project on a weekly basis. This gives the team a chance to share success stories, and Corvera ensures that everyone knows that their hard work and dedication are appreciated.

"On a personal level, since we are a smaller company, I can meet with everyone in my group at least twice a year to discuss how they are doing, and to discuss their goals as well as the goals of our group and the company," he says. "Good communication within our own group as well as with our clients benefits everyone. We strive to maintain good communication."

Contribution

Although the overall contributions of Precision Antibody will benefit human health, the role of every project is specific and targeted, with each one aimed at a unique medical application.

"We hope in the end that it will have a large impact in the scientific community and the community at large," Corvera says. "On an academic level, we can provide antibodies to study novel targets for research in new fields. In pharmaceutical research, we can provide antibodies as diagnostic tools, as control reagents, and as validation antibodies, and in some cases as an early stage antibody candidate that can be modified downstream for development in a therapeutic antibody program."

"The work will hopefully impact individual lives downstream based on the products and programs the work supports," he adds.

Sara Goudarzi is a freelance writer based in New York City. Her Web site is www.saragoudarzi.com.

All photos courtesy of Precision AntibodyTM





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For more information, visit www.ssi.shimadzu.com. Mark Taylor, GC product manager, can be reached at cmtaylor@shimadzu.com, or by phone at 800-477-1227 x.1896.

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HOW IT WORKS O

TRANSFECTING B-CELL LYMPHOMAS WITH siRNA

Problem: Using small interfering RNAs (siRNAs) to exploit the mechanism of RNA interference (RNAi) has become a powerful tool to study gene function in cell culture and *in vivo*. These small RNA molecules are designed to target the mRNA with a complementary sequence in order to achieve degradation. Chemically synthesized 21-nucleotide siRNAs have been shown to induce RNA interference in mammalian cells. This can be useful in suppressing cancer cells like B-cell lymphomas, which are cancers derived from lymphocytes and constitute 85% of all non-Hodgkin's lymphomas. For reasons that remain unknown, transfecting B-cell lymphomas has not been achieved with traditional techniques using lipids, chemicals and viruses. Progress has been made with electroporation, but this process results in a high rate of cell death.

Solution: Jessica Alluin, a Research Associate in the Department of Molecular Biology at The City of Hope, used Bio-Rad's Gene Pulser MXcell electroporation system to successfully transfect two cell lines of B-cell lymphomas with siRNA against the HPRT1 gene. The Gene Pulser MXcell electroporation system is designed to ensure highly efficient delivery of molecules such as siRNA into a variety of mammalian cells, including primary and difficult-to-transfect cells.

Critical to the success of any electroporation experiment is the ability to optimize experimental conditions. This leads to increased transfection efficiency while maintaining cell viability and the need for less precious sample. Unlike other electroporation systems, every critical parameter is programmable with Bio-Rad's Gene Pulser, from waveform to number of pulses, enabling researchers to easily find the ideal set of conditions for their specific cells. Alluin appreciated the Gene Pulser's distinctive ability to vary and test multiple electroporation conditions on one plate, fine tuning for both transfection efficiency and cell viability.

Specifically, she suspended B-cell lymphoma cell lines JEKO-1 and

SUDHL-6 cells in Gene Pulser electroporation buffer and divided into sets of two: one control and one experimental. Each set consisted of buffer and cells whereas the experimental tube had the addition of HPRT1 synthetic siRNA to determine RNAi knockdown. Each set was

and SUDHI

↑ The Gene Pulser MXcell electroporation system delivers molecules efficiently into mammalian cells—especially into primary and difficult-to-transfect cells—in a multi-well plate or in a cuvette."

separated into the wells of a 24-well electroporation plate and electroporated with the Gene Pulser MXcell system using a resistance of $1,000\Omega$, varying the waveform, voltage, capacitance or duration and number of pulses to determine the optimal condition for each cell type. The electroporated cells were transferred

into a 6-well plate and incubated at 37°C.

At 48 hours post-transfection, aliquots were taken from each set of transfected cells to determine cell viability under a microscope. Cells with a viability of 50% or greater were processed to determine HPRT1 mRNA expression levels and therefore the transfection efficiency. The Gene Pulser MXcell electroporation system proved to be effective in transfecting B-cell lymphomas once the conditions resulting in minimal cell death were identified. Electroporation conditions 16 and 9 demonstrated the best siRNA delivery methods in JEKO-1 and SUDHL-6, respectively, with

minimal cell death.

A comprehensive set of electroporation protocols for mammalian cell lines submitted by scientists worldwide is available through Bio-Rad's website at www.bio-rad.com/transfection-protocols.



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HOW IT WORKS O

NUCLEIC ACID CONTAMINATION SOLVED WITH EXITUSPLUS™ TECHNOLOGY

Problem 1. Incomplete degradation of DNA: Advanced experiments in gene technology demonstrate that even small amounts of free DNA molecules are sufficient to cause infections, recombination or biological transformation. The complete decontamination of equipment and surfaces from DNA molecules is important for biological containment and safety, as well as preventing artifacts in PCR amplification experiments. Commercially available DNA decontamination reagents DO NOT destroy DNA molecules efficiently, despite their corrosive or even toxic properties.

Problem 2. Corrosion: Elimination of nucleic acids depends on the use of corrosive and toxic substances that cause irreversible damage on surfaces of costly equipment.

Problem 3. Autoclaving does NOT fully destroy nucleic acids: PCR analysis demonstrates that even after autoclaving, larger DNA fragments can be identified, especially when nucleic acids are protected by protein envelopes (e.g. viruses) or within microorganism cell walls (e.g. bacteria). Nucleic acids from viruses and bacteria are not properly inactivated by simply autoclaving.

Solution 1: DNA-ExitusPlusTM uses a unique nucleic acid decontamination technology, based on chemical rather than enzymatic activity. Therefore, its effects on fragmentation are totally independent of the size and sequence of the DNA fragments.

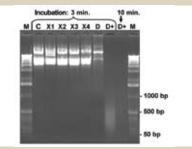
PCR analysis shows that, after treatment with DNA-ExitusPlus™, no amplifiable DNA templates are present, proving there was a highly efficient degradation of DNA molecules. Only by using PCR analysis in combination with a sensitive DNA degradation test can one be sure that the DNA is NOT merely modified or masked.

Spraying DNA-ExitusPlusTM on lab surfaces will ensure complete decontamination. Moreover, the reaction time for DNA-ExitusPlusTM corresponds to the drying time after spraying on a surface (10 - 20 minutes).

Solution 2. DNA-ExitusPlusTM shows no metal corrosion, when compared to conventional decontaminants. DNA-ExitusPlusTM therefore offers a gentle and environmentally safe alternative that degrades and removes all DNA molecules with high efficiency without being toxic nor corrosive.

Solution 3. Autoclave-ExitusPlusTM, an ExitusPlusTM-based powder mixture,

66

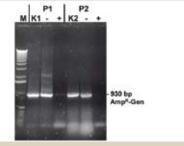


200 ng of CCC plasmid DNA each, were treated with 5 μ l of the indicated reagent for 3 min and 10 min respectively. C = control (treated with water); M = Molecular weight marker; X1, X2, X3, X4 = competitors' products; D = conventional DNA-Exitus TM ; D + DNAExitusPlus TM . For a complete protocol of the experiment please see our brochure: "Contaminations by Nucleic Acids: Problems & Practical Solutions".

can be used as an additive for the decontamination of liquid waste. Due to its chemical composition, Autoclave-ExitusPlusTM is not heat-sensitive and does not contain volatile or harmful ingredients.

Autoclave-ExitusPlusTM leads to an efficient degradation of bacterial DNA, while under standard autoclave conditions, there is always undegraded/partially degraded DNA.

Summary: Only PCR analysis in combination with DNA degradation assays show the true decontamination potential of a reagent. In addition, the use of autoclaving to eliminate DNA from microorganisms requires Autoclave-ExitusPlus™ for complete removal of viral and bacterial nucleic acids.



▲ Figure 2. Analysis of E. coli cultures by PCR, after autoclaving with Autoclave-ExitusPlus.

Recombinant E. coli cultures containing a plasmid with the ampicillin resistance gene (AmpR-Gene) were used. Aliquots (2 µl) of the cultures were analyzed by PCR for the presence of the complete AmpR gene. (-) = E. coli plus water; (+) E. coli plus Autoclave-ExitusPlus™; (K) = E. coli plus Autoclave-ExitusPlus™ plus 2 ng template for the AmpR gene (positive control to prove that PCR is working); (M) molecular weight marker.

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HOW IT WORKS O

USING CRYOGENIC LIQUID ARGON DEWARS COST-EFFECTIVELY

Problem: To reduce operational costs in today's unstable economy, a lab or facility manager with a new ICP/Mass Spec system must cost-effectively use cryogenic liquid argon dewars to supply gaseous argon.

When it comes to specific critical gases requirements, one attractive option is the use of cryogenic liquid cylinders, commonly called dewars, to supply gaseous argon to ICP and ICP/Mass Specs. Argon's unit cost per cubic foot/gaseous liter is much lower when delivered to your facility in cryogenic liquid form in dewars. However, since these containers store the gas in a cryogenic form until it is dispensed as a gas, there are two issues that can decrease the cost-effectiveness of using this mode of supply.

Since the argon is stored in self-pressurizing containers with relief valves and the cryogenic liquid is boiling inside, reserve containers waiting for the primary container to empty on a system will, over time, build internal pressure until the relief valve setting is reached and then begin to vent excess gas at a rate of 2 to 3 percent per day. This is the NER or Normal Evaporation Rate, referred to in the industry as the "use it or lose it" phenomenon. At this rate, if the reserve cylinder of argon contains 4,500 cubic feet of gas, it equals losing 135 cubic feet every day it sits in reserve. It wouldn't take long to eat up whatever savings resulted from the lower unit cost.

Since most of the gas is in cryogenic form, the pressure in the container does not indicate if the unit is full, half full or empty. The small liquid level indicators on top of the dewars are hard to read and not very accurate. Since most gas distribution systems rely solely on pressure to change from primary to reserve cylinders, false low-pressure readings can cause lab personnel to remove containers with as much as 25 percent of the contents still inside.

Solution: CONCOA's Intelligent Gas Distribution System IntelliSwitch II continuously monitors your reserve container's pressure, using programmed software logic to determine if a container is truly empty or contains residual product. IntelliSwitch II 538 Series is the latest in the line of computer-controlled gas distribution switchover systems using very accurate transducers to monitor both primary and reserve inlet pressures. Proprietary software logic uses this information to drastically reduce evaporation loss by switching to the reserve dewar to supply the gas to the instrument before the relief valve opens, drawing down pressure in the container to a programmed point, and then returning to the primary dewar. This



"economizer function" can virtually eliminate losses in the reserve dewar.

Additionally, when primary dewar pressure drops below the point at which the system switches to the reserve, IntelliSwitch II does not immediately conclude that the container is empty. It waits a programmable amount of time and while supplying the system from the reserve, watches the pressure reading on the primary. If the pressure rises above the switchover point in that time period, the computer concludes residual liquid was left in the container and switches back to it to supply the instrument. It does this repeatedly until the dewar fails to build pressure above the programmable switchover point, at which time it switches to the reserve, and sounds an alarm to indicate the primary is now truly empty. This "look-back feature" reduces the residual discarded when using dewars to less than 2 to 3 percent.

By eliminating evaporation loss and reducing the residual left in empty containers, CONCOA's IntelliSwitch II optimizes the cost savings of using cryogenic argon to supply gas to ICP or ICP/Mass Specs.

For more information, visit www.concoa.com, or contact Larry Gallagher, 800-225-0473, larry.gallagher@concoa.com.



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HOW IT WORKS O

BENCHTOP FLOW CYTOMETRY

Problem: To fully understand cellular processes such as pathway activation and phenotypic change, scientists need tools to monitor the expression of multiple proteins per cell simultaneously. The technique of flow cytometry, in which cells are optically counted and examined while suspended in a stream of fluid, has emerged as a powerful cell analysis tool that can satisfy requirements for speed and reliability while also providing multiparametric information on individual cells.

Despite the power of flow cytometry, the size, complexity and cost of conventional instruments have historically confined this technology to the core lab and limited its use to experts.

Solution: Benchtop, micro-capillary flow cytometers, paired with ready-to-use cell analysis kits, enable any researcher to leverage the power of flow cytometry, regardless of expertise or access to a core facility. These systems accommodate smaller sample volumes, generate less waste, have lower operating costs, and are easier to set up and run than traditional flow cytometers.

Guava Technologies, part of Millipore, developed the first commercially available micro-capillary flow cytometer and helped to launch benchtop flow cytometry. Today, Guava® flow cytometers span a broadening range of sophistication, from simple, two-color detection of single samples, to four-color detection of multiple tubes or 96-well plates. In fact, these are the only benchtop flow cytometers capable of 96-well format data acquisition and analysis.

Guava flow cytometry instruments incorporate innovative microcapillary flow cell technology that eliminates the need for "sheath fluid"—the liquid used to carry the cells through the laser beam. This innovation allows researchers to use smaller samples and results in a minimal amount of liquid waste (from liters per day to less than 50 mL per day). The technology results in an instrument much smaller than con-

70

ventional flow cytometry systems, which means the Guava instrument can easily fit on a benchtop.



▲ Guava EasyCyte Flow Cytometer

Along with changes in instrumentation, the commercialization of turnkey assay kits and specialized software has made flow cytometry analysis easy for scientists with no prior experience with the technique. Millipore has developed a portfolio of reagent kits validated specifically for use on Guava flow cytometers. More than 20 FlowCellect™ assay kits are available for measuring chemokine receptor levels, stem cell phenotypes, cell viability, apoptosis, cell cycle progression, proliferation and toxicity. Because all necessary reagents are included in the kits, no assay development is required. Assay-specific software modules

enable researchers to get meaningful data even more quickly.

Sophisticated cell analysis enabled by flow cytometry is now a powerful "on demand" tool for researchers looking for answers to increasingly complex questions about protein activity, function and interaction.

When characterizing mixed cell populations, it may be insufficient to determine gross protein levels across an entire cell population. Biological processes can manifest themselves as shifts in relative expression or signaling events between subpopulations of cells. The ability to quantitatively distinguish subpopulations of cells according to their protein expression profiles and elucidate complex cell signaling pathways using bench-top flow cytometry opens up new opportunities for researchers seeking to understand biological processes and diseases at their most fundamental

The availability of benchtop, microcapillary flow cytometry has allowed this powerful cell and protein analysis tool to be accessible to researchers of any skill level, right at the lab bench. The traditional barriers of cost, extensive assay development and challenging software have been eliminated, allowing flow cytometry to be integrated directly into the research setting and into protein expression workflows.

For further information, please visit www.millipore.com/flowcytometry.

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PARTING POINTS

Takeaways from this month's issue:



The Online Lab Manager, p. 10

Lab managers are under increasing pressure to do more with less, and with a host of online tools at their fingertips, they can. Here are some of the ways online resources are helping managers increase lab productivity and reduce costs:

- Screening employment candidates using online job boards and Web 2.0 technologies
- Online purchasing through vendor or "emporium" websites
- Benchmarking specific functions, such as technology costs, against competitors
- Making use of online meetings and webinars as alternatives to expensive business travel
- Using online software based on remote servers for LIMS



Ask the Expert, p. 34

Dr. Michael D. Hopkins, Professor of Chemistry at the University of Chicago, helped in renovating the Searle Chemistry Building, which received a LEED Gold certification for its "green" attributes. Some of those attributes include:

- At least 75 percent of the building (walls, floors, roof) was reused
- The entire building is supplied with 100 percent outside air so no chemicals or vapors are recirculated through the labs
- Water use was reduced by 33 percent through high-efficiency toilets and low flow faucets
- Vegetative and reflective roofs were used to minimize the heat island effect



Conflict Management, p. 20

It's important for managers to be able to confront and resolve conflicts. In order to do so, the causes must first be understood. Here are some possible sources of conflict:

- Value differences: Most of us share a majority of personal values, but minor differences can lead to conflict
- Role pressures: Demands from various sources (work, family, personal) can be daunting, and fitting it all together can lead to tension and fatigue
- Goals: While they may be clear to everyone, individual, divisional or departmental goals can vary, and can bring staff into conflict
- Perception differences: We all see things differently, based on diverse experiences, emotions and values
- Status: Threats to our status are seen as attacks on the values we have accepted



The Economic Realities of Lab Automation, p. 48

Automated instrumentation, equipment and software have a major impact on lab productivity. Before the move toward a fully automated lab is made, the following issues should be addressed:

- Standards development: Consider building on the HL7 and ASTM/CSLI standards
- Education: This includes user-level material (working with automation systems) and management-level material (how to plan for automation, impact, regulatory issues, etc)
- Planning: Consider gradual introduction of automated devices into the lab, or evaluate the procedures you're using and determine if they're suitable for automation



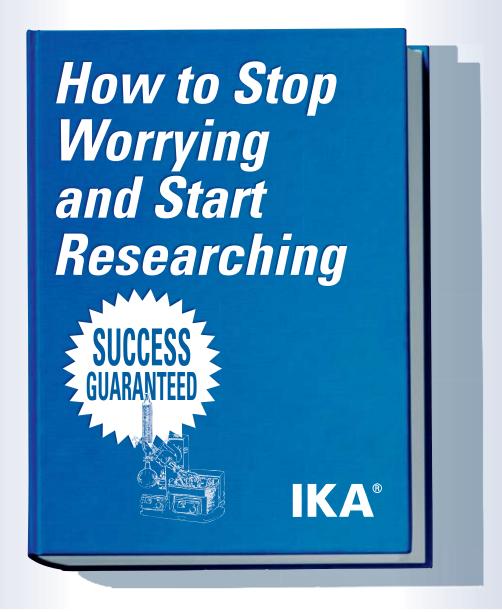
74

Scanning the Scene, p. 30

Three-dimensional scanning, a new tool in laboratory construction and renovation, moves the process along much faster. Here are some of the benefits:

- Safety: Surveying staff are less likely to have to climb ladders or balance on lifts. In many cases, crews can simply set up the equipment and walk away
- Accuracy: The scanners measure millions of data points very accurately, reducing the need to make return field visits
- Validation: For facilities that need validation from authorities, laser scanning provides real coordinates, fully documenting every part of the system
- Compatibility: Data can be converted into other building modeling software programs

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