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By using metrics effectively, laboratory managers can better focus their R&D efforts and be more effective in improving their firms' sales and profitability. This is essential, now more than ever, given the slow recovery from the "Great Recession." 10

John Borchardt

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The Devil in the Details

Laboratory benchmarking entails comparing the auglity of one lab to measures taken from a range of other laboratories. or from the standard bearers. It's the details involved in the benchmarking process, however, that can be maddening.

Rernard Tulsi

PRODUCT SHOWCASE LIVE

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EDITOR'S NOTE



Happy New Year!

"Maximizing profits" and "competing for market share" are not phrases typically associated with laboratories. Right? Well, maybe they should be.

Welcome to the first issue of Lab Manager Magazine for 2011. Well into our third year of publication as part of the LabX Media Group, we wanted to begin the New Year by focusing on our key editorial mission — to help you "Run Your Lab Like a Business." For that, both our feature article, "Maximizing ROI," and our Business Management article, "Good Laboratory Benchmarking Means Controlling Variables," look at the very business-specific practices of metrics and benchmarking.

In John Borchardt's cover story, he shows how metrics can be used to improve a lab's product development and co-development programs, better manage R&D outsourcing relationships, and conserve laboratory resources. Bernard Tulsi, in his Business Management article on page 62, explains the growing need to do benchmarking as "laboratories, especially in the bigger companies, are always under pressure to improve their quality, excellence and competitiveness." Benchmarking, he says, is particularly useful in measuring energy costs, especially for pharmaceutical companies "very keen on managing costs and increasing profits." While obviously useful in specific applications, both authors warn against an over reliance on either metrics or benchmarking, with Borchardt saying, "One should be careful of having too many metrics and of turning metrics into an overly bureaucratic exercise."

In addition to being the beginning of a new year, January is also LabAutomation month (January 29 to February 2, Palm Springs, CA). Apropos of that, we have devoted significant editorial to the topic of laboratory automation, beginning with Joe Liscouski's Technology & Operations article, "Automating Science," in which he takes a look at the fast-changing skill set that automation requires. "Laboratory managers need to be conversant with automation and informatics technologies and the planning needed to design effective programs for the use of the technologies available. Beyond that they need to understand their future needs well enough, and how those needs match-up against current product capabilities, to advise vendors on how product characteristics and functionality has to be changed," says Liscouski.

When asked how to determine what sort of automation a lab needs, this month's "expert," Marc Ferrer, answered: "Try to get opinions from several people. Get critical information related to versatility, robustness, technical support and training; this is going to be very important in getting the infrastructure up and running. You have to do your homework and find out what people are happy with, before talking to the vendors and making any kind of investment."

And finally, a real-world example of what happened when a biotech company decided to automate the time-consuming task of agitating small glass media bottles for a set amount of time, weighing the bottle and its contents, and recording the weight. In "Robots to the Rescue," (page 28) George Aux, technical development representative for Syngenta Biotechnology Inc. (Research Triangle Park, NC), tells us that through the use of a robotic system they have been able to "increase the speed of data collection and interpretation, ask and answer questions previously not addressed using other technologies and most importantly derive more value from the same work."

So if you're looking to improve your lab's bottom line or invest in automation systems, our January issue provides an abundance of good information to help you do both. And if you're planning to attend LabAutomation 2011, please stop by the Lab Manager booth and say hello.

Allhan

Pamela Ahlberg Editor-in-Chief

Correction: In the December issue's Table of Contents we mistakenly attributed the cover article, "Managing Change" to Bernard Tulsi when the author was John Borchardt.

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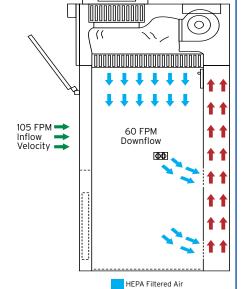


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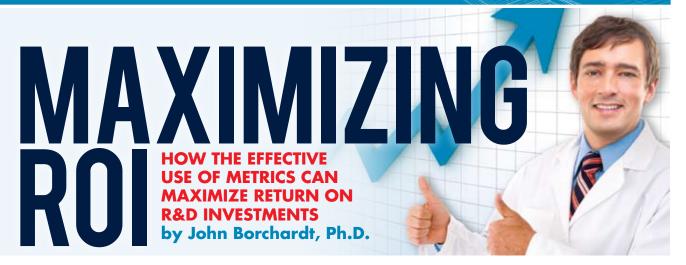






Contaminated Air

Room Air



By using metrics effectively, laboratory managers can better focus their R&D efforts and be more effective in improving their firms' sales and profitability. This is essential, now more than ever, given the slow recovery from the "Great Recession." An American Productivity & Quality Center (APQC) study indicates that the opportunity for improved laboratory performance to increase sales and profits is substantial at many companies. The results summarized in Table 1 indicate that the top 20 percent of the companies surveyed had achieved substantially higher revenues and profits than the overall average for all 105 companies surveyed. These metrics can be used to benchmark and improve the effectiveness of your own firm's R&D efforts.

PERFORMANCE RESULT	AVERAGE COMPANY	TOP 20% OF COMPANIES
% of revenue from new products	27.5%	38.0%
% of profits coming from new products	28.4%	42.4%
% of projects commercially successful	60.2%	79.5%
% of products commercial failures	20.8%	8.1%
% of projects launched on schedule	51.1%	79.4%
% of projects on budget	57.1%	79.0%
time late (% of schedule)	35.4%	17.2%
% of projects meeting profit objectives	56.0%	77.1%
% of projects meeting sales objectives	55.4%	71.5%

▲ Table 1. Results three years after commercialization of new products

The results of this survey indicate that many firms can substantially improve the effectiveness of their new product development programs. Only 44 percent of firms' product development projects meet their financial objectives, according to the APQC study. Meanwhile, 32 percent of the businesses surveyed rated their new product development (NPD) speed and efficiency as "very poor," and only 27 percent rated their NPD profitabilityrelative-to-spending as "high." In addition, 28 percent of businesses do not even measure their NPD results. Dr. Scott J. Edgett, CEO of the Product Development Institute, has gone so far as to say, "New product management is in trouble."

Effectively defining and using laboratory metrics can improve this situation. Some metrics, and the percentage of companies (surveyed by the Goldense Group) that use them, are presented in Table 1 of Reference 1. They include:

68%

Red spending as 70 or sales	00 /0
Total patents filed/pending/awarded	50 %
Current year % of sales of new products developed last N (usually three) years	ped 47%
Number of new products released	46%
% increase/decrease in R&D headcount	43%
Number of products/projects in active development	42 %
% resources/investment devoted to new product development	41%

These metrics enable companies to benchmark and judge the overall effectiveness of their product development programs. More detailed metrics can be applied to individual laboratory projects.

Defining R&D metrics

R&D spending as % of sales

The use of metrics is more suitable for applied research and technical service projects (see below). It is difficult to apply metrics to basic research, in which

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answers are uncertain and goals evolve during the course of a project.

Simple metrics are useful even if they do not measure all of the laboratory activities on a given project. However, too many or overly complex metrics can become an excessively bureaucratic exercise that reduces productivity rather than increasing it. In addition, spending an excessive amount of time on metrics can be counterproductive. Without a convincing explanation of the need for metrics, laboratory staff members can become cynical about the entire metrics process.

Timely updates of metrics data is essential if the metrics are to drive project planning and execution. If they are not measured in a timely fashion, the use of metrics

can become a retrospective process only. However, timely data can be used to take immediate, corrective action rather than just to determine what went

"The use of metrics is more suitable for applied research and technical service projects."

wrong after excessive
amounts of time, money and effort have been expended on a project.
The most commonly used metrics
for individual product or manufacturing process development projects involve

setting project milestones and completion date targets. The number of staff members working on a project, their skills and the project budget supporting them are the three primary determinants of whether project and performance target milestones will be met. It is essential when designing projects to include milestones that are both important and occur early in the project. These allow prompt remedial action to be taken to ensure that the project proceeds as desired. Remedial action can include terminating projects when failure to achieve milestones indicates that large amounts of additional time, increased staff levels or much additional funding will be required to succeed.

Metrics for outsourcing R&D

For many firms, outsourcing means capitalizing on the capabilities of other organizations in order to achieve their R&D goals. Processes once performed by the "core firm"—concept development, all or part of the R&D and commer-

cialization—can be contracted to other firms if it increases cost effectiveness and speed of commercialization.

Wayne Mackey, principal, Product Development Consulting, Inc., offers a hierarchy of partnership types. The most basic type is what he terms the "directive" partnership, in which a contractor builds or develops to the contracting organization's specifications. All decisions at all levels reside with the contracting organization. The next level up the hierarchy is the "interactive" partnership, in which the contracting organization specifies the desired outcome of the partnership but not how the contractor achieves this outcome. All decisions reside with the contracting organization. Mackey terms these two categories "outsourcing."

Outsourcing relationships are easier to manage than the two types of co-development relationships that are further up in the hierarchy. The first is "collaborative," in which the contractor and contracting organization

jointly design the project and split its ownership. One party still receives a fee from the other. At the top of the hierarchy is "risk-reward sharing," which incorporates the collaborative relationship but both parties also share the financial risks and rewards. Co-development partnerships often evolve into the contracting organization taking an equity stake in the contractor or even acquiring it. This has often been the case in co-development projects between large pharmaceutical firms and relatively small biotechnology contractors.

Mackey recommends that a "partnership coordination council" be established at the beginning of a co-development project, and that it be defined in the contract between the two organizations. For example, the partnership coordination council would include one technical manager and one project representative from each partner. The technical managers are concerned with resource allocation and strategy. This includes intellectual property concerns, information flow and other technical issues. The project representatives are concerned with the cost and schedule of the project. The council defines the metrics to be used in the project.

As noted in the second paragraph of this article, Dr. Edgett notes that an effective and profitable R&D process achieves a good balance between the number of projects and the available resources. This can be consid-



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In touch with life

ered a ratio, with the number of projects in the numerator and, in the denominator, weighted factors representing the number of R&D staff members, their skills and the facilities available (e.g., number of laboratories, number of hoods and amount of specialized instruments and equipment).

To improve this ratio and add innovative ideas and technology, lab managers increasingly rely on outsourcing and co-development. These programs require the preparation and management of R&D contracts between the organizations. Lab managers should be involved in setting the terms of these contracts, particularly the metrics used to set performance standards and define success.

Factors to consider in outsourcing and co-development contracts include the obvious one—stating what your organization needs. This can be more difficult than it sounds because your organization may have competing demands. As part of the negotiations, both parties must clearly define the innovation strategy and how goals will be achieved. The level and detail of information required from the contractor as the project proceeds, and how this information is to be delivered, should also be specified. Determining how well an outsourcing or codevelopment partner fulfills a contract requires metrics.

The primary metrics are milestones and the dates of their achievement. Performance factors such as process yield and product performance can be made a part of these milestones, as well as economic factors such as project spending for each milestone. Incentive payments may be written into contracts as rewards for achieving milestones in a timely fashion. Milestones, and the metrics for their successful achievement, must be clearly defined and communicated to project participants.

Edgett notes that companies are now doing more than writing milestones and timing into their outsourcing R&D contracts. They are defining specific metrics to be used in determining project progress and milestone achievement. These need to be defined very early in the co-development project. However, one can "kill innovation by putting too much rigor into metrics at the front end," Edgett warns.

Conserving laboratory resources

Outsourcing and judicious selection of new product development projects are important ways to make better use of your laboratory's resources. Lab managers should guard against pursuing too many projects, resulting in consumption of too much lab time and staff being spread too thin. Another concern is undertaking projects of low value to the company. Managers must use metrics to winnow out these marginal projects; metrics that could be used include anticipated revenues, profits and return on investment should the project be successful. The estimated likelihood of a project being successful is another factor to consider. One can design an equation using weighting factors to assign values to projects and employ spreadsheets to rank projects.

Another way to conserve resources for the most important projects is to design projects so that key decisions (for example, to proceed with the project or terminate it) are made as early as possible in the life of the project, before large sums have been expended. A good time to make these decisions is when the project hits early, major milestones. Answers to the following questions can help determine whether a project meets the company's metrics and will be allowed to proceed:



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- Does reevaluation indicate whether project success will have a substantial impact on the company's bottom line?
- Does the manner in which the project has proceeded indicate it still has a chance of success that is consistent with the company's requirement?
- Is the project achieving milestones on schedule and on budget?

It is essential to have the right senior-level staff conduct the reviews that will result in making these key decisions. People working directly on projects often have an emotional stake in them that can affect decision making.

One also must manage the department or laboratory portfolio of projects in its entirety to be sure it has the appropriate mix of projects to satisfy the company's metrics while meeting strategic priorities and goals.

Technical service work

Technical service work is an important component of the workload at many laboratories. It is easy for

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lab managers to agree to do technical service work, even though it may not justify itself in terms of customer retention or additional sales to new or existing customers. A parameter must be used to define appropriate technical service spending for each customer. When spending reaches this level, lab managers have to consider carefully whether additional work is justified. If it is not, one runs the risk of alienating a customer. An alternative is to request that the customer pay for technical service work beyond the limiting metric set by the lab manager.

This metric can be established by setting technical service spending as a percentage of sales or profits derived from each customer. Reviewing lab records from previous years can provide a historical record of technical service spending for each customer and whether business retention or a sales increase resulted. A sharp increase in technical service work can provide justification for asking the customer to contribute to technical service costs. On the other hand, a major customer's low level of technical service requests in previous years may serve as justification for not using a standard metric to limit spending on a technical service project.

Another strategy to justify spending beyond a set metric on a technical service project is obtaining the customer's agreement to let your firm use the data in a technical service bulletin or conference presentation. Customers will often require that their names be kept confidential. These bulletins and presentations can be useful sales tools.

Technical bulletins and conference presentations

Technical bulletins, conference presentations and trade magazine articles can serve as other metrics to measure the lab's creativity and effectiveness in promoting additional product sales. In many cases, laboratory managers review their firm's needs and make plans to do the laboratory work needed to prepare specific deliverables in these areas in the upcoming fiscal year.

The dark side of metrics

Time is one of the lab manager's most important resources. However, an overemphasis on time-based metrics can result in an excessive focus on short-term projects, steering managers and staff members away from long-term projects that drive the major innovations essential to the long-term health and profitability of the business. In particular, time-to-market metrics, which should measure time from new product or process conception to commercialization, can result in an excessive focus on short-term

projects that, while improving revenues and increasing profits, do not have a major effect on the company's business.

An overemphasis on inappropriate metrics in other parts of the firm also can have a negative effect on the laboratory manager's ability to be effective in conducting the R&D and technical service work the company needs. For example, too much focus on quarterly results and "making the numbers" can result in laboratory budget cuts at some firms. This can starve laboratories of the resources—people, instrumentation, other equipment and outsourcing capability—that lab managers need to innovate successfully. Overemphasis on reducing staffing levels, and their associated costs, can reduce the ability of laboratories to carry out the thoughtful, often time-consuming work that is required for major innovation and effective

Wrap-up

new product development.

Simple metrics are useful even if they do not measure all of the project activities. One should be careful of having too many metrics and of turning metrics into an overly bureaucratic exercise. Finally, timely updates of metric data are essential if the metrics are to drive project planning and progress.

USING METRICS TO PROVE YOUR WORTH TO STAKEHOLDERS

By John K. Borchardt

Managers of contract analytical labs and other technical services can use metrics to ensure their worth to the companies using their services. "You want to satisfy the needs of the stakeholders since that is what you are paid to do as a project manager," says consultant Simon Buehring with the U.K. firm Knowledge Train. "If the objectives aren't defined, then you won't be able to meet those needs through your project."

Bradford Goldense, president of the Goldense Group, Inc., notes firms should "bring in suppliers and customers to be part of the product development process." This can strengthen stakeholder support. Notifying customers early of problems and changes in projects is also helpful in maintaining support for a new product or when disappointing developments occur later.

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1. J.K. Borchardt, "Using Research Metrics Helps Get More Bang for Your R&D Buck," *Lab Manager Magazine* (April 2007) www.labmanager.com/articles.asp?ID=67.

Dr. John K. Borchardt is a consultant and technical writer. The author of the book Career Management for Scientists and Engineers, he often writes on career-related subjects. He can be reached at jkborchardt@hotmail.com.



GOOD LEADERS, GOOD ACTORS

USING "SITUATIONAL LEADERSHIP" TO MANAGE ANY CHALLENGE WITH THE RIGHT LEADERSHIP STYLE

by Lee Froschheiser



On June 5, 1944, just hours before D-Day was to begin, General Dwight Eisenhower paid a visit to the paratroopers of the 101st Airborne. He walked among the men, shaking their hands, patting them on their backs, cracking jokes and boosting morale. In his pocket, however, he carried a prepared message in which he took full responsibility for the mission's possible failure. He expected the casualty rate to climb as high as 70 percent, yet the decision to move forward with the plan had been made. Late that evening, the future president saluted each plane as it roared off the runway. Then he cried. Eisenhower knew that so many of those brave soldiers, whom he'd praised and pumped up just hours earlier, would never return. At that very moment in time, a sacrifice was in the making.

"A good leader acts in the moment, choosing the best style for the challenge at hand."

This story provides a classic example of how good leaders must be good actors; specifically, they must be proficient in what's called "situational leadership." Plain and simple, situational leadership means having the skills and understanding to assess the scenario you're facing and manage it with the right leadership style. Considering that there are three basic types of leadership—authoritative, participative and hands-on—a good leader acts in the moment, choosing the best style for the challenge at hand.

Situational leaders are good actors because they know how to adapt their leadership style. They can mask fear, panic and worry with a great sense of self-confidence both in themselves as well as those they must inspire and motivate. However, to assume the role, they must become great believers in whatever leadership approach they've chosen, and they must exude extreme self-confidence as they reflect on that decision.

Like good actors, good leaders "become" the character in that moment, and their success depends greatly on the purity of their belief. If they don't believe in what they are doing and the type of leadership role they've adopted, they'll come



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across as a fake. Ironic but true, good acting is one of the strategies good leaders use to communicate with credibility, build trust among their people and motivate others. Had Eisenhower cried in front of the troops that fateful summer day, or shared the message in his pocket, the consequences of D-Day could have been quite different. Instead, he put on his poker face, saving his tears for a more private, appropriate moment.

Good leaders and good actors aren't simply born

If you are in the camp that believes good leaders are made, not simply born, it's important to note that situational leaders possess key characteristics that are, essentially, the qualities of a great leader. In addition to confidence, there are 11 other attributes of leadership, including clear vision, integrity, empathy, sense of humor, humility, passion, courage, style and the ability to recognize potential in others, develop trust and encourage excellence. Some of these attributes might be innate, but many good leaders find they must develop at least some of these qualities. Doing so comes with time, experience, failure, success, coaching and mentoring, and a genuine desire to develop leadership qualities.

For instance, while there's nothing wrong with reading books on the subject of leadership, consider reading books *about great leaders* or making a list of effective qualities in the leaders you know personally. Adopt some of their ways, test them out and see what works. While good leaders actively study and prepare for their roles as such, they also make great strides by acquiring the necessary experience (e.g., climbing the chain of command and taking on greater leadership responsibilities).

Coaching and mentoring clearly support leadership growth, but good leaders and good actors must also develop a strong sense of self-awareness. Understanding shortcomings and strengths provides a launch pad for improvement and, hopefully, excellence. In becoming a good leader, or a good actor, it's likely that you'll have to work on issues around "emotional intelligence." Use 360-degree evaluation to discover how effective your leadership

style is and, notably, how you communicate. Good actors know that when it comes to delivering a message, 7 percent of it is the content of the message itself, 38 percent is your tone of voice and 55 percent is about the visual presentation, which includes a self-confident persona. Therefore, how you sound, look and carry yourself makes up 93 percent of what goes into being an effective communicator-a critical component to leadership success.



"Situational leaders possess key characteristics that are, essentially, the qualities of a great leader."

Playing the role throughout tough times

At a dinner party just prior to World War II, President Franklin D. Roosevelt was sharing friendly words with Orson Welles, whose career as a

famous actor, film director, writer and producer was just starting to take off. Welles was seated next to the 32nd president of the United States, possibly discussing the serious events of the day or chatting about Welles' radio adaptation of *War of the Worlds*. Regardless, the conversation inspired Roosevelt to lean over and whisper, "Mr. Welles, you and I are the two best actors in America." To run the country, arguably one of the greatest presidents of all times confessed that he had to act, and not just act

but be one of the best in the national show. Roosevelt led the country through an extremely rough period in United States history during which there was a great degree of uncertainty and economic peril not unlike that of today. We are, in fact, in a time of war and recession.

"How you sound, look and carry yourself makes up 93 percent of what goes into being an effective communicator."

And in these more contemporary, yet very tough, economic times, great leadership still requires great acting. It's about company presidents, CEOs and managers weathering hardships with a sense of calm. When the opportunity warrants, it's also about making the choice to throw an occasional fit or communicate frustration, disappointment and even anger in a planned, controlled sort of way.

The role that's played depends on the situation at hand, yet to evolve into a truly good leader, you must learn to thrive in the moment presented, managing it with purposeful grace. Doing so is a talent, for sure, but it's also a practice—one that almost any impassioned individual can learn given time, experience, self-belief and a genuine confidence in this "art" as a business strategy.

Lee Froschheiser is president and CEO of Management Action Programs (MAP). He is also co-author of "Vital Factors, The Secret to Transforming Your Business - And Your Life." For over 50 years, MAP has helped 160,000 leaders and 13,000 organizations create sustainable results using the powerful combination of the unique MAP Program, business coaching and consulting services. For more information, visit www.mapconsulting.com or call 888-834-3040.

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- 1. Clear vision 2. Recognizes the potential in others 3. Develops trust
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Lab Manager Academy



WHY ALL-STAR TEAMS FAIL

FOUR KEY STRATEGIES TO GETTING EVERYONE TO PLAY NICE IN THE SANDBOX

by Gregg Gregory



Bobby was selected to his County All-Star high school baseball team. He was so excited; he was going to get to play with all of the other great players from his region. There was no shortage of talent on the All-Star Team either. Each of the boys selected had scholarships to colleges across the U.S. and they were all tops in their positions, including Bobby.

This County All-Star Team was invited to play against another county. This county did not select an all-star team-rather Bobby's team was going to face the thirdplace team in its division. Bobby and the rest of the team were psyched at the fact they would destroy their opponents. By all accounts on paper they should win going away. Only a couple of the opposing team's players received any scholarships. It was a hot afternoon late in May when, to the amazement of everyone in attendance, Bobby's team lost by the slaughter rule in just five innings. What went wrong and why did they fail? Let's look at this from several different levels.

Let's start with the personal level. There is something to the old expression, "Show me someone who has not failed and I will show you someone who has not taken risks." We have all failed at some point in our lives. Think back to your childhood and when you were learning to ride a two-

wheeler. Were you one of those kids (you know the type) who never used training wheels? Most of us needed our training wheels; now what about when you took them off—what happened?

If you were like the majority, you fell—a lot—and did you give up? Most likely not. You kept going and learning from your mistakes. Failing on an individual basis is different than an all-star failing. Individuals gain insight and can grow greatly from failures. All-star teams, on the other hand, come to the table with significant individual accomplishments already behind them and the level of expectation to succeed is much greater.

Look at the U.S. basketball team in the world championships last year. With a team full of NBA stars, 12 to be exact, they finished third in the world games and lost to Greece, a team with no NBA stars on the team. The sports reporters were saying things like, "show me a team of misfits playing like a team and they can beat a team of superstars any day".

Generally, in order to be on an all-star team, you usually are selected because of the talents you displayed in the work environment. This environment can be a playing field of sports or the daily grind in the office.

Let's look at why many all-star teams fail.

This can be broken down into a four strategic areas:

The organization has not built a culture of trust and respect

As mentioned above, All-Star teams are usually built from stellar performers; and that means enormous egos, which sometimes translates into a lack of trust of others. Suppose you know for a fact that Sarah is lying to Jonathan on the team. How well will you trust what Sarah says to you in the future?

When there is solid trust and respect, you even have outstanding conflict resolution. Without conflict how can the team move forward? Yet poor conflict resolution can lead to animosity and increase the lack of trust. Poor conflict resolution can be as simple as not accepting the other person's point of view and then allowing the conflict to become personal. Once it becomes personal, the likelihood of moving forward is diminished greatly.

Failure to recognize the chemistry necessary to succeed

In the movie "Miracle" staring Kurt Russell as U.S. Olympic Team coach Herb Brooks, he says "I am not looking for the best players, I am looking for the right players." This is a critical part of why the

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U.S. Olympic team defeated the Soviets in 1980 at Lake Placid. The chemistry was right. They had a group of no names all working together and defeated what many call the greatest sports dynasty ever.

It is still possible to have the right players on the team and if they are not doing the job that best suits him/her then it is just as much a failure. Randy was a good loan originator in the mortgage industry, but not a stellar producer. When his supervisor suggested that he become processor, he felt like he was being brushed off. After explaining that this was because his talents would allow him to better serve the team from that position and he would likely experience greater success in the long run, Randy agreed to make the move.

After just about 18 months he realized he actually was better working on the inside. He quickly became an underwriter and later became director of operations for the same mortgage company. This was a classic example of right team wrong position. Had the original leader not recognized the chemistry mismatch, Randy's career could have take a very different path.

Lack of mutual accountability

It is one thing for the leadership to hold everyone accountable, (and they should) it is another when members hold each other accountable. Some of the best teams are those whose leaders are only there to be a resource in the event of a problem. Team members take care of the basic problems as they arise by holding each other 110 percent accountable. The Hillstone Restaurant Group which owns Houston's, Gulf Stream, and Bandera restaurants among others follows this strategy perfectly. Each server in the res-

taurant is responsible for his/her tables, yet, in essence, it is the responsibility of everyone to serve every table and at the end of the shift the servers do not share in the tips. They constantly hold each other accountable.

Poor team language

Listen to how the team members talk. Are they saying things like, "I do not get this" or "I think it should have been done this way". How about "I want to see more of...?"

This is individual-centered language and is not healthy for a team to move forward. On the other hand, they might say things like, "We can make this work", or "if we do it this way then..., or when we get through this section we can..."

These are more team-based statements and the language indicates that the team is in charge and is balanced.

Let's face it—we will never get along with everyone. On the other hand, if we can understand the other person's behaviors a little better then we as a team can become better producers, and that is the little secret of playing nice in the sandbox.

With over 25 years of experience, Gregg Gregory has helped organizations, such as U.S. Naval Research Laboratory; National Institutes of Health; Chesapeake Bay Research Consortium and Bridge Pharmaceuticals, develop a greater focus, more cooperation, increased productivity, and a greater impact. Gregg's programs are peppered with anecdotes, inspirational stories and filled with humorous real-life examples to energize and engage everyone and focus on moving the team forward, building trust and collaboration across department lines. Gregg can be reached at 301-564-0908 or at his website www.teamsrock.com.

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HOW CHANGING TECHNOLOGIES ARE CHANGING JOB REQUIREMENTS by Joe Liscouski

Would you hire someone with out-of-date skills? You might be doing just that. We are in the midst of a transformation of the way laboratory work is done. Those changes are not going to be incremental; they will require a major change in the skills and experience people need in order to be effective. This article takes a look at what working in an automated laboratory will be like and what the needed skills are based on the experiences of those working in facilities dependent upon successful implementation of automation technologies (which include laboratory informatics).

Automation has been shown to be an effective tool in improving productivity and reducing the cost of labor-intensive work. This has been demonstrated not only in manufacturing environments but also in clinical laboratory systems and contract testing labs where laboratory automation has been effectively implemented.1

During e-mail and telephone conversations with people at contract testing labs, made in preparation for this article, the phrase "We couldn't work profitably without automation" would come up. One lab stated that their prices would be two to three times higher without automation. The driving factor in clinical chemistry automation has been to improve productivity and reduce costs (Mt. Sinai Medical Center reported a ninefold increase in sample throughput with a fivefold per-test cost reduction.)² These are the same issues that drive any organization.

Properly done, laboratory automation is a useful tool in both research and testing environments. In fact, most laboratories would find it difficult to function without automation and computer systems. While some measurements are difficult to make in an automated environment (the effect of lotions on skin, for example), most laboratory instrumentation work is done by equipment with embedded computers in addition to data acquisition/reduction/reporting and management functions.

How will lab work change?

Automation has already had an impact on laboratory work. Those working in chromatography, for example, no longer measure peak areas or heights by hand, constructing calibration curves, or evaluate results manually. That work is done by computer systems, with the results shown on printouts or transferred to other systems. In many cases, sample preparation work is done by robotic systems that relieve people from labor-intensive efforts. An autosampler was released last year that carries out sample preparation functions within a small

> footprint. For the most part, however, these systems represent incremental changes to lab work, with people still providing linkage—the integration between one automated task and another. Ideally, in a fully automated laboratory workflow, the system would carry out all steps of the analysis from the initial sample to the final result. This is not fantasy. This type

of work is going on in clinical chemistry and contract testing laboratories today. In clinical applications, the systems are the result of decades of work in standardization and client vendor cooperation. We see the results of standardization in life science workflows that use micro-titer plates with standardized plate formats, allowing vendors to create a range of equipment with different capabilities (stackers, washers, readers, etc.) that can be put together into functioning systems.

The increased use of automated systems does raise one concern: trusting the automated equipment too much—the development of "push-button science." We cannot let the complexity of systems intimidate us into not asking questions about how they work and produce results. As you will see below, laboratory professionals need to be educated so that they can challenge vendors and ensure that they are using the right products for their work. The fact that a vendor has produced a software package doesn't mean it is right for your application. End users need to understand how it works, how it is convert-

"The fact that a vendor has produced a software package doesn't mean it is right for your application."

Lab Manager January 2011

TECHNOLOGY & OPERATIONS



ing instrument output into results, and whether it fully fits their needs.

One of the major changes in lab work is that people will be less involved in the execution of tasks and put more effort into managing systems. However, that is not the only change. The introduction of automated systems changes the way one thinks about laboratory work. For example:

- The development of testing methods has to be done with an eye toward their
 ability to work in an automated environment. This means one needs to think about
 how things are being done and whether or not they lend themselves to implementation and routine use with automated equipment. Techniques that are easily
 automated will be preferred.
- People will be concerned about both the science and the implementation of automated systems (e.g., whether they are functioning properly and tracking down problems). The work will be more along the lines of managing a production environment than typical hands-on task execution. This will require training that is more sophisticated, since they will need to understand how things work in addition to the science. As Diana Mass³ of Associated Laboratory Consultants put it, "What I have observed is that automation has replaced some of the routine repetitive steps in performing analysis. However, the individual has to be even more knowledgeable to be able to troubleshoot sophisticated instrumentation. Even if the equipment is simple to operate, the person has to know how to evaluate quality control results and have a quality assurance system in place to ensure quality test information."
- More time can be spent evaluating results. The shift from hands-on task execution to knowledge-based work has been one of the promises of automation.

Changing skill sets

Questions about skills needed for work in an automated facility were posted last summer (2010) on LinkedIn discussion groups. The following are examples of some of the responses from clinical, pathology, pharmaceutical, and biotechnology professionals:

- "The ability to troubleshoot/think and validation experience are now the two skills that I look for most when hiring an experienced chemist."
- "For today's modern lab practices you should equally know all about your lab automation and their troubleshooting. Knowing in detail the software program of the instrument is a must. Good knowledge of the technical aspects will always put you in a better position."



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- "Risk management techniques, best laboratory practices and [being] software literate are skills that are required in a clinical laboratory at every level (technicians through managers) plus good old-fashioned ingenuity and critical thinking."
- "Though automated systems have replaced manual work, I feel, the key personnel should have a basic understanding of the process. Software skills are essential and also the interpretation of the output data. I am writing this with my experience in R&D biotechnology. The technicians should also have basic knowledge on trouble-shooting. We generate so much information through the automated systems that interpretation of important information becomes very critical and the onus lies with the supervisors."

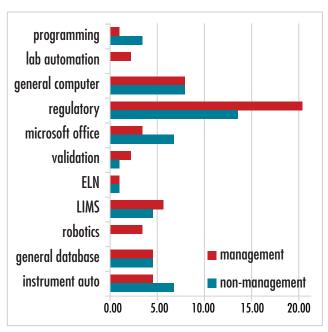
The following quote from Martha Casassa, Laboratory Director, Braintree Rehabilitation Hospital, (Braintree, MA) gives a contrast between clinical and non-clinical environments:

"Having a background both clinical (as a medical technologist) and non-clinical (chemistry major and managing a non-clinical research lab), I can attest to the training/education being different. I was much more prepared coming through the clinical experience to handle automation and computers and the subsequent troubleshooting and repair necessary as well as the maintenance and upkeep of the systems. During my non-clinical training the emphasis was not so much on theory as practical application in manual methods. I learned assays on some automated equipment, but that education was more to obtain an end product than to really understand the system and how it produced that product. On the clinical side I learned not only how to get the end product, but [also] the way it was produced, so I could identify issues sooner, produce quality results, and more effectively troubleshoot. I do not believe a specific degree level or amount of education is the key to success with automation in a lab setting. It is the type of training and the curriculum's approach that [are] critical."

We need to think differently about the education of laboratory managers and lab personnel. Business as usual is not going to cut it. We did a review of 88 job descriptions posted last summer for open positions, looking to see what backgrounds people were asking for. The bulk of the positions were in life sciences and evenly split between management and non-management positions. We were looking for keywords that pertained to automation and a regulatory environment. The chart above shows the results:

The list on the left contains the keywords that occurred (with one exception) versus the percentage of the number of job descriptions in which they occurred. The exception was "instrument automation," which was an aggregate of occurrences (interestingly, some noted specific vendor products).

For an industry that is moving toward the increasing use of automation and informatics technologies, these are low numbers. We have moved past the point where "general computer," word processing, and spreadsheet skills are a reasonable basis for competence in a modern laboratory.



▲ Frequency (%) of automation-related keywords occurring in a review of 88 job descriptions.

Personnel requirements

Laboratory managers need to be conversant with automation and informatics technologies and the planning needed to design effective programs for the use of the technologies available. Beyond that, they need to understand their future needs, and how those needs match up against current product capabilities, well enough to advise vendors on how product characteristics and functionality have to be changed. This last point is essential to forging effective vendor-customer relationships. Vendors have their views of what the market needs based on what they see, but having customers who can articulate technology needs and integration requirements will advance the field much more quickly.

That point was noted in a recent meeting in which representatives from Velquest, LabWare, Accelrys and Rescentris discussed "Future Directions in Lab Informatics." They agreed that more input and involvement from customers was needed in their planning and the shaping of the evolu-

tion of informatics systems.⁴ Successful vendor-customer relationships are going to be critical as laboratory work moves from manual effort to full automation.

Laboratory automation engineers are needed to assist in the planning, design, implementation, and support of laboratory automation systems. This is something the ILA has been working on for some time.

Laboratory personnel need to be trained in the products and technologies as well. We need to move beyond the ability to use preplanned settings for equipment, to having them understand what the equipment does "under the hood" so that problems can be traced or avoided. They need to understand how things work—not at the programming level, but how data is acquired from instruments, how peaks are detected, how baselines are drawn, and how setup parameters can affect those functions.

The move toward automated laboratories is more than purchasing equipment. It is the effective use of products and technologies by people educated to work competently in that environment.

Joe Liscouski, executive director, The Institute for Laboratory Automation, can be reached at liscouski@InstituteLabAuto.org or by

phone at 978-732-5122.

The Institute for Laboratory Automation is a nonprofit organization focused on education and the development of methodologies for successful lab automation programs, and the development of the field of laboratory automation engineering. For more information, visit http://www.InstituteLabAuto.org.

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ROBOTS TO THE RESCUE AUTOMATED DATA COLLECTION SYSTEM DRIVES RESEARCH IN NEW DIRECTIONS by Kim Norris

Syngenta Biotechnology Inc. (SBI), located in Research Triangle Park, North Carolina, is the key North American site for Syngenta's biotechnology and crop genetics R&D, with approximately 400 scientists and support personnel employed at the facility. A portion of these research activities includes the monitoring of various types of fermentation processes by the direct measurement of products over a period of time de-

Apart from representing a bottleneck in the overall pace of the research, the slow rate of data collection does not allow scientists to develop a clear understanding of the reaction kinetics. To increase the rate of data collection, Syngenta faced the prospect of having to assign many personnel to work continuously for 24 hours to agitate and weigh the bottles and record the data. According to George Aux, technical develop-

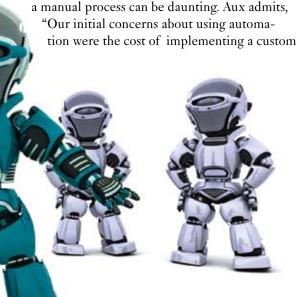
"In some research projects, dozens of samples need to be continuously processed between 12 and 72 hours."

ment representative for SBI, a neighbor who worked at Aisin WA Co. Ltd., suggested the idea of using industrial robots to automate the process. After a site visit to the

fined by a scientist acting as a principal investigator. The products in the research application are primarily mixtures of various carbohydrates, either liquids or slurries used in the commercial production of ethanol. The manual process for taking direct measurements of these substrates involves agitating small glass media bottles for a set amount of time, weighing the bottles and their contents, and recording the weight of each bottle. In some research projects, dozens of samples need to be continuously processed between 12 and 72 hours, making the task of collecting the data

Aisin WA Co. plant in Durham, North Carolina, which widely uses FANUC and other types of robotics, the SBI team became familiar with a variety of available robots and their strengths and weaknesses. Because of the quality of their equipment, SBI called FANUC Robotics North America to help SBI automate their processes, and FANUC referred them to ESS Technologies, Inc., an authorized system integrator for FANUC.

For many companies, the prospect of automating



extremely time-consuming.

solution and the complexity of integrating the components needed to do the job." ESS outlined for SBI the advantages of robotics automation in their application. Robotic systems are ideal for the type of laboratory research conducted at SBI's facility. Tedious, repetitive processes are susceptible to variances as a result of decreased concentration caused by human fatigue and boredom. As the task wears on, the possibility of human

error increases and concentration wanes. Robots, in comparison, easily take on repetitive processes and offer consistent handling and timing. For SBI, this meant that all samples were ensured of receiving the same amount of agitation and the weighing of the samples could be performed at a consistent pace, increasing throughput. Robots can work 24/7/365 with minimal routine maintenance, and their programming can easily accommodate multiple test setups for handling the agitation rates and weigh cycles for various product samples. Robotic modules also offer a compact footprint, allowing the system to fit into existing laboratory space.

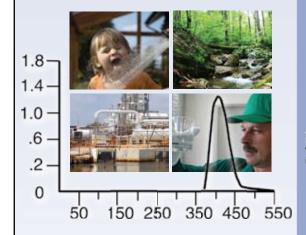
"Robots easily take on repetitive processes and offer consistent handling and timing."

As a first step in designing an automated solution, ESS performed a thorough analysis of the process to be automated, to develop a clear understanding of what SBI hoped to achieve. According to Aux, "The staff at ESS was able to collect all key design elements and bundle them in such a way as to make the use and upkeep of the system as simple as possible. Various interactions took place over the life of the project, which ensured not only a high degree of transparency but also served to troubleshoot some of the unique features our system employed."

The final solution integrated a FANUC

LR Mate 200iC robot with ESS-designed gripper-style end-of-arm tooling (EOAT) and a Model WM3002 weigh scale from Mettler Toledo. The system interfaces with any PC running a Windows® XP operating system to record the weight of each bottle. ESS mechanical engineers designed a custom tray to hold the glass media bottles, allowing the robot to precisely pick the bottles and replace them after the data is col-

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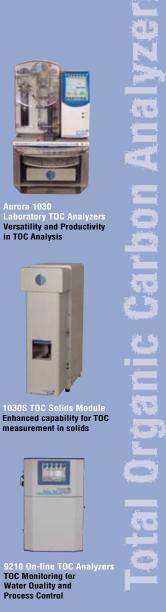


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lected, while the PC interface easily tracks each bottle and its corresponding weight according to its location in the tray. The six-axis design of the LR Mate 200iC robot offers the flexibility the software engineers needed to create a program that could pick a bottle and agitate it in an up-and-down as well as a circular motion. In early system tests at ESS headquarters in Blacksburg, Virginia, the media bottles were partially filled with water and a few drops of colored dye to verify that the agitation by the robot was sufficient to thoroughly mix the product. After the agitation cycle is complete, the robot places

► FANUC LR Mate 200iC robot agitates the laboratory bottle before the bottle is weighed.



After the bottle is agitated, the robot places it on an integrated scale that records data to a PC.

the bottle on the integrated weigh scale. The weight

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Applied Scientific Instrumentation 29391 W Enid Rd, Eugene OR 97402 Ph: (541) 461-8181 US/Canada: (800) 706-2284 www.ASlimaging.com of the sample is recorded by the PC interface, and the robot returns the bottle to the tray. The robot handles 6-10 cycles per minute, depending on the required agitation and the grid size.

The advantages of the robotic data collection system quickly became clear to the scientists at SBI. As Aux explains, "One valuable product of the fermentation process, ethanol, is measured by physically removing a sample from the reaction, purifying it through filtration and then applying one of several off-line analytical tools to determine its concentration. Another product of fermentation is carbon dioxide gas. The amount of carbon dioxide gas released from the reaction is directly proportional to the amount of ethanol, providing researchers with an indirect means to measure ethanol accumulation. The amount of evolved carbon dioxide gas can be determined gravimetrically by using precision balances.

"The primary purpose for automating our research activity was to dramatically increase the precision and number of the measurements of the fermentation performance of many reactions being run simultaneously between 12 and 72 hours without a scientist being present for the sample collection, processing and analyses. Furthermore, by leveraging the relationship between carbon dioxide evolution and ethanol production during the fermentation process, we can avoid having to use more sophisticated and expensive analytical techniques to generate the necessary data to make performance assessments."

According to Aux, "The most positive results [of automating the data collection process] came in terms of the type of data, its quantity and quality. The raw data flow increased several thousand percent. The data itself has driven the research we do into new areas and has enabled a much more comprehensive understanding of our processes. Through the use of our robotic system, SBI has been able to increase the speed of data collection and interpretation, ask and answer questions previously not addressed using other technologies, and, most important, derive more value from the same work. These benefits mean that the robotic system paid for itself in less than one year, not something we can say about most analytical tools we use at our facility today."

"The most positive results [of automating the data collection process] came in terms of the type of data, its quantity and quality."

The clear success of implementing a robotic solution has changed how SBI views the idea of automating its research processes. Aux says, "Our experience with ESS exceeded our expectations during all phases of the design, construction and installation of our robotic system. We would certainly consider automated solutions for other applications in our research platform. For us, the key to considering the use of a robotic system is the duration of a research project and the need for the continuous routine manipulations of materials. Having successfully utilized an automated solution for this project helps other members of our organization see the potential of robotics and understand how to best use this technology."

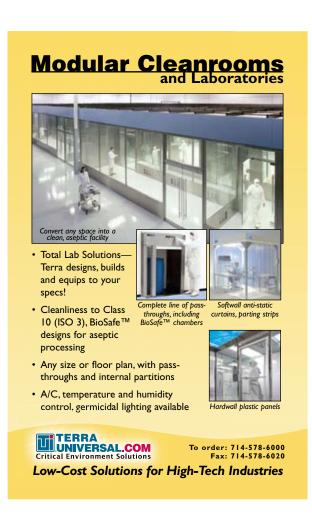
By making the transition from a manual to an automated process, SBI gained more than it had initially hoped for. The robotic solution not only automated a tedious and time-consuming manual process, but the system also allowed SBI scientists to extract more information from the data being collected. This new insight has allowed the scientists to take their research in new directions without burdening the company with either the high cost of additional personnel or expensive analytical tools. The added value of

the robotic system quickly allowed the customer to realize a return on their investment and take research projects to a new level.

Kim Norris, sales project coordinator at ESS, can be reached at knorris@esstechnologies.com or by phone at 540-961-5716.

Syngenta Biotechnology Inc.'s ambition is the development of practical and commercial solutions for the problems farmers are facing today. Another objective of the agricultural biotechnology research at SBI is to improve the quality and nutritional benefits of food crops. For more information about SBI, please go to www.syngenta.com.

ESS Technologies, Inc. is an authorized FANUC Robotics system integrator. In addition to robotic automation solutions, ESS specializes in complete packaging line design, manufacture and integration. To learn more, visit www.esstechnologies.com.



EVOLUTION OF THE CLEAN ROOM BY JOHN BUIE

Although the principles of clean room design go back more than 150 years to the beginning of bacterial control in hospitals, the clean room itself is a relatively modern development. It was the need for a clean environment for industrial manufacturing during the 1950s that led to the modern clean room as we know it.

A clean room is a rigorously controlled environment that has a low level of environmental pollutants such as dust, airborne microbes, aerosol particles and chemical vapors. The air entering a clean room is filtered and then continuously circulated through high efficiency particulate air (HEPA) and/or ultra-low particulate air (ULPA) filters to remove internally generated contaminants. Staff wearing protective clothing must enter and exit through airlocks, while equipment and furniture inside the clean room is specially designed to produce minimal particles.

While more than 30 different industry segments utilize clean rooms, 70 percent of U.S. clean room floor space is in the semiconductor and other electronic components, pharmaceutical, and biotechnology industries.

1970s

By the early 1970s the principle of "laminar flow" had been translated from the laboratory to wide application in production and manufacturing processes.

In the late **1950s**, Sandia Corporation (which later became Sandia National Laboratories) began investigating the excessive contamination levels found in clean rooms. Researchers found that clean rooms were being operated at the upper practical limits of cleanliness levels and identified a need to develop alternative clean room designs.

In 1962, Sandia Corp. launched the Whitfield Ultra-clean room, which was publicized in Time Magazine, creating a great deal of interest. Instead of simply using filters to clean incoming air, Whitfield used filtered air to keep the room clean by introducing a change of ultra-clean air every six seconds. By **1965**, several vertical down flow rooms were in operation in which the air flow ranged between 15 m (50 ft)/min and 30 m (100 ft)/min. It was during this time that the specification of 0.46 m/s air velocity and the requirement for 20 air changes an hour became the accepted standard.

1940

1939 - 1945

32

Development of the modern clean room began during the Second World War to improve the quality and reliability of instrumentation used in manufacturing guns, tanks and aircraft. During this time, HEPA filters were also developed to contain the dangerous radioactive, microbial or chemical contaminants that resulted from experiments into nuclear fission, as well as research into chemical and biological warfare.

While clean rooms for manufacturing and military purposes were being developed, the importance of ventilation for contamination control in hospitals was being realized. The use of ventilation in a medical setting gradually became standard practice during this time.

1950s - 1960s

1950

The evolution of clean rooms gained momentum as a result of NASA's space travel program in the 1950s and 1960s. It was during this time that the concept of 'laminar flow' was introduced, which marked a turning point in clean room technology.

1960

In 1960, Blowers and Crew in Middlesborough, UK was the first to improve contamination control by creating a unidirectional airflow from an air diffuser fitted over the entire ceiling in an operating room. In practice, the airflow was disturbed by air currents and the movement of people, but the idea of unidirectional flow was born.

Also in 1960, McCrone Associates began developing advanced particle handling techniques using tungsten needles and collodion. These techniques, which later became industry standards, were incorporated into the McCrone Associates Class 100 clean room.

In **1966**, Patent No. 3273323 was submitted and issued for the "laminar flow airhood apparatus."

1970

In **1962**, Patent No. 3158457 for the laminar flow room was issued. It was known as an "ultra clean room."

In 1961, Professor Sir John Charnley and Hugh Howorth, working in a hospital in Manchester, UK, managed to significantly improve unidirectional airflow by creating a downward flow of air from a much smaller area of the ceiling, directly over the operating table.

Also in 1961, the first standard written for clean rooms, known as Technical Manual TO 00-25-203, was published by the United States Air Force. This standard considered clean room design and airborne particle standards, as well as procedures for entry, clothing and cleaning.

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In 1987, a patent was filed for a system of partitioning the clean room to allow zones of particularly high-level cleanliness. This improved the efficiency of individual clean rooms by allowing areas to adopt different degrees of cleanliness according to the location and need.

1980s - 1990s

The 1980s saw continued interest in the development of the clean room. By this stage, clean room technology had also become of particular interest to food manufacturers.

During the late 1980s, STERIS (formerly known as Amsco) developed the use of hydrogen peroxide gas for the decontamination of clean rooms, and marketed the idea under the trademark VHP (vaporized hydrogen peroxide). Hydrogen peroxide gas rapidly became the most widely used method of sterilization, due to its unique combination of rapid antimicrobial efficacy, material compatibility and safety.



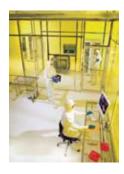
In 1991, a patent was filed for a helmet system that can be used in a medical clean room in which the user is protected from contaminated air in the environment, while the patient is protected from contaminated air being exhausted from the user's helmet. Such a device decreases the possibility of operating room personnel being contaminated with viruses carried by the patients being operated upon.

ln 1998/1999,

CRC Clean Room Consulting GmbH introduced the clean room filter fan. This involved the integration of a filter fan unit, with filter, ventilator, and motor directly into the clean room ceiling. In 2003, Eli Lilly pioneered the development of a new system for the prevention and containment of cross-contamination during the manufacture of pharmaceutical powders using a specially designed "fog cart". This allows the operator to be covered by an exceptionally fine fog of water on exit from a critical area, virtually eliminating the risk of transferring dust traces beyond their proper confines.

1980

In **1980**, Daldrop + Dr.Ing.Huber developed an innovative clean room ceiling, known as 'Euro Clean', to meet the rising challenges from industry at the beginning of the 80s.



2000s

2000

The pace of clean room technology transformation has accelerated over recent years. Since the year 2000, there have been significant advances in new clean room technology, which have helped to streamline manufacturing and research processes, while also reducing the risk of contamination. Most of the technological developments of the past decade have been directed towards the manufacture of sterile products, particularly aseptically filled products.

1990

In 2009, The University of Southampton, UK opened a Nanofabrication Centre containing a clean room with nanofabrication facilities, making it possible to manufacture high-speed and non-volatile "universal memory" devices for industry that could process information faster than anything achieved with conventional technologies.

2010

Photos courtesy of Terra Universal

THE FUTURE OF CIFAN ROOMS

Clean room facilities in the United States have been predicted to grow fourfold from a baseline of 1998 to the year 2015, to an estimated 180 million square feet in 2015.

The most common applications of clean rooms currently are in the manufacture of semiconductor and other electronic components, as well as in the pharmaceutical and biotechnology industries. In addition to these traditional applications, clean room technology has more recently been applied to micro- and nano-system processes, and this looks certain to be an area of growth in coming years. The development of clean room technology is likely to continue to be driven by certain key factors including the increasingly technical use of exotic physical and biological phenomena, the central role of increasingly fine structures, the creation and use of materials of the highest purity, and the increasingly broad-based utilization of biotechnology. Given the scale of these challenges, clean room technology looks set to remain indispensable to production in coming years.

REDUCING, DISTILLING, RECYCLING, AND CONCENTRATION by Angelo DePalma, Ph.D.

Rotary evaporators have for decades been staples in labs and industries performing chemistry, including labs in the chemical, environmental, materials, life science and forensics industries. Key applications include sample concentration, solvent recycling, extractions, and separation of solvent mixtures.

In their simplest embodiment, "rotovaps" consist of a temperature bath, rotating flask, condenser, collection flask, and vacuum source. Solvent distills from the sample under the combined effects of heat and vacuum, and collects after condensation in the collector. Recovered single-phase organic solvents may be dried and re-used; binary, tertiary, or quaternary solvent mixtures are also re-used but may need adjustment for composition.

Water is the fluid of choice for the bath, but some laboratories use oils to reach heating temperatures of up to 180°C. Several choices are available for the condenser coolant. Until about 10 years ago, almost evervone used house water. Concerns over water consumption caused many labs to switch to a chiller to recirculate coolant into and out of the condenser coils. Chillers provide more precise cooling, greater control over condensation, a greatly reduced environmental footprint, and are overall less expensive to use than water. High-efficiency trapping

34

of low-boiling solvents is achieved with a "cold finger" charged with dry ice and acetone. are turning to more sophisticated vacuum control, which Kristof O'Connor, product manager at

"Water is the fluid of choice for the bath, but some laboratories use oils to reach heating temperatures of up to 180°C."

Vacuum options

Of all the rotovap options, vacuum is probably the broadest. At one time, water aspirators were the most common vacuum sources. That practice has gone by the wayside for the reasons given for water coolers and due to environmental concerns related to solvent vapors venting down the drain.

The next most common source is house vacuum, which is limited but inexpensive and reliable. Users typically insert a Woulff bottle or cold trap between the vacuum spigot and the rotovap, to trap volatiles that the condenser missed and protect the house vacuum system.

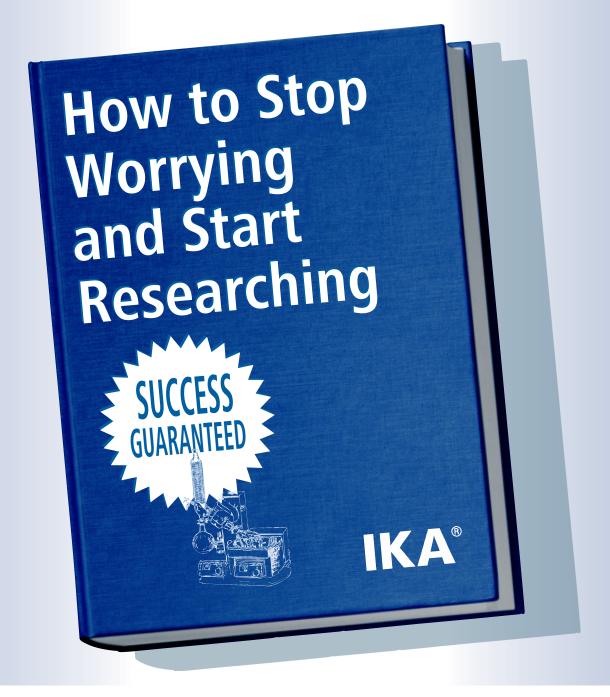
Increasingly, users employ vacuum pumps to achieve reproducible and rapid solvent removal. The vacuum must be applied carefully, however, to avoid bumping and foaming.

Traditionally, vacuum control was achieved by slowly closing a glass stopcock. Increasingly, users

Heidolph Brinkmann (Elk Grove Village, IL), describes as "probably the number-one improvement in rotary evaporators over the past two decades." Control became necessary, he says, because "vacuum pumps are very stupid machines. They try to achieve as high a vacuum as they can, as quickly as possible, which often results in bumping and foaming."

Lisa Sprenger, account manager at IKA Works (Wilmington, NC), agrees on the importance of vacuum control and the full and volume-regulated distillation method implementations, and adds the following:

- Larger graphic displays with increased data storage capacity
- Additional safety features to regulate heating baths and motor units
- Implementation of full and volume-regulated distillation methods
- Motorized lift systems
- Clockwise and counterclockwise rotation of the distilling flask to increase speed and efficiency for powder drying applications





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years, glassware and wearing parts exclude

Newer rotovaps may incorporate thermocouple-controlled tion, in which a pump integrates with a controller and a thermocouple located in the vicinity of the condenser coils. As the coil temperature rises through heat transfer between the condenser and the evaporated solvent, the vacuum is bled out through valving to maintain steady distillation. Another technique, known as "RPM" control, speeds or slows the pump's inner workings to control the delivered vacuum.

Whereas valve control is generic, RPM control locks users into pumps from a single manufacturer. "Our RPM control pump only works with our precision controller," Mr. O'Connor tells Lab Manager Magazine.

Coupled with software and solvent databases, vacuum control allows users to plug in bath temperature and solvent for ultimate fine-tuning of evaporation rate, to the point of allowing fractional distillation of multi-component solvents, followed by final drying.

"These features provide reproducibility, and make it easier and faster to optimize operating parameters," Mr. O'Connor says.

Purchase factors

Potential purchasers should consider several vacuum and condenser cooling options before buying a ro-

Cooling method, which dictates the type of condenser used, should be decided based on the expected solvent load. More vigorous cooling is demanded for high volumes, rapid distillation, and very low-boiling solvents like ethyl ether.

Purchasers should consider whether automated, volume-dependent rotary evaporation is desired. This feature combines precise distillation with walk-away automation.

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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As part of our Lab Products Survey series, Lab Manager Magazine has compiled the responses of more than 120 lab professionals regarding the use of rotary evaporators in the lab. The first rotary evaporator was manufactured and sold by Walter Büchi of Basel, Switzerland in 1957, and by the early 1960s, the device had become a standard fixture of the organic and biochemical laboratory. Today, more than 50 years later, evaporation and distillation are still the most frequently used separation methods.

Rotary evaporators are commonly used by synthetic and purification chemists to dry solutions prior to redissolution in another solvent or prior to long-term storage of the finished product.

A typical rotary evaporator has a water bath that can be heated in either a metal container or crystallization dish. This keeps the solvent from freezing during the evaporation process. The solvent is trapped by a condenser and is collected by a vacuum for easy reuse or disposal. Most labs use a simple water aspirator vacuum on their rotary evaporators, so a rotary evaporator cannot be used for air and water-sensitive materials unless special precautions are taken, i.e. additional traps are used. In the lab, the house vacuum line, a circulation bath or a membrane pump is used as the source for the vacuum.

In purchasing a new rotary evaporator, respondents identified a number of factors and features that influence the decisionmaking process—the top five of which are reliability, low maintenance (easy to clean), price, ease of use and safety.

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itomber of folding craporators be	ing oscu in respondents lubs.
1 to 3	65%
4 to 6	8%
6 to 9	2%
10 or more	4%
None	21%

Primary purpose for rotary evaporators in the lab:

Research	72 %
Processing	15%
Quality Control	8%
Clinical	1%
Other	4%

Primary applications for rotary evaporators in the lab:

i illiary applications for folding craporators	iii iiic ius.
Concentration of substrates	24%
Distilling of low-boiling solvents	18%
Extractions	15%
Distilling of temperature-sensitive substances under vacuum	12%
Recycling of solvent waste	8%
Separation of material mixtures	7 %
Drying of powders	7 %
Chemical synthesis under reflux	4%
Distilling of oxygen-sensitive substances under inert gas	2%
Other	2%

Types of rotary evaporators respondents use in their labs:

c	 1.4	
Other		1%
Motor lift		40%
Hand liff		59%

Size of rotary evaporator heating bath respondents use in their labs:

Less than 1 liter	8%
1 liter	19%
2 liters	23%
3 liters	15%
4 liters	15%
5 liters	11%
10 liters	5%
More than 10 liters	3%

Rotary evaporator components respondents use in their labs:

Digital bath	17%
Condensate trap	13%
Diaphragm pump	13%
Recirculating cooler	12%
Vertical condenser	10%
Diagonal condenser	9 %
Reflux condenser	9 %
Chiller	8%
Dry ice condenser	4%
Cold finger condenser	4%
n ./ ./ .	

Respondents' budget for purchasing a new rotary evaporator:

Less man \$2,500	35%
\$2,000 to \$3,500	23%
\$3,500 to \$5,000	21%
\$5,000+	21%

Respondents' annual budgets for related equipment, parts, maintenance, service and repairs:

Less than \$500	49 %
\$500 to \$1,500	20%
\$1,500 to \$3,000	8%
\$3,000+	5%
Don't know	18%

Respondents' purchasing plans for a new rotary evaporator:

Starting the review process	8%
Plan to purchase in the next 1 to 6 months	13%
Plan to purchase in 6 to 12 months	9%
Plan to purchase in 12+ months	5%
No current purchasing plans	58%
Don't know	7 %

Respondents' reasons for purchasing a new rotary evaporator:

Addition to existing systems; increase capacity	40%
Setting up a new lab	21%
Replacement of an aging rotary evaporator	26%
First-time purchase	10%
Other	3%

Factors/features that influence the decision-making process when buying a rotary evaporator:

Low maintenance (easy to clean)	
	91%
Price	90%
Ease of use	88%
Safety	84%
Low cost of ownership	78%
Versatility	70%
Service and support	69%
Warranty	66%
Temperature sensitivity	62%
Ease of installation	54%
Energy efficiency	49%
Quiet drive motor	48%
Built-in vacuum controller	47%
Coated glassware	46%
Small footprint/size	45%

Environment	15%
Biochemistry and biology	16%
Chemical	25%
Quality control	5%
Food and beverages	2%
Pharmaceutical industry	14%
Hospital/Medical center	1%
Metal industry	2%
Plastics	3%
Forensic labs	1%
Fuels	0%
Other	17%

QUANTIFYING ORGANICS THROUGH OXIDATION, DETECTION

by Angelo DePalma, Ph.D.

Total organic carbon (TOC) analyzers are a mainstay in industries that need to detect and quantify carbon content from a variety of samples and sources. Unlike spectroscopy, which measures specific carbon species from their unique interactions with light, TOC analysis does not tell which specific carbon-containing species are present. Nevertheless, it does provide information on impurities, which is invaluable in evaluating environmental samples. TOC analysis is mandatory for many labs, particularly in semiconductors

inorganic carbon; oxidation occurs either through direct, high-temperature (1300°C) or catalytic (680°C) combustion, or through a technique involving either ultraviolet radiation or thermal oxidation in the presence of persulfate.

The detector is the heart of TOC analyzers. Two main techniques are used to quantify carbon dioxide: conductivity and non-dispersive infrared (NDIR). Conductivity is a straightforward measurement involving either direct measurement or membrane-

(SPC), a relatively recent NDIR development, provides improved sensitivity and precision by concentrating the oxidized sample and measuring it all at once instead of through a flow cell.

One emerging trend in TOC is the analysis of solids, for example soils. Jeff Lane, a TOC specialist at OI Analytical (College State, TX), tells *Lab Manager Magazine* that his company is working on a new solids module that captures CO₂ in a sampling bag that collects oxidized material from replicate samples. "Solids work because

samples are not always as homogeneous as liquids or suspensions," says Mr. Lane. "A collector bag helps overcome heterogeneity."

Once the gas is collected, it can feed into a cavity ring spectrometer or even

a mass spectrometer, which provides both TOC values and ¹²C¹³C isotope ratios, which are useful in determining the geographic origins of carbon-containing materials. Environmentalists have considered using isotope ratios from feathers or droppings to map bird migration, forensic food scientists use it to pinpoint the origins of high-value products such as olive oil, and pharmaceutical companies employ isotopes to detect counterfeits.

"NDIR should be considered the detection method of choice because it is interference-free and directly measures TOC generated during the oxidation step."

for process water, or in regulated industries that work with ultrapure water for processing, instrumentation, cleaning/cleaning validation, or human drugs. Other industries that regularly employ TOC analysis include pharmaceuticals, foods, forensics, oil and gas, and the life sciences.

TOC analysis involves sample acidification and oxidation down to CO₂, followed by detection and quantification. Acidification is used to remove

38

based analysis. Direct conductivity has a limited analysis range but is inexpensive, does not require carrier gas, and is sensitive to parts-per-billion (ppb) levels. Membrane-based conductivity is somewhat more complicated and takes longer, but is more robust and provides a greater analysis dynamic range.

NDIR should be considered the detection method of choice because it is interference-free and directly measures TOC generated during the oxidation step. Static pressurized concentration

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PRODUCT FOCUS: TOC ANALYZERS

As it catches on, TOC analysis on solids could replace approved, legacy test methods that were developed years ago for materials not normally thought of as carbon-bearing, such as concrete. This will take time, Mr. Lane says, because "only a certain number of people are willing to overcome inertia."

Competing technologies

Customers considering the purchase of a TOC analyzer, and particularly wondering whether to acquire a combustion or persulfate oxidation model, should consider potential down time and ongoing direct costs together. Although OI Analytical sells both instrument types, Mr. Lane suggests that persulfate may be superior to combustion for samples other than ultrapure water and measurements of very high molecular weight compounds, due to deterioration of various components over time. Nevertheless, he says the economic impact of various oxidation methods is difficult to quantify.

Although persulfate oxidation is preferred over combustion for some samples, the technology has shortcomings for very low-concentration measurements. According to Christopher Smith, senior product manager at Lab Synergy (Goshen, NY), Analytik

Jena's North American distribution partner, trace levels of carbon in the persulfate reagent may interfere with measurements or create difficulties in preparation of blanks. "It's hard to get persulfate clean enough," he says. "The reagent's carbon content becomes a limiting analvsis factor."

Lab Synergy has solved this problem by employing a very high energy, dual-wavelength UV source that oxidizes carbon-containing samples without persulfate.

Another Analytik Jena innovation is VITA, a software algorithm that compensates for changes in the flow of gases past the IR detector, which is flowdependent. This approach, Mr. Smith says, allows analysts to "vary sample size without affecting precision analysis. You can even achieve multipoint calibration with a single standard."

"Although persulfate oxidation is preferred over combustion for some samples, the technology has shortcomings for very lowconcentration measurements."

> 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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40 Lab Manager January 2011 www.labmanager.com



As part of our Lab Products Survey series, Lab Manager Magazine has compiled the responses of 175 lab professionals regarding the use of total organic carbon (TOC) analysis.

A mainstay of environmental and auglity control chemistry, TOC analyzers measure the carbon content of dissolved and particulate organic materials in water. The carbon measured may arise from any combination of living or dead organisms and chemical contamination.

TOC often serves as a surrogate for more difficult measurements, for example, contamination from petrochemicals, solvents, pharmaceuticals, chlorinated industrial chemicals and pesticides. It can also act as a screen for additional analysis. For example, pharmaceutical manufacturers might use liquid chromatography-mass spectrometry to analyze water samples containing unacceptable TOC values. As a quality measure, pharmaceutical regulatory authorities in the U.S., Europe and Japan require TOC analysis of ultrapure water used in biotechnology to ensure the absence of contaminating bacteria.

Purchasers of TOC analyzers value ease of use, throughput, and automation features. Based on the survey, respondents want to be able to set up a group of samples and walk away while the instrument does its thing. Another desirable feature is some sort of reporting and/or control function, which can be achieved by connecting analyzers to LIMS (laboratory information management systems), or for critical monitoring applications to a SCADA (supervisory control and data acquisition) or Ethernet network, whose supervisory functions will close down a plant or process when serious excursions occur.

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Number of TOC analyzers currently in respondents' labs: Respondents' plans for purchasing a new TOC analyzer:

	-	_	-	
None				30%
1				47%
2				13%
3				4%
5 or more				3%

Primary purpose for TOC analyzers in the lab:

Research	29%
Quality control	34%
Clinical	1%
Processing	10%
Other	27%

Types of TOC analyzers being used in respondents' labs:

Benchtop	75 %
Portable	11%
Online	13%
Other	1%

TOC analyzer components being used in respondents' labs:

, ,	•	
Autosampler		59 %
Inorganic carbon remover		30%
Soil sampling devices		6%
Other		6%

Respondents' preferred technology:

Wet chemical UV method	59 %
High-temperature combustion	41%

Respondents' interest in using total nitrogen (TN):

•	•	•	•	•
Using				11%
Not using, but interested				40%
Not using, and not interested				49%

Respondents' annual consumables budgets for items such as reagents, solvents and water standards:

Less than \$3,000	55%
\$3,000 to \$10,000	29%
\$10,000 to \$15,000	10%
\$15,000 to \$20,000	3%
\$20,000 +	4%

Starting the review process	9%
Plan to purchase in the next 1 to 6 months	9%
Plan to purchase in 6 to 12 months	6%
Plan to purchase in 12+ months	7 %
No current purchasing plans	60%
Don't know	10%

Primary reasons for purchasing a new TOC analyzer:

Replacement of an aging TOC analyzer	31%
Addition to existing systems; increase capacity	29%
Setting up a new lab	16%
First-time purchase	19%
Other	5%

Respondents' budget ranges for a new TOC analyzer:

	•
Less than \$10,000	28%
\$10,000 to \$20,000	31%
\$20,000 to \$30,000	19%
\$30,000 to \$40,000	14%
\$40,000+	9%

Factors/features that influence the decision-making process when buying a TOC analyzer:

Reliability	87%
Accuracy	87 %
Ease of use	84%
Low maintenance/Easy to clean	83%
Low operating cost	80%
Service and support	79 %
Price	71%
Warranty	60%
Speed	56%
Ease of installation	50%
Small footprint/size	37%
Energy efficiency	32%
Other	14%

Respondents' fields of work:

Environment	35%
Pharmaceutical industry	17%
Quality control	10%
Biochemistry and biology	8%
Chemical	7%
Hospital/Medical center	5%
Fuels	4%
Other	14%

ILLUMINATING THE MICRO AND NANO WORLDS

by Angelo DePalma, Ph.D.

During many decades of serving the life science, materials, medical, forensics, and environmental industries, microscopes have become an icon of laboratory work.

Microscope technology has diverged into three branches. Light microscopes, which view objects illuminated by visible light, have been around for centuries. Related are instruments that image nonvisible infrared or ultraviolet radiation, or ones that view fluorescence or Raman effects. All of these use optics to focus light into a viewing field, detector, or camera lens. Visible light microscopes, by far the most common type, are the subject of this article.

The second major microscope group consists of electron microscopes that use high-energy electrons to visualize objects at very high resolution. The third category, scanning probe microscopes, forms images by scanning a surface with a microscopic probe. Prices of electron and scanning surface microscopes have fallen remarkably over the last twenty years, but these techniques are primarily the domain of basic research groups at universities or high-level corporate R&D.

The technology behind visible light microscopes, arguably the oldest true laboratory instruments, has not changed much in fundamental opera-

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tion in two hundred years. Microscopes still consist of a light source, optics, and a stage for holding the specimen.

That does not mean that microscopy, and microscopes, are not evolving, says Lorne Davies, group manager at Olympus America (Center Valley, PA). "Some people believe that since microscopy has been around so long, it must be a stagnant industry. It's not obvious that you can make important changes to an old technology."

Mr. Davies admits that innovation tends to be incremental rather than earthshaking, but each stage of improvement "enhances what users are looking for, which is crisp, high-quality images."

How they've improved

Advances in optics, mainly of precision lenses, are difficult to come by due to the physical limitations of glass. Improvements do occur, most resulting in improved numerical aperture (the range of angles over which lenses can accept light).

But for medical and diagnostic laboratory workers, a special focus of Olympus, the most critical improvement is ergonomics. Microscopists working in a cytology or pathology laboratory sit at their instruments for many hours at a time. Ergonomically friendly microscopes help users maintain comfortable body positions, minimize repetitive stress, and lessen fatigue on shoulders and eyes.

"Today, all microscopes from reputable manufacturers are very good at producing high-quality images, so ergonomics becomes a differentiator and for some, a pivotal factor in purchase decisions," Mr. Davies tells *Lab Manager Magazine*. Ease of use is another related feature in high demand.

One exciting development in light microscopy has been the widespread adoption of fluorescence techniques. Fluorescence microscopy requires specialized reagents and equipment, including a camera to capture fleeting events. One fluorescence method, fluorescent in situ hybridization (FISH), enables investigators to identify and locate specific DNA sequences on chromosomes.

Another emerging technique is whole slide or "virtual" microscopy. This involves capturing microscope images and making them available on computer screens for later examination by one or more individuals. Virtual methods are useful for collaborative work, particularly in medical diagnostics.

Lab Manager January 2011 www.labmanager.com

What should potential buyers look for before purchasing a microscope? Mr. Davies puts a vendor's reputation, service, and support high on the list. "People have close relationships with their microscopes, and that closeness extends to companies selling them."

SEM resolution in a light scope?

This past year, Ravikiran Attota, Ph.D., a research engineer at NIST (Gaithersburg, MD), discovered a software technique that he claims provides the resolution of scanning electron microscopy (SEM) or atomic force microscopy (AFM) through a conventional light microscope. The technique, through-focus scanning optical microscopy (TSOM), uses a software trick, and no additional hardware, to reconstruct images rapidly and at low cost.

In fact, Dr. Attota claims that his method improves on SEM and AFM in that it combines their strengths. "SEM excels at lateral resolution, while AFM is best for vertical resolution," he says. TSOM achieves both through a paradoxical approach.

Optical microscopes cannot clearly visualize nanometer-scale features because the wavelength of visible light is larger than the object being imaged. Dr. Attota acquires many of these outconductors. "But TSOM should be of great interest to anyone who does microscopy," he says, particularly those involved in nanomaterials or nanostructures. For life scientists, the technique is particularly applicable to objects that change at different locations, for example cells.

"Prices of electron and scanning surface microscopes have fallen remarkably over the last twenty years."

of-focus, or "through-focus" images anyway, at different focal points. The computer program he wrote combines the images and reassembles them into a TSOM image with spectacular depth capabilities. Where AFM provides depth resolution of only 1 micron, TSOM easily reaches 100 microns and in tests has produced images with 200-micron depth resolution.

Dr. Attota's group works on nanometrology, "the measure of small things," with an emphasis on semi-

Dr. Attota has been working with Sematech, Intel, and several universities on the new technique.

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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LAB MANAGER'S INDEPENDENT GUIDE TO PURCHASING AN OPTICAL LABORATORY MICROSCOPE

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UPRIGHT

Modern microscopes are available in two basic frame types: the upright and the inverted, with the upright microscope being the most common type. An upright microscope has the illumination system below the stage and the lens system above the stage



The basic non-polarizing microscope offers lower magnification useful for many applications, including situations in

nchtop microscopes are the work horses of laboratory microscopes. They have an enormous range of applications in biomedicine, metallurgy and industrial sciences

A polarizing microscope uses polarized light for investigating the optical propertie of specimens. It was originally used in petrographic and mineralogical research, although it has now come to be used in such diverse fields as biology, medicine, polymer chemistry, liquid crystals, magnetic memory and state-of-the-art materials.

The basic, standard polarizing upright microscope is a cost-effective option and suitable for many basic applications including optoelectronics, developmental biolog marine biology, forensic science, medical devices, microelectronics and rocks/minera

Basic microscopes tend to offer magnification within the range 5x to 400x.















Advanced polarizing microscopes are suitable for digital imaging, including option of the foundation of the following including options:

hey tend to offer magnification in the range 40x to 5000x for observational application























MT9000 / MT9900 Se

7700 Series Pol







which a greater area of the sample must be viewed simultaneously.











4000 Series Labor

scopes are the most common type of upright microscope, and have many clinical and biological applications, including cell biology, molecular pathology, immunology, veterinary, formulation science, cytology, histology,

These microscopes are suitable for digital imaging, including options for fluorescence and darkfield. hey tend to offer magnification in the range 40x to 5000x, which is suitable for most laboratory purposes.











Motorized upright microscopes can be equipped with a motorized objective nosepiece, motorized fluorescence filt ube turret, motorized transmitted light condenser, or a motorized attenuation wheel for fluorescence excitation, or any

digital controller allows the synchronous operation of the motorized accessories for improved accuracy and ease of us











START HERE INTRODUCTION:

Microscopes have been used by scientists for centuries, and are now more widely relied upon than ever. Optical microscopes are the most common type of microscope found in a standard laboratory. They use optical lenses in order to magnify the image generated by the passage of a wave through the sample or reflected by the sample.

The typical magnification that can be achieved by a standard optical microscope in the visible light range is up to 1500x, with a resolution limit of around 0.2 µm. Resolution is limited by the wavelength of the radiation used. The spatial resolution of an optical microscope can be improved by using shorter wavelengths of light, including ultraviolet radiation.

INVERTED

Modern microscopes are available in two basic frame types: the upright and the inverted.

An inverted microscope has the illumination system above the stage and the lens system below the stage. Inverted microscopes are suitable for looking through thick specimens, such as dishes of cultured cells, because the lenses can approach closer to the bottom of the dish where the cells grow.

Motorized
The motorized inverted microscope provides options such as a motorized condenser, fluorescence filter turret, transmitted and reflected light shutters, and filter wheels.









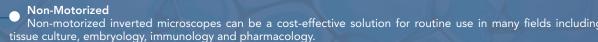








































STREAMLINING ROUTINE, REPETITIVE PIPETTING TASKS

by Angelo DePalma, Ph.D.

Automated liquid handlers (ALHs) are one of the truly enabling technologies of modern life sciences, particularly in medical testing, biological research, and high high-throughput screening. Ap-

plications in combinatorial chemistry and materials investigations were considered emerging a decade ago, but these markets remain small.

Liquid handlers use robotically controlled pipettes to deliver precise quantities of liquid reagent to reaction vessels, more often than not to microtiter plates. Major instrument manufacturers include Beckman Coulter, Tecan, PerkinElmer, Eppendorf, QIAGEN, and the two firms interviewed for this article.

"Automated" is the functional word in ALH markets. Once a method is entered, robots are expected to deliver fluids continuously and precisely (both in terms of location and quantity), with extremely high reproducibility, often nearly continuously.

Simplicity but not simplistic

Manufacturers of ALHs are feeling pressure to simplify, to offer prod-

ucts that resemble workstations rather than stand-alone instruments. "That doesn't mean they want simplified capabilities," says Isaac Meek, technical specialist at Caliper Life Sciences

"Manufacturers are feeling pressure to offer products that resemble workstations rather than stand-alone instruments."

(Hopkinton, MA). "They want the features and functions, but they also want to be productive without having to be programming experts."

Caliper and other vendors therefore "encapsulate" or standardize methods to liquid handler configurations, thus multiplying the instruments that can benefit from specific methods. Users need only dial up the method and apply it to their workflow, without investing a lot of effort into becoming an automation or methods development expert. "Nobody wants to become intimately familiar with details like those," Mr. Meek says. "We see demand for this from several corners of the industry, including genomics, proteomics, and compound management."

Another significant trend, according to Mr. Meek, is shrinking instrument size

and discrete systems rather than complex, cobbled-together devices reaching across an entire lab. "Users want desktop-sized instruments that will not interfere with other equipment." With

> more-compact footprints have come software improvements that positively affect usability.

> Users increasingly look for true walk-away automation, a

capability that, according to Mr. Meek, has been often touted but rarely delivered. Increasingly, instruments can handle complex operations without human intervention and send a text message to indicate that the job is complete.

All these benefits are a result of a common factor in lab instruments: the disappearance of the instrument specialist. Organizations used to have core mass spec or microscope facilities. "Those days are gone," says Mr. Meek. "Now we're seeing a genomics core consisting of several pieces of high-tech instrumentation, where workers are expected to be familiar with several instruments. We've gone from an instrument or methods focus to an application focus."

Another important trend, which first became prominent during the high-

throughput screening era in pharmaceuticals, is the ability to track and monitor samples as they wind through the workflow. "This began with screening, then became common in genomics, and now it's everywhere."

Accuracy

Pipetting accuracy and calibration, which go hand in hand, are significant operations or features, depending on one's perspective, in automated liquid handling.

Calibration is usually done gravimetrically, but the weakness of this approach is that by weighing the entire plate (the standard method) one obtains the average volume delivered but no inkling of tip-to-tip variability.

"When we introduced our first liquid handler in 1990 for emerging high-throughput screening applications, there was greater concern for coefficient of variation than for absolute accuracy," says Tom Astle, president of Tomtec (Hamden, CT). "Users wanted and expected all samples to be the same. Today, with the emphasis on bioanalysis, accuracy is king."

Issues in delivery accuracy vary depending on the type of displacement used. Air displacement, which uses disposable tips, creates the most pipetting variation, according to Mr. Astle. "Depending on how the tips are made, you can have considerable variation, depending on whether the tip surfaces wet or not and how much liquid clings to them."

With positive displacement pipetting, the piston plunges to the bottom of the tip's orifice, so there is no air gap or dead air volume that can affect dispensing. Positive displacement delivers superior tip-to-tip reproducibility, Mr. Astle says, but by necessity it requires tip cleaning, another possible source of error.

Purchase decisions

Mr. Meek mentions three factors that potential buyers should consider when shopping for an automated liquid handling system:

• Software versatility and ease of use: How easy is it to learn? Does the instrument come with useful software

- content or methods? How steep is the learning curve?
- Instrument size and configuration: Liquid handlers should not require special tables or space, or dedicated hoses or power supplies.
- · Flexibility, expandability, and ability to integrate with other systems if needed. These benefits are important if labs expect increased throughput needs or if methods change.

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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SOURCES OF ELECTRICAL ENERGY FOR ELECTRONICS TESTING

by Angelo DePalma, Ph.D.

Power supplies provide steady, precisely controlled electrical energy to electronic equipment. Anyone who has built or worked with a desktop computer recognizes the power supply—typically the bulkiest component—sitting behind the electrical inlet socket.

One type of supply, the uninterruptible power supply, powers electronics in the event of an emergency such as a blackout by keeping a battery constantly charged. When the main power goes out, the battery takes over before the equipment can power down.

which enable users to plug them into a common electrical wall outlet. The power supply first uses a rectifier to convert house alternating current (AC) into direct current (DC), the only type that common instruments and devices use. It then adjusts the current and/or voltage upward or downward to meet the needs of the instrument. Throughout the device's circuitry, additional power circuits step up or step down the current according to the various subcircuits' needs.

One way to differentiate power supplies is to look at how they operate.

Switching power supplies use a switching generator to harness efficiencies when converting electrical energy

from the grid's AC to specific DC current and voltage requirements. Switching supplies work by rapidly turning on and off. Linear power supplies operate at constant, precisely controlled voltages.

Switching power supplies are common as embedded supplies for personal computers because of their high efficiency and small footprint, but they tend to be electrically noisy and don't regulate as well as linear power supplies, says David Pereles, marketing segment manager at Tektronix (Beaverton, OR).

Stand-alone power supplies, including uninterruptible supplies, do make sense in non-electronics labs when a lot of equipment runs on the same voltage, says Mark Swift, business development manager at Universal Electric (Canonsburg, PA). "It's easier to provide the right electrical energy from a single piece of gear." Other benefits are ease of connectivity and protection against heat or loss of power.

Physics and chemistry labs, particularly R&D and academic labs, use power supplies to drive basic equipment, for example in electroplating and electrochemistry work, or to supply direct current in much the same way as a battery. Biology laboratories, for example, employ power supplies to drive gel electrophoresis equipment.

Electrical/electronics lab power supplies come in three major types, depending on the work being done. Constant voltage supplies provide configurable DC voltage that is adjustable over a specific range that includes zero voltage. Constant current supplies output-regulated current independent of the voltage. Constant voltage/constant current devices provide either voltage or current.

"Most common lab instruments have their own integrated power supplies, which enable users to plug them into a common electrical wall outlet."

Uninterruptible power supplies are rather uncommon in most labs, except for stand-alone computer equipment that might suffer from data loss. Academic and industrial research organizations usually have house backup generators for heavy equipment and instrumentation, and backups for both computer power and data.

Most common lab instruments have their own integrated power supplies,

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But by far the most common venues for power supplies are electrical testing, design, and fabrication laboratories. As they are being built, prototype circuits lack a pre-packaged power supply, so the designer will utilize one of the three power supply types according to the circuit's specifications. Power supplies are also used to design and troubleshoot subcircuits, and to repair or diagnose problems with instruments or circuits whose power supplies have failed.

Varying voltage or current is common when prototyping an electrical circuit to do a particular task, such as timing, counting, or signal processing. "Certain circuits rely on variable voltage thresholds," Mr. Pereles says. "Changing the voltage is useful when performing a comparison of how the circuit operates at different voltages, or in supplying accurate reference voltages or currents."

Purchase decisions

Mr. Pereles says that choosing the right power supply should follow a "fairly predictable sequence or decision tree."

The first consideration is what voltage and current are needed. "The answers to those two questions will narrow the field quite a bit."

"Most laboratory bench units supplying outputs on the order of 30V and 5A sell within a narrow price range, typically \$400 to \$1,200."

Next, users should consider how many outputs they need. An uninterruptible power supply connected to a single computer might only need half a dozen, while a supply shared by two or three technicians in a repair or testing facility should have two or three times that number.

Price is often a second-tier consideration, since most laboratory bench units supplying outputs on the order of 30V and 5A sell within a narrow price range, typically \$400 to \$1,200.

Then come the finer points: accuracy, output noise, the ability to respond to load changes, stability when the AC voltage changes, and variable output. "Certain lab procedures may require changing the current or voltage over time," says Mr. Pereles. Some power supplies are computer-controlled for such operations and require a separate voltage or current meter. Some have these functionalities built in, as well as microprocessor control. "Power supplies are getting smarter, displays are getting better, and the units generally can

do more with each succeeding generation," Mr. Pereles observes.

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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As part of our Lab Products Survey series, Lab Manager Magazine has compiled the responses of 460 lab professionals regarding the use of laboratory balances in the lab. Today's analytical lab balance is a product of over 60 years of continuous innovation from a handful of equipment manufacturers around the globe. Each improvement has aimed to increase the analytical lab balance's precision, accuracy or reliability for researchers. The origins of the modern analytical lab balance date back to the short-beam analytical assay balance produced by Sartorius in the early 1900s.

Balances and scales used in laboratories today come in various shapes and sizes. Although often used interchangeably, scales and balances have different uses. A balance compares the mass of two sets of objects, while a scale determines the mass of an object or set of objects. The most common types in use today are beam balances, spring balances, top-loading balances, analytical balances, precision scales, and moisture analyzers.

In purchasing a new lab balance, respondents identified accuracy, versatility of use, and the need for precision as the most important factors that influence the decision-making process.

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Number of balances used in respondents' labs:

1	13%
2	23%
3	18%
4	12%
5 or more	39%

Primary purpose for balances in the lab:

Research	42%
Quality control	29%
Production	13%
Clinical	7%
Other	10%

Types of balances respondents use in their labs:

Analytical balance	38%
Microbalance	8%
Portable balance	8%
Precision balance	23%
Top-loading balance	23%
Other	1%

Balance components respondents use in their labs:

Moisture analyzer	11%
Vibration isolation table	15%
Balance enclosure	19%
Balance printer	10%
Calibration weights	42%
Other	2%

Respondents' purchasing plans for a new balance:

Starting the review process	5%
Plan to purchase in the next 1 to 6 months	9%
Plan to purchase in 6 to 12 months	9%
Plan to purchase in 12+ months	7%
No current purchasing plans	61%
Don't know	8%

Primary reasons for purchasing a new balance:

Replacement of an aging balance	39%
Addition to existing systems; increase capacity	38%
Setting up a new lab	16%
First-time purchase	1%
Other	5%

Budget range for the purchase of a new balance:

Less than \$500	13%
\$500 to \$1,500	20%
\$1,500 to \$3,000	42%
\$3,000 to \$9,000	19%
\$9,000+	7 %

Factors/features that influence the decision-making process when buying a balance:

Reliability	98%
Durability	94%
Low maintenance	90%
High precision	88%
Price	87%
Easy cleaning	82%
Reputation	81%
Past experience	78%
Auto calibration	72 %
Sealed control panel	57 %
Currently using	55%
Recommendation	51%
Large display	34%
Communication port	33%

Respondents' fields of work:

•	
Automotive	2%
Biochemistry and biology	19%
Building materials chemistry	3%
Detergents, surfactants and cosmetics	4%
Energy and power plants	2%
Environment	11%
Fertilizers, base materials and explosives	2%
Food and beverages	5%
Forensic chemistry	2%
Fuels	2%
Metal industry	3%
Organic chemistry	8%
Paints, lacquers and solvents	2%
Paper and pulp	1%
Photography and optics	0%
Plastics	3%
Plating and galvanics	1%
Semiconductors and electronics	2%
Textiles, leathers and ceramics	2%
Toxicology	4%
Other	13%

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SK THE EXPERT

YOUR NEEDS by Tanuja Koppal, Ph.D.

Marc Ferrer, Ph.D., Team Leader at the Chemical Genomics Center, which is part of the National Human Genome Research Institute at the National Institutes of Health, talks to Tanuja Koppal, Ph.D., contributing editor at Lab Manager Magazine, about the need for automation in various laboratory settings. Ferrer emphasizes the need for using "fit for purpose" automation and addresses the key questions that factor into the decision making. He also highlights the issues that impact the effective implementation and use of automation once the decision has been made.

Why should lab managers consider bringing automation into their laboratories?

A. The first thing that people need to think about is what it is that it to do, and what is the ultimate goal. That is really going to determine why and how much automation they really need. The advantages of automation are obvious in terms of achieving sample throughput, experimental reproducibility, gaining time and reagent savings, all of which translate to cost savings. Those are some of the direct benefits, but there are also some indirect benefits to automation. Once you start thinking about automation, you start thinking about next steps. You think about reagent stability, assay readouts, assay windows and miniaturization,

and that leads to the development of more reliable and robust assays.

How do you decide on how much you need to automate?

↑ • How much automation you need really depends on where you are, whether in industry or academia, in a small lab or a big lab, in an individual lab or a centralized core lab. and what it is you are trying to achieve. If you are in a centralized high-throughput screening (HTS) group in a big pharmaceutical lab, then you probably need an integrated robotic system, with good compound management coupled to a robust Laboratory Information Management System (LIMS). If all you are looking for is increased throughput and you don't really have to deal with diverse assays and readouts, then you want to think about miniaturization. If you are in a small biotechnology lab where you work on a specific therapeutic area, or if you are in a core academic lab, you may still need an integrated robotic system, but you will also need more flexibility in terms of assay readouts and formats. If you are a principal investigator (PI) in an academic lab, bringing in automation can be expensive, and it would then make sense for a few Pls to get together and jointly buy liquid handling or reader capabilities. You don't need the equipment to be integrated, because integration comes coupled with LIMS and

having expertise and trained personnel to run the robots. So with a few nonintegrated pieces of equipment, you can get the throughput you need without a huge investment.

How do you decide what you need in terms of automation?

 $oldsymbol{\Lambda}$ • First define your goals, then talk to the **H** experts about the type of automation you need. Go to automation meetings and conferences, or go to your local HTS groups and explain what you are trying to do and get their advice. Ask lots of questions about what instrument works best for what assays, and then decide what would best serve your needs. We all have our own favorite vendors and equipment, so try to get opinions from several people. Get critical information related to versatility, robustness, technical support and training; this is going to be very important in getting the infrastructure up and running. You have to do your homework and find out what people are happy with, before talking to the vendors and making any kind of investment.

How do you set budgets and priorities and allocate costs?

A: Define your scope, talk to the experts and find out what you are going to need. Once you have set a mandate, you will know what you need but you may not know

Marc Ferrer received his B.Sc. in Organic Chemistry from the University of Barcelona, Spain, in 1989. In 1994, he earned his Ph.D. in Biological Chemistry from the University of Minnesota, Minneapolis, working on new methodologies for peptide synthesis and studying the molecular basis for protein folding. He then moved to the Department of Molecular and Cell Biology at Harvard University, Cambridge, as a postdoctoral fellow, where he used combinatorial chemistry and phage display methodologies to identify peptides and peptidomimetics that blocked HIV infection. In 1999, he joined the Department of Automated Biotechnology, the Central HTS group at Merck Research Laboratories, developing assays and implementing high-throughput screens for lead and target identification. For the last ten years, he developed extensive expertise in assay development and miniaturization to implement small molecule high-throughput screening in 1,536- and 3,456-well formats for lead identification. He also implemented siRNA HTS for target identification, developing new automation-friendly siRNA transfection protocols, improved data analysis tools for hit selection, and strategies for better on-target hit validation. He also used large-scale chemical genomics approaches for more efficient target and lead identification and pathway mapping in physiologically relevant cellular systems, combining assays with multiplexed readouts with compound/RNAi libraries. Recently, he joined the NIH Chemical Genomics Center, where he is a Team Leader in the Biomolecular Profiling and Screening group, and where he continues to develop and implement chemical genomics approaches using small molecule and siRNA screens to identify tools to functionally probe biological systems and develop new therapeutics for rare and neglected diseases.

what it is going to cost. Then go to the vendors and tell them what you are looking for, and start getting quotes on the equipment needed. You can then go back to the source that is funding your investment and tell them what it's going to cost. It's an iterative process, with sets of reality checks on what is doable and what is not. If you are in a small lab, work with your core group to see if they can demonstrate

In your opinion, what are some of the biggest mistakes that people make when it comes to automation?

A. Some people try to do it themselves and build everything from scratch by putting together bits and pieces of equipment with the help of someone who is technically savvy. The problem there is you then spend more time building and maintaining the system than

actually using it. So when you identify what you need, leverage the vendors to get you going rapidly. The do-ityourself approach, without the right support and expertise, has led to some of the biggest and most costly mistakes made. Don't reinvent the wheel; instead, choose a vendor who can provide prompt, affordable service to minimize any downtime. Establishing good relationships with the vendors is critical for the day-

to-day running of these instruments, which are quite sophisticated and not always easy to fix. Sometimes, people also forget about the data management involved. There are different sets of tools for data processing, data mining and data

visualization, and you cannot build the hardware infrastructure without thinking about how you are going to track and analyze the data. Finally, think about automation beyond your current application and build an infrastructure that can be easily modified for other applications.

How do you plan for downtime for routine maintenance and equipment breakdown?

With time and experience, you can estimate how much buffer time you need to build in for preventive maintenance and downtime. In a centralized core lab, you can get historical data to help you plan things out and have good backup systems in place. Having an infrastructure to minimize downtime is critical.

What is the current trend in lab automation?

A • I think the trend these days is toward "fit for purpose" automation. People are not buying a fully automated robotic system just because they can afford to do so. People are thinking early and more clearly about what they need and are building the infrastructure around it. The trend is to buy smaller integrated systems that are more flexible and will allow you to do more biology and more assay readouts. The large, centralized HTS groups may still rely on big integrated systems, but for most other screening groups the flexibility to adapt to different assays is becoming important.



Fully automated, ultra-high-throughput robotic screening systems from Kalypsys Inc., currently in use at the laboratories of the Chemical Genomics Center at NIH. (Source: Marc Ferrer, Ph.D.)

what works for you and what doesn't. On the other hand, if you are in a core group, identify your customers and find out what they need and how you will be working with them.

MIND MAP FOR INCREASING By John Buie GC OUTPUT INCREASES IN GC OUTPUT CAN OFTEN BE ACHIEVED THROUGH RELATIVELY MINOR ADJUSTMENTS IN OPERATING PARAMETERS

This MIND MAP outlines some thought processes designed to help identify potential performance-enhancing changes.

GC is an important analytical and preparative technique, requiring skill and experience to operate effectively. However, no matter how skilled or experienced the operator, GC output can often be improved by simple adjustments in the set-up or selected operating parameters.

The following MIND MAP offers some suggestions for how GC output can be improved relatively easily. The different components and settings that are likely to have the biggest influence on output are discussed, together with suggestions for modifications to improve overall performance.

IN-HOUSE

Some training companies offer in-house training courses where users may be trained on the equipment available. This is a particularly appealing option if several users need to be trained at one time.

ONLINE

Some courses are available online for users to follow at their own convenience. Particularly suited to theoretical training. Considerable resources are also available online.

BUY NEW EQUIPMENT

For current models and latest technology.

BUY REFURBISHED EQUIPMENT

For cost savings, while still enjoying much of the functionality of newer models.

EVENTS

Conferences and meetings are a useful way to expose staff to the rigors of GC.

THERMAL CONDUCTIVITY (TCD)

Universally selective, with a detectability of around 1 ng.

INSTIGATE USER TRAINING

GC is a complex technique requiring skill and experience to derive the best outcomes. If output is falling below what is expected, consider instigating staff training, particularly if users are new or inexperienced. Staff training is an essential part of GLP compliance. It may also contribute to Continuing Education.

ELECTRON CAPTURE (ECD)

Selective for halides, nitrates, nitriles, peroxides, anhydrides and organometallics. Detectability is around 50 fg.

CONCENTRATION DEPENDENT DETECTOR

The signal is related to the concentration of solute in the detector, and does not usually destroy the sample. Dilution with make-up gas will lower the detector's response.

GC DETECTOR

Many detectors are available, offering different types of selectivity. Selective detectors respond to a range of compounds with a common physical or chemical property and specific detectors respond to a single chemical compound. Consider varying the GC detector for improved output.

FLAME PHOTOMETRIC (FPD)

Selective for aliphatics, aromatics, ketones, esters, aldehydes, amines, heterocyclics, organosulfurs and some organometallics. Detectability is around 2 pg.

FLAME PHOTOMETRIC (FPD)

Selective for sulfur phosphorus, tin, boron, arsenic, germanium, selenium, chromium, using hydrogen and air as support gases.

Detectability is around 100 pg.

FLAME IONIZATION (FID)

fected by the make-up gas.

Selective for most organic compounds, using hydrogen and air as support gases. Detectability is around 100 pg.

MASS FLOW DEPENDENT DETECTORS

NITROGEN-PHOSPHORUS

Selective for nitrogen and phosphorus, using hydrogen and air as support gases. Detectability is around 10 pg.

HALL ELECTROLYTIC CONDUCTIVITY

Selective for halide, nitrogen, nitrosamine and sulfur, using hydrogen and oxygen as support gases.

COMPREHENSIVE TWO-DIMENSIONAL CHROMATOGRAPHY (GCXGC)

The signal is related to the rate at which solute molecules enter the detector. The

sample is usually destroyed. The response of a mass flow dependent detector is unaf-

As each "fraction" emerges from the first GC column, it is cryofocused (condensed and concentrated with a burst of very cold air) and then applied to a second, orthogonal column, with a narrow internal diameter and fast flow rate. The result is both higher, sharper peaks, and enhanced chromatographic separation.

STIR BAR SORPTIVE EXTRACTION (SBSE)

A dynamic variation of SPME in which a spinning glass-covered magnetic bar is used to adsorb analytes, which can be removed by thermal desorption in the gas chromatographic injection port.

SOLID-PHASE MICROEXTRACTION (SPME)

Used for gaseous and liquid samples. A fused-silica polymer coated fiber is exposed to the stirred sample. The shielded fiber is then inserted into the injection port of the gas chromatograph.

INVEST IN NEW EQUIPMENT

Any of the components of the GC system, or the entire system, may need to be replaced at some time. At this stage, the principal decision is whether to buy a brand new system or component, or a refurbished version. Refurbished equipment can often have similar specifications to newer models but may be available for a greatly reduced capital outlay. Many refurbished models also carry a guarantee.

SOLID-PHASE EXTRACTION (SPE)

This technique is used to concentrate analytes from gaseous or liquid samples. The adsorbed analytes can be eluted with a solvent or thermally desorbed.

IMPROVE SAMPLE PREPARATION

Sample preparation is an essential step in gas chromatography and can be the most errorprone and labor-intensive task in the process. A number of techniques for GC sample preparation are available, and GC output can be greatly enhanced by selecting the most appropriate method and accurately following it. Most sample preparation techniques for GC are based on variations of extraction theory whereby the sample solvent, temperature, pressure, phases or volume may be altered.

ACCELERATED SOLVENT EXTRACTION (ASE)

Used for solid and semi-solid samples. Elevated temperatures and pressures used in these techniques cause hydrogen bonds and dipole interactions to be reduced, and surface wetting is increased.

MICROWAVE-ASSISTED EXTRACTION (MAE) (OR MICROWAVE-ASSISTED SOLVENT EXTRACTION (MWE))

Similar to ASE. The extraction container must be microwave transparent, while the solvent used may be either microwave absorbing or non-microwave absorbing. Ultrasonic vibrations may be used to assure good contact between sample and solvent in ultrasonic extraction (USE).

INCREASE MY GC OUTPUT

STATIC HEADSPACE TECHNIQUE

Volatile analytes are equilibrated in a closed vial at a specified temperature and pressure. A gas-tight syringe is used to transfer the headspace sample into the gas chromatographic injection port.

DYNAMIC HEADSPACE TECHNIQUE

Analytes are swept or purged onto an adsorbent platform and then thermally desorbed into the gas chromatograph.

MULTIDIMENSIONAL GC

Multidimensional gas chromatographs have been developed for more efficient separation than can be achieved with a single column.

When refining GC technique, the most appropriate detector or detectors will depend largely on the expected application, and anticipated sample throughput.

VARY EXPERIMENTAL CONDITIONS

Effective GC depends on the appropriate selection of components and conditions.

- Column size
- Stationary phase
- Mobile phase

INJECTION TECHNIQUE

Several injector types are available. Good injection technique is essential for efficient GC output and should:

- allow accurate and reproducible injections of small amounts of representative samples
- induce no change in sample composition
- not exhibit discrimination based on differences in boiling point, polarity, concentration or thermal/ catalytic stability
- be applicable for trace analysis as well as for undiluted samples.

HEART CUTTING

Selected sections of the sample that emerge from one column are introduced into a second, orthogonal column (one whose separation medium differs from that of the first column).

DIRECT INJECTION

A sample is injected, flash vaporized, and passed directly to the column. However, it can be difficult to reliably inject small sample volumes.

SPLIT INJECTION

Only a fraction of the injected sample passes to the column; the rest goes to waste.

SPLIT-SPLITLESS INJECTION

The amount of analyte injected can be varied using software before an injection is made. This is called the split ratio and is a function of the ratio of gas flow through the GC's injector, as controlled by pressure/gas flows in the injector.



DECIPHERING MSDS

WHAT THEY ARE AND WHY YOU NEED THEM by Vince McLeod

A little more than one year ago, an entirely preventable tragedy occurred when a UCLA research assistant was burned over 43 percent of her body and died 18 days later in a hospital burn unit. While using a plastic syringe to extract a small amount of t-butyl lithium—a chemical compound that ignites instantly when exposed to air—she was engulfed in a flash fire when the syringe came apart in her hands. The accident was attributed

to poor technique, improper method, poor training and a lack of supervision. A quick reading of the compound's MSDS might have prevented this terrible loss.

A good system for chemical management begins with a complete inventory of the laboratory's chemicals and an MSDS collection for those materials. This column explains what an MSDS is, what information it contains and how to best use that information.

MSDS is an acronym for material safety data sheet. The purpose of the MSDS is to inform chemical users of the potential hazards encountered with a chemical's use. Both the Occupational Safety and Health Administration

(OSHA) and the Environmental Protection Agency (EPA) have published regulations dealing with MSDSs. However, most chemical products packaged for consumers and general household uses are exempt from these requirements. We will focus on the OSHA regulation as it applies to all employers and their workplaces. We will begin first with a little history.

MSDS history and regulations

In the 1940s, the Chemical Manufacturers Association (CMA) began producing chemical safety data sheets (CSDSs) for many chemicals used in commerce. These were very detailed in their coverage, the longest of which was some 46 pages. CSDSs are no longer produced or supported by the CMA.

In 1985, the OSHA Hazard Communication Standard (29 CFR1910.1200)² became effective, requiring manufacturers and distributors to provide MSDSs to their customers. In 1987, this was expanded to "all employers with employees exposed to hazardous chemicals in their workplaces." The OSHA definition of a hazardous chemical is broad—"any chemical which is a physical hazard or a health hazard." We do not know many

chemicals that would fall outside that definition. Do you?

Although the hazard communication standard (HCS) does not require a particular format for the MSDS, it does specify what information must be included. Since the HCS does not specify a format for MSDSs, wide variation existed in the order and completeness of the required information by the many different manufacturers and distributors. Recognizing this problem, the CMA worked on developing a voluntary guidance document in an effort to improve the completeness, accuracy and consistency of MSDSs. In 1993, the American National Standard Institute

published the first standard for preparing material safety data sheets on hazardous industrial chemicals (ANSI Z400.1-1993)³, an MSDS format containing 16 sections. The current standard is now Z400.1/Z129.1-2010.

MSDS content

The ANSI Z400.1 format for MSDSs incorporates all the information required under the OSHA Hazard Communication Standard (plus a few extras). The ANSI format lists sections in a logical sequence and has gained acceptance by most manufacturers and distributors. Thus, our discussion and comments on MSDS content will follow the ANSI design.

"In 1993, the American National Standard Institute published the first standard for preparing material safety data sheets on hazardous industrial chemicals."

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Section 1: Chemical Product and Company Identification

The contents of this section are obvious: the chemical and/or product is named here along with the manufacturer or distributor, and should include the company mailing address and telephone number. A key to this section is that it should relate the MSDS to the container label and shipping documents. Other useful information that is usually included is a brief description of the chemical or product and its general use. Most companies will also give the date the MSDS was written or the date it was last revised.

Section 2: Composition, Information on Ingredients

This important section identifies the hazardous components and amounts of each for the product. This is where you look to see what you are dealing with. The chemical abstract service (CAS) number should be given as this number provides positive identification of each component. The CAS number is important with the many different naming conventions and pseudonyms in use. This section also provides information on published exposure limits, if applicable, such as OSHA permissible exposure limits (PEL), American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit values (TLV), and others like IDLH (immediately dangerous to life and health) limits. If any of the components or their amounts are trade secrets, it must be stated here.

Section 3: Hazards Identification

The material's appearance, odor, health, and physical and environmental hazards are listed in this section. The information here expands on the previous section, providing details on each component's hazards, routes of exposure, symptoms for both acute and chronic exposures, and target organs for each exposure route. Information on flammability, reactivity and proper personal protective equipment should also be given.

Section 4: First Aid Measures

Instructions on emergency and first aid procedures are provided for each potential route of exposure, e.g., inhalation, ingestion, skin or eye contact. They should be concise and written in easily understood layman's language. If there are specific medical steps, then a "Notes to Physician" section is provided for this information.

Section 5: Firefighting Measures

Described in this section are the fire and explosive properties of the chemical or product components. The proper extinguishing media is given, along with any special protective equipment needed and unusual decomposition hazards. Additional information such as flashpoint, autoignition temperature and flammable limits in air are helpful depending on the chemical components.

Section 6: Accidental Release Measures

Addressed in this section are the proper responses to any spill or leak of the material. The information presented is usually intended for emergency response personnel. It describes the personal protective equipment needed and any special precautions—such as ventilation or evacuation, cleanup methods and environmental considerations.



Section 7: Handling and Storage

This section and the following one are very important for laboratory personnel and chemical managers. This section contains guidance for minimizing potential hazards while handling and storing the material. Addressed here are requirements for types of containers and dispensing equipment as appropriate. Also covered in this section are conditions to avoid, such as temperature extremes, secondary containment, and work and hygiene practices.

Section 8: Exposure Controls, Personal Protection

Discussed in this section are the engineering controls and personal protective equipment (PPE) to be used when handling the material. The need for any ventila-



DON'T ALLOW EXPERIMENTS TO RUN UNATTENDED UNLESS THEY ARE FAILSAFE

By James A. Kaufman

There are surely going to be times when experiments must continue running on their own while you do other things (go out to lunch or home to sleep). At these times, it's important to consider all the things that could go wrong in your absence and to prepare for them.

For example, what would happen if there were a power or compressed air failure and the stirrer were to shut down? What if the water gets turned off or a cooling hose detaches? Get the idea? Cooling hoses need to be clamped or wired on.

What about the water shut down? Do you need a special sensor for water, temperature, pressure, fluid level, etc. to control the experiment in your absence?

The name, address, and phone number of the person responsible for an experiment should be prominently displayed. In addition, clear directions should be provided on how to safely shut down the experiment in your absence. Special hazards and precautions should be noted. Your experiment shouldn't become someone else's land mine.

Unattended experiments should be set up in such a way that they "fail safe." They automatically shut down if a failure occurs rather and create a runaway situation (overheating or over pressurizing).

Source: Kaufman, James A., Laboratory Safety Guidelines - Expanded Edition, The Laboratory Safety Institute, www.labsafetyinstitute.org

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tion or special exhaust systems is covered, along with requirements for eyewash and safety showers. Laboratory personnel should focus on PPE instructions, which provide proper eye, hand and body protection, and whether respiratory protection is needed.

Section 9: Physical and Chemical Properties

Of particular interest to chemists, the information presented here assists users in determining proper PPE, handling and storage. General appearance, odor and physical state (liquid, solid or gas) are given in addition to pH, vapor pressure and density, specific gravity, boiling point and others depending on usefulness. Any warning properties (i.e., how to detect the substance via smell, taste or feel) should be well noted.

Section 10: Stability and Reactivity

Although more important for emergency responders, users should also be familiar with the information in this section, which depicts potentially hazardous reactions or decomposition products. Examples include evolution of hazardous gases or production of heat if involved in a fire. Any incompatibilities that could lead to hazardous conditions should also be discussed here.

"Laboratory personnel should focus on PPE instructions, which provide proper eye, hand and body protection, and whether respiratory protection is needed."

Section 11: Toxicological Information

Information listed in this section is drawn from both animal testing and human experience, and should include all known toxicities of the material. Included are both acute and chronic effects on skin, eyes, immune system and reproductive system, as well as from inhalation or ingestion. Data on irritancy, sensitization and carcinogenicity should also be stated.

Section 12: Ecological Information

Potential impacts should the product be released to the environment are presented here. Data on the expected environmental fate and whether degradation occurs is given, along with effects on plant, animal and aquatic life.

Section 13: Disposal Considerations

Guidance given here is intended for use by both technical and waste management people—to evaluate waste treatment options. Usually a reference is made to follow all applicable federal, state and local regulations.

Section 14: Transport Information

This section provides information for shipping the material. In general, this means following the U.S. Department of Transportation (DOT) regulations contained in 49CFR172 and includes listing the proper shipping name, hazard classification number and description, UN identification number, and North American Emergency Response Guidebook number, as applicable. Information on international shipping may also be given.

Section 15: Regulatory Information

The chemical or product's regulatory status is presented in this section. Included are the reporting requirements, threshold planning quantities, release reporting quantities and inventory status under the U.S. Superfund Amendments and Reauthorization Act (SARA); Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA); Toxic Substances Control Act (TSCA) and other federal and state regulations, as applicable.

Section 16: Other Information

This section is intended for material that does not fit into any of the preceding sections; yet, the preparer feels it is pertinent. Usually included are the preparer's name and contact information, revision dates, references and definitions of terms and acronyms.

Final Words

As you can now see, MSDSs are complex and take some work to understand. But if you make the effort to get to know the layout and information they contain, they can provide valuable information and be a reliable asset that you turn to in times of need.

- "Deadly UCLA Lab Fire Leaves Haunting Questions," Christensen, Kim, Los Angeles Times, March 1, 2009, http://www.latimes.com/news/local/la-me-uclaburn1-2009mar01,0,3624028.story.
- 2. Hazard Communication, US Department of Labor, Occupational Safety and Health Administration, Washington, D.C., February 1996, http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10099.

 American National Standard for Hazardous Industrial Chemicals—Material Safety Data Sheets—Preparation, ANSI Z400.1-1993, American National Standards Institute, New York, 1993.

Additional Resources:

http://www.ehs.cornell.edu/msds/msds.cfm—excellent page of links to various MSDS locations and sites

http://www.msdssearch.com/—another great web page for searching MSDS

Vince McLeod is an American Board of Industrial Hygiene—certified industrial hygienist and the senior industrial hygienist in 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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LAB SAFETY AUDITS EXPOSED

OUTSIDE EVALUATIONS REVEAL CRITICAL ISSUES AND CONCERNS by James A. Kaufman, Ph.D.

Over the past 30 years, I've conducted thousands of audits and inspections of laboratories and other workplaces. In addition to labs, those inspections have included storage rooms, classrooms, and areas such as fire departments, artist studios, crime labs, jails, libraries, and theaters. I have also been training personnel in how to conduct these audits and inspections.

This article is a portion of a Laboratory Safety Institute (LSI) publication, *Audits and Inspections: A Summary of Recommendations*, summarizing the recommendations from my audit and inspection reports over the past several years. Some general lab safety recommendations have also been added. It is intended to provide a broader overview of the types of issues and concerns raised during these consultations.

Having an outsider evaluate your workplace can be very helpful, as an outsider is not unbiased but differently biased. An outsider questions and compares in ways that insiders may not feel comfortable.

There's another issue. It's very difficult for insiders' voices to be heard. Colleagues are often unable or unwilling to hear the insider's voice. So, having an outside review can be very helpful in getting the message across to colleagues and management/administration.

Summary of Audit/Inspection Recommendations

Biological and Animal Hazards

- 1. Use dissecting specimens preserved with non-formaldehyde (formalin) preservatives.
- 2. Store scalpels all pointing away from you.
- 3. Store syringes in locked drawers or cabinets.
- 4. Ensure proper care for live specimens during vacations.
- 5. Seal specimen containers with vinyl electrician's tape.

Chemical Disposal

- 1. See if a rendering company will take biological specimens to make glue.
- Some items (carbon disulfide, ammonium dichromate) should be returned to central storage or kept only with permission.
- Collect hazardous wastes in clearly labeled containers which are kept sealed at all times except when waste is being introduced.
- 4. Keep waste containers closed except when waste is being introduced.

Chemical Handling

- Do not permit the preparation and consumption of food or beverages in areas where chemicals are handled or stored.
- 2. Properly label all chemicals and containers.
- 3. Install additional fume hoods as noted.
- 4. Put warning labels on hazardous chemicals.
- 5. Resecure labels with wide, clear shipping tape.

Chemical Storage

- 1. Store oxidizing acids (nitric and perchloric) separately from other acids (formic, acetic and butyric acids are organic fuels).
- 2. Store corrosives and other hazardous chemicals below eye level.
- 3. Post "No Food Storage" signs on all chemical and biological storage refrigerators.
- 4. Store mercury in closed containers.
- 5. Store corrosives separately from other chemicals.
- 6. Store oxidizers separately from other chemicals.
- 7. Corroded storage cabinets need to be cleaned and repainted with epoxy paint.
- 8. Store flammables in approved flammables cabinets.
- 9. Establish a system-wide method for chemical arrangement.

Compressed Gases

- 1. All compressed gas cylinders should be chained to avoid falling over.
- Transport liquid nitrogen in freight elevators or using passenger elevators as dumbwaiters.
- 3. Use a regulator to remove gas from cylinders when the pressure is above 30 psi.
- $4. \;\;$ Keep the protective cap in place at all times except when the gas cylinder is in use.

Electrical Hazards

- 1. Repair faulty electrical receptacles and equipment as noted.
- 2. Eliminate the use of two-prong unpolarized plugs on all electrical devices.
- 3. Install additional receptacles as noted. Do not use extension cords for permanently installed equipment.
- 4. Upgrade circuit breakers to GFI circuit breakers.
- 5. Repair plugs with missing ground prongs.

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Emergency Facilities

- 1. Install eyewash fountains, safety showers, first aid kits and fire blankets as noted.
- 2. Provide signs to designate the location of emergency equipment and emergency facilities.
- 3. Make sure emergency equipment and facilities remain unobstructed.
- 4. Clean, tag and date eyewash facilities and safety showers regularly.
- 5. Make sure safety showers are useable (i.e. have chain attached).
- 6. Repair emergency facilities as noted.

General Facilities

- 1. Install guards on paper cutters and fans as noted.
- 2. Repair damaged facilities as noted.
- 3. Belt/pulley guards are required on all vacuum pumps.
- 4. Provide running water and electricity to labs as noted.
- 5. Turn off gas and electricity when not in use.
- 6. Clean and defrost refrigerators as noted.
- 7. Install alarm systems for computer room security.
- 8. Reduce overcrowding by assigning fewer students to science classes.

Glassware

- 1. Discard broken glassware in designated containers.
- 2. Store glassware below eye level.
- 3. If beakers and flasks must be stacked, use a sheet of corrugated cardboard between the layers.

Housekeeping

- $\label{eq:continuous} \textbf{1. Provide general clean-up for the noted areas.}$
- 2. Store heavy objects on lower shelves.
- 3. Stored materials and equipment should not stick out from shelving.
- 4. Where electrical cords must run across walkways, provide covers to avoid tripping hazards.

Lasers

1. Use the ANSI Z-136.1 Standard as the guide for laser safety.

Safety Equipment

- 1. Use only chemical splash goggles in chemistry and biology laboratories.
- 2. Use impact goggles for physics and shop.
- ${\it 3. \ Use \ sanitizer \ cabinets \ between \ classes \ to \ disinfect \ goggles.}$

Ventilation

- 1. Install additional fume hoods as noted.
- 2. Repair fume hoods as noted.
- 3. Make sure that all labs and storage rooms have proper ventilation.
- 4. Keep fume hoods clean of paper and other items.

Miscellaneous

- 1. Secure file cabinets to wall to eliminate tip over hazard.
- 2. Do not store materials on the floor and in aisles or walkways or within 24 inches of the ceilings.
- 3. Make sure alcohol burners have caps.
- 4. Make sure sharp objects (knives, scissors, syringes etc.) are pointing away or stored.
- 5. Repair or discard cracked fish tanks.

Safety Program

- 1. The school should have a written safety and health policy that is endorsed and supported by the principal and superintendent.
- There should be assigned responsibility for the school's health and safety program. That person should report directly to the senior administrator.
- 3. There should be a written safety program describing the various activities that will go on to help ensure that the policy in #1 is implemented.
- 4. These activities should include:
 - a. A safety committee
 - b. Regular inspections
 - c. Taking corrective actions
 - d. New employee safety orientation
 - e. Recordkeeping and reporting
 - f. Accident investigation and reporting
 - g. Safety meetings
 - h. Written rules and regulations (like an emergency procedure for dealing with spills).
 - Regular safety and health training as mandated by the state and federal laboratory standard, hazard communication standard, right-to-know and Workers Compensation Regulations.
 - j. Emergency planning
 - k. Rewards
 - I. Enforcement
 - m. Performance evaluation
 - n. Student and staff rules agreements, which include the four critical parts: read, understood, agree, and realize

This article is based on LSI's publication *Audits and Inspections: A Summary of Recommendations.* Approximately half the recommendations are presented in this article. Interested readers may contact LSI (severin@labsafety-institute.org) to order the full publication.

James A. Kaufman, PhD, is founder and President/CEO of the Laboratory Safety Institute. LSI is a non-profit educational organization dedicated to making health and safety an integral and important part of education, work and life. The Institute provides training programs, consultation services and a wide range of publications for organizations throughout the world. Since 1977, Dr. Kaufman has been writing, lecturing and answering questions on laboratory safety and effective lab safety programs. Email your questions to jim@labsafetyinstitute.org.



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stablished in 1993, Kansas State University's Biotechnology/Proteomics Core Lab is a facility that provides services to researchers at the university and other research and development (R&D) institutions. The lab assists scientists with projects related to new protein identification, protein modifications, protein-protein interactions and enzyme substrates.

"Because of the agricultural emphasis at Kansas State University, many of our projects center on arthropods and plants," says John M. Tomich, director of the Biotechnology/Proteomics Core Lab. "Some of the systems we work on include various strains of bacteria; the red flour beetle, tobacco horn worm and yellow meal worm; crickets, aphids, mosquitoes, ticks and thrips; wheat, soy beans and rice; and Arabidopsis."

These projects involve processes such

as annotating the genomes—looking at where and when certain proteins are expressed developmentally or in which tissue—or identifying enzymes involved in an insect's biological processes such as digestive systems, immune systems, exoskeleton development and hormone signaling.

"In plants, we have identified proteins that are affected by various growing conditions, insect or microbial attack, and storage conditions," explains Tomich.

The lab also synthesizes peptides, chromophoric enzyme substrates, fragments for antibody production, antigens and flavor enhancers and acts as a brokerage for buying and selling oligonucleotides, or polymers with a short sequence of nucleotides.

"This lab has been in existence for 18 years and has dramatically changed during that period," says Tomich, who helped found the lab and has been heading it since. "Initially we carried out oligonucleotide synthesis, amino acid analysis, automated Edman degradation and peptide synthesis. Of those tasks, only peptide synthesis remains. In 2005, we received money from the National Science Foundation (NSF) to equip the proteomics lab."

Lab structure

As director, Tomich oversees the entire facility and is in charge of the peptide synthesis and protein characterization elements. Working with him is Associate Director Yasuaki Hiromasa, who, with the help of an assistant, takes care of the proteomics section.

"My background is in bio-organic (peptide chemistry) and bio-analytic chemistry, while the associate director's training is in enzymology and his



assistant's training is in biomedical engineering," Tomich says.

Together, they run the core lab, which occupies approximately 1,500 square feet of space in two separate rooms, and two offices. "One room houses the mass spectrometers and high-performance liquid chromatography (HPLC) systems, while the second room houses our electrophoresis and robotics units for picking spots," says Tomich.

Within this facility, Tomich and his staff assist clients who are mostly within Kansas State University and the nearby United States Department of Agriculture (USDA) Agricultural Research Service (ARS) facilities. The lab does, however, take samples from other institutions and industries.

"In 2009, we had 93 projects [that] used the oligonucleotide service, 40 projects that used the mass spectroscopy service, 12 projects that used the peptide/protein synthesis/separation service and 10 other projects that used other services provided by the core lab," explains Tomich.

In the areas of plant and arthropod biochemistry, proteomic studies are at the forefront of research. The proteomics work that Tomich and his staff conduct in these areas has helped a number of their clients receive federal grants for their projects.

"It has given us great satisfaction to see our clients receive new funding and international acclaim for these projects," he says.

Tomich and his staff receive orders daily. The oligo orders are processed through Integrated DNA Technologies, which sends samples back within 48 hours. By centralizing orders, the lab can provide competitive prices and free shipping. Orders involving peptides

usually take several weeks to fill, while the proteomics work is usually turned around within 10 days.

One reason that operations run so smoothly is because Tomich relies on his competent staff—he says they do not require much supervision.

"I give my people lots of independence and let them know that it is the completion of projects that matters more than them punching a clock," he says. "Flextime is the buzzword here. Folks come and go to make sure that everything is moving forward at a reasonable pace.

"I give the two staff people total independence to schedule the projects and maintenance of the instruments. I even give them time to establish independent collaborations and publish independently."



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Academic lab

Equipped with \$3 million worth of scientific instruments, Biotechnology/Proteomics Core Lab is not just used for providing services to plant and animal researchers on campus and in industry, but is also used as a teaching tool for students in the field.

"We like to engage students and have them work with our instruments so that they will have a better idea of where problems arise, as well as have a working knowledge so that when they present their data they know what they are talking about," Tomich says.

For example, two graduate students—both with chemistry backgrounds and nearing the completion of their degrees—help with peptide synthesis projects.

Not only does their work help the lab, but both of these students use peptide synthesis in their own research as well, Tomich explains. This type of involvement allows the students to be part of important research and have a chance at having their work published.

"With the exception of the nano-LC MS/MS, proteomics students and faculty researchers can train on our instruments and [also] sign up to use them as time permits," Tomich says.

Through support from Kansas University's upper administration, Tomich and his staff have been able to offer their proteomic services at a greatly reduced cost to junior investigators and those seeking to change the focus of their projects.

"All we charge are replacement costs for the consumables," Tomich says. "Through this mechanism, we have helped a number of junior investigators get extramural funding and advance in their careers."

The lab is also used for Tomich's own federally funded research. "We have three different projects that look at bioactive peptides that function either as drugs or help deliver drugs. My research uses most of the instrumentation housed in the core lab."

Inventory, maintenance, hiring

The core lab is divided into proteomics, peptide synthesis and protein characterization.

Within the area of proteomics, the lab staff primarily uses two different types of mass spectrometers to analyze protein samples partially separated using 1d and 2d gel electrophoresis. Specifically, Tomich and his staff use a Bruker Ultraflex III MALDI TOF/TOF—an instrument for accurate mass determination that requires miniscule amounts of the sample and is capable of MS/MS analyses of certain high-abundance peaks. The team specifically uses this machine for peptide mass fingerprinting (PMF) and in-sourcedecay (ISD) analyses to identify proteins and some post-translational modifications (PTMs).

"Our other instrument is a Bruker HCT-Plus, which we use for nanoflow LS MS/MS analyses on in-gel digested proteins that are cut out of gels," says Tomich of the instrument they routinely use to generate peptide sequences. "All of the workflow is processed by the Bruker program, Proteinscape, with the aid of the search engines Mascot and Phenyx."

"For peptide synthesis we are set up to perform either FMOC or t-BOC chemistries. We prepare full-length bioactive compounds, chromophoric enzyme substrates, fragments for antibody production, antigens and flavor enhancers," Tomich adds. They can be linear or cyclic and can contain heavy atom labels, dyes, biotin, cholesterol and other specific molecules.

"We automated Applied Biosystems Inc. peptide synthesizers that run our proprietary synthesis programs."

For protein characterization, the team has a number of instruments with various

uses, including circular dichroism (CD), Fourier transform infrared (FT-IR), fluorescence, plasmon resonance and analytic ultracentrifugation to look at either protein secondary structure or protein-protein interactions.

In order to ensure that all these processes run smoothly, the team has to stay on top of inventory and maintenance. The associate director, Hiromasa, maintains the inventory and ensures that the lab is well stocked for smooth operation. Because the lab is situated in a location that isn't in the vicinity of many service companies, Tomich and his staff maintain most of the instruments themselves.

"This past year we purchased a oneyear service contract on the two MS instruments to have them repaired and upgraded," Tomich says. "For our older peptide synthesizers, I am always on the lookout for old units that can be used for parts."

Tomich also takes care of the hiring. Although he says that in the 18 years of the lab's existence, he's seen minimal turnover.

"The former associate director took a tenured faculty position in Japan and two assistants have moved on to other positions for family reasons."

Challenges and rewards

Tomich finds that a big challenge is to constantly remain relevant to the research interests of his client base. Because of this, the lab staff is continually modifying services to meet industry needs and actively seeking funding to keep up with the field.

"This is why we dropped certain analyses and added others," Tomich says. "We are just beginning to get requests for post-translational modification analyses and will need to get new instrumentation to fulfill these requests."

In addition to the physical tools that the lab seeks, Tomich employs another valuable tool—communication.

"Communication is very important; making sure that the staff understands exactly what the clients are asking for is critical," he says. "We insist that all requests be in writing."

Another way to ensure that the client's needs are being addressed is to meet with all the clients on a regular basis—to go over their needs, procedures and schedule of charges. Tomich also sends his clients any updates that might aid their research.

"Additionally, it is important that the clients know both our strengths and limitations. If they want something that we cannot do, I refer them to other labs that can provide the service."

For Tomich, being the director of Kansas State University's Biotechnology/Proteomics Core Lab is rewarding because in addition to conducting his own internationally recognized projects, he gets to participate in the projects of other researchers.

"These can be both mentally stimulating and challenging," he says. "No two days are ever the same. Every day brings about some new discovery or problem to overcome."

But it's the overall contribution of the lab to society and science that makes the hard days and challenges worth it.

"Many of the projects that we are working on have implications in pest management and crop plant nutritional value," Tomich explains. An example is clients that seek to find species-specific enzyme targets for a new generation of environmentally safe pesticides.

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



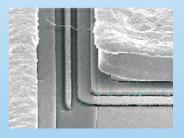
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THE DEVIL IN THE DETAILS

GOOD LABORATORY BENCHMARKING MEANS CONTROLLING VARIABLES by Bernard Tulsi

The concept of laboratory benchmarking is easy to grasp. It simply entails comparing the quality of one lab to measures taken from a range of other laboratories or

from the standard bearers—the top performers in the field. The details involved in the benchmarking process, however, can be quite maddening.

For most laboratories, "Benchmarking is always an issue, and it is not as simple as it sounds," says Niek Klooster, senior global consultant to laboratory management and benchmarking with Intertek (Analytical and OCA Divisions). Part of the reason is that labs have quite different backgrounds, functions and objectives, and these differences make it difficult to compare them in an objective, like-to-like manner.

Paul Mathew, staff scientist with the Lawrence Berkeley National Laboratory, who specializes in energy benchmarking in laboratories, concurs. "In principle, benchmarking is simple. It starts with a selected metric such as total annual energy use per square foot per year, which can be simply and inexpensively calculated and compared for a number of laboratory buildings." The goal generally is to identify

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opportunities for improvements in efficiency.

"Where it gets complicated is in the details," Mathew continues. "Each lab building is unique, so how to normalize for the differences associated with each setting—climate, installed equipment and other programmatic elements—becomes a key question." Each of these

attributes influences the outcomes in benchmarking, so controlling for different variables is always a major hurdle, according to Mathew.

"Benchmarking is really a first step in helping to identify opportunities."



Chemical analysis at the lab.

Still, Klooster says, "Lab managers should not be afraid of benchmarking. I see fear at the beginning of each project with laboratory directors. They are afraid of having the discussion because they believe the benchmarking results will cause everything in their labs to change—and they don't want that."

Typically, laboratory benchmarking involves a short study, which could take as long as a week, during which there are discussions about the organization, its quality, information technology (IT) and maintenance, among other subjects. "After collecting a variety of data on the number of tests and methods, and on different protocols, a report is generated for the management of the company," says Klooster.

"Intertek's benchmarking staff would typically prepare such reports for laboratory directors in the base chemical, petro chemical, refinery and related industries, where the same tests are done on a regular—daily or weekly—basis. We get most requests for benchmarking work from site management teams; they

decide when to request our services to help them work out their efficiency and benchmarking issues."

Among the top reasons for benchmarking laboratories are to improve quality; to satisfy payer, regulatory and accreditation requirements; and to enhance the competitive position of companies. These are perennial goals,

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according to Klooster, who is based in the Netherlands, and who has also served as the chairman of the Dutch Laboratory Managers Association.

He says that laboratories, especially in the bigger companies, are always under pressure to improve their quality, excellence and competitiveness, and that this is the main driver behind the growing need to do benchmarking. Today, Intertek oper-

ates 1,000 labs in 100 countries, and employs about 26,000 people worldwide.

Turning to the mechanics of how benchmarking projects

are initiated, Klooster says that to support the contention that their labs are performing at 100 percent efficiency and cannot be any more productive, lab directors perform benchmarking exercises, often with the help of external specialists, to prove their case to top management.

Related to that approach are the situations in which top management officials indicate to their lab directors that their facilities could be more efficient than they are currently. To support their position, they will request benchmarking, which in turn could provide specifics on the extent of current deficiencies and pinpoint areas of weakness.

"Third, and for an entirely different purpose, which we at Intertek call outsourcing, is another important reason for doing benchmarking," says Klooster. In such situations, Intertek will take over an entire laboratory, including the staff, all the assets, and the rent or lease for the site and facilities. In such situations, the laboratory is transitioned from an in-house operation to an outsourced one. This could be advantageous for the original owners because they are no longer responsible for any of the fixed costs.

"Intertek performs a lot of outsourcing, and the company is continuously in discussions for additional outsourced labs. In all these situations, we perform benchmarking of the laboratories to ascertain their levels of efficiency and the reasons behind any deficiencies," says Klooster.

As practiced today, laboratory benchmarking is not an ongoing exercise. Rather, it generally takes the form of a site study that culminates in a report that, depending on the circumstances, could point out that the laboratory is not making the most efficient use of its resources because tests take longer than the normal time required for the method being used. "In such circumstances, the report to the lab's management will recommend that

steps could be taken to improve efficiency—and specific recommendations for improvement are then transmitted down to individual managers," says Klooster.

"This is always a one-time exercise, and it is hardly ever the case that complete benchmarking exercises are done every year or every other year," he says.

According to Mathew, there are two broad categories

"Pressure to improve quality, excellence and competitiveness ... is the main driver behind benchmarking."

of benchmarking. One form, cross-sectional benchmarking, essentially compares one laboratory and its facilities with other labs and the buildings in which they are located. Longitudinal benchmarking, on the other hand, requires the study of one lab facility over time. In the case of energy, this means comparing usage over a



number of years and selecting one as the baseline year.

Turning to the approach used by Intertek to conduct benchmarking, Klooster says the first step is to obtain a variety of information about different aspects of a laboratory, including its financials, a menu of the analyses it performs and details of its IT system, among other information.

"A number of city and state agencies are making performance according to benchmarked standards mandatory."

"Then there is a series of meetings with site managers on a selected number of areas of concern such as work flow, number of samples handled per unit time and related questions," says Klooster.

"On the basis of all that information, we organize site visits during which we interview the financial team, the technical staff, the IT team and the maintenance team, among others, depending on the areas of concern we identified," he says. During these visits, the consulting team also ensures that its members

interview some of the most important participants in this process—customers and other key stakeholders such as vendors and suppliers.

"All the different views and positions are then coordinated and compiled into the benchmark report and given to the appropriate decision makers," he says.

"What actions are taken after the benchmark-

ing is conducted depends on the laboratory management that reviews the report." He notes that a well-prepared report should have some commentary on best practices collected from labs at other similar and different industries, and provide some recommendations on how to

streamline organizational roles and improve efficiency. There should be enough information to provide management with a basis to take appropriate action, according to Klooster.

"Still, this is not obligatory, and just represents recommendations on which site management can base their decisions," Klooster adds.

Mathew agrees. "Benchmarking is really a first step in helping to identify the opportunities. It is not the last step; it helps to point in the right direction and

to figure out which areas need to be improved."

Eight years ago Mathew and his colleagues launched the Labs 21 *Energy Benchmarking Tool*, based on the recognition that there was no publicly available data on laboratory buildings for benchmarking. At the request of several labs, they started collecting relevant data, and today have more than 200 laboratories in their core data set.

"Today, we can filter the data set for certain key characteristics because the tool has six different filters—lab area ratio (lab area relative to the building area),occupancy, lab type, lab use, climate zone and data type (such as real versus estimated data)," he says.

This is still the only publicly available tool for laboratory energy benchmarking in the United States. "The idea behind the tool is not to



set standards but to create a basis for comparisons with other labs. The idea is to let the benchmarking data speak for themselves," Mathew says.

"After labs discover, for example, that there is scope for improvement, they may go on to benchmark individual systems such as lighting, ventilation, heating and cooling to discern the areas that are deficient and where action is needed."

Mathew says that many pharmaceutical companies focus sharply on benchmarking. "They are very keen on managing costs and increasing profits, and one of the ways to manage costs is to reduce utilities. So anything that helps them get a grasp on how they are faring in the energy sector is of value to them.

"Interestingly enough, the top five or six big pharmaceutical companies have gotten together and done benchmarking studies on their laboratories—this sends a strong signal that there is growing interest in energy benchmarking," he adds.

In fact, another major sector in the healthcare field, the clinical laboratories, initiated quality benchmarking measures more than 60 years ago, when about a dozen laboratories in Philadelphia cooperated on

a plan to compare their results for hemoglobin testing, which were widely discrepant at the time. Over the years, a number of accreditation standards have emerged for clinical labs, including the Clinical Laboratory Improvement Amendments of 1988 and some of the rules developed as part of the Joint Commission's patient safety and quality improvement goals.

Meanwhile, a number of city and state agencies are making performance according to benchmarked standards mandatory. LEED, an environmental certification system for buildings, which espouses performance improvements across metrics such as energy savings, efficient water use, carbon dioxide emissions and better use of resources, is one of the solid drivers of benchmarking. Furthermore, a number of state and federal laws are making such efforts mandatory.

For a variety of reasons, Intertek's Klooster foresees an increase in benchmarking activity, and he notes that in 2009 the requests his company received

for benchmarking from labs increased. Globally, he sees quite different patterns in how benchmarking will be approached by U.S., Canadian and European labs compared to those that are located in the rapidly developing Asian countries (the tigers).

"In the Western developed nations, the benchmarking issue will be about efficiency, and the big financial question will be whether to keep the practices of the last 50 years. These will be the key questions for some time, especially now that their economies are in a tough position," he says.

"The Asian tigers are quite different because they've passed all the stages in the economic development cycle much faster than we have. They have different interests—their focus is to grow, grow and grow."

Bernard Tulsi is a freelance writer based in Newark, Del. He may be contacted at btulsi@comcast.net or 302-266-6420.



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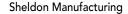


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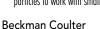
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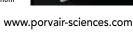


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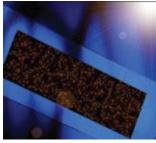
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microscopy system enables high-throughput shear flow assays. The automated microscopy station provides high-performance imaging in brightfield, phase, DIC and fluorescence. An integrated CCD camera permits high-resolution, low-noise data acquisition.

"Typical flow cell systems require cumbersome protocols for setup, experimental runs, and cleaning/sterilization," said Michael Schwartz, Program Director, Fluxion Biosciences. "BioFlux 1000Z saves time and effort since the system is already pre-configured and ready to go to work for a variety of validated cellular assays."

The integrated experiment scheduler allows for unattended imaging and overnight assays for kinetic and time-lapse high-content screens. BioFlux Montage software offers control for all components in a single package. All screening experiments and analysis is controlled from a single user interface.

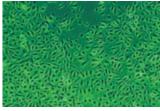
Able to run up to 96 shear flow assays in parallel, the BioFlux 1000Z is ideal for life science research and drug discovery applications, including cell and platelet adhesion, biofilms, stem cell research and cell migration and invasion.

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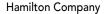
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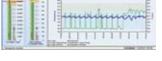
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- Previous version was released in English and German
- Eleven more languages have been added: Bulgarian, Chinese, Traditional Chinese, French, Italian, Japanese, Korean, Polish, Portuguese, Russian and Spanish
- New language updates are available free of charge from Metrohm.com (installation of MagIC Net is required first)

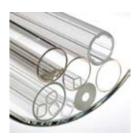
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HOW IT WORKS



Real-Time Monitoring of **Pipetting Processes**

Problem: Automation solutions offer a great alternative to laborintensive manual processes. Liquid handling automation eliminates human errors and process inconsistencies over extended periods of time, resulting in an increased robustness compared to manual processes. It is important, however, to use the appropriate controls to monitor the accurate and reliable implementation of a robotic process. A key component of success in automation is the use of samples that have been well qualified. Robotics can only run a process consistently when the appropriate samples and volumes are fed into the system. For example, if there is a missing sample or there is insufficient sample in a well, the robot may still perform its function but cannot deliver volumes into the source plate as expected. Often times, this poses a challenge to the end user. How does the user know whether the robot is aspirating and dispensing volumes accurately? How does he know if there are wells with insufficient volumes, or if a tip gets clogged?

Solution: Hamilton Robotics addresses these problems with a unique solution that uses TADM (Total Aspiration and Dispense Monitoring) technology described below. It offers real-time monitoring of aspiration and dispensing, allowing customers to have a record profile of all the pipetting steps in each of the wells.

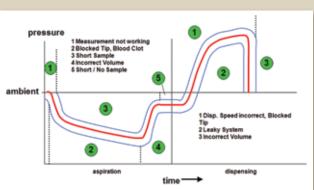
TADM increases the accuracy and robustness of the pipetting process. A pressure sensor inside each individual pipetting channel constantly records the pressure in the system during aspiration and dispensing. The software generates a pressure-over-time curve (Figure 1) that is different for each liquid class and each volume pipetted.

The values obtained by the pressure sensor during a pipetting step (aspiration or dispense) can be compared to user-defined values, thereby enabling realtime monitoring of the pipetting process.

The TADM feature would not be feasible if the pressure curves obtained were instrument-, weather- and altitude-dependent. Therefore, the reference point of the pressure curve is zeroed automatically by the software before pipetting commands are executed. Because the pressure value is not re-zeroed between consecutive aspiration steps, TADM curves from the different aspiration cycles will be shifted. In other words, the reference point for the start of an aspiration curve will always be the pressure value

obtained before the tip was picked up. Since the pressure value is rezeroed between consecutive dispensing steps, curves will be obtained, where the curves from all consecutive dispense cycles are not shifted.

By examining the TADM curves of many aspiration or dispense steps, it becomes apparent that curves obtained from a normal, error-



▲ Hamilton Robotics – TADM Technology

free pipetting step are distinctively different from curves from erroneous pipetting steps. These differences are quite obvious and can be used to distinguish between correct and erroneous pipetting steps. Some of the common pipetting errors during aspiration and dispense cycles and the corresponding pressure curve behaviors are listed in Table 1.

For more information, go to www.hamiltonrobotics.com

Pipetting step	Error type	Pressure curve
Aspiration Step	clot detected short or no sample foam leaky system	pressure below normal pressure above normal zigzag behavior, pressure above/below normal aspiration pressure above normal
Dispense Step	blocked tip not enough liquid foam leaky system	pressure above normal retarded rise in pressure, pressure below normal zigzag behavior, pressure above/below normal dispensing pressure below normal

▲Table 1

HOW IT WORKS O



An Automated Liquid Handling System

Problem: Popular 96- and 384-well microplate-based applications are often not ideally suited for manual pipetting methods. Although readily available in most laboratories, manual pipette use in these formats is neither efficient nor consistent.

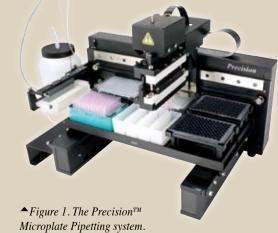
Of chief concern is the lack of reproducibility from user-to-user and plate-to-plate. Even proficient operator technique runs the risk of improper pipetting, incomplete well mixing, cross-contamination, and pulling from or dispensing into the wrong sample. Additionally, manual pipetting is time consuming, hampering throughput and increasing labor costs that could otherwise be used for data interpretation and other tasks.

Solution: Automated liquid handlers, such as the PrecisionTM Microplate Pipetting System from BioTek Instruments (Figure 1), offer the high reproducibility necessary for microplatebased applications. Since the process is automated, the technician is free to devote attention to data analysis and interpretation, or other laboratory tasks. Additionally, automated liquid handling systems eliminate repetitive strain injuries that lead to lost productivity and add to insurance costs.

Precision and accuracy (Figure 2) are normally ensured through the same air displacement technology found in manual pipettes. Dispensing, aspirating and mixing protocols are programmed via integrated software, eliminating technician-to-technician variability and increasing reproducibility within and between plates, and even from multiple users. Complex processes such as serial dilution, plate replication and plate-to-plate or inter-plate sample transfer may also be programmed for automated operation.

Some liquid handlers offer bulk single- and multichannel liquid dispensing in addition to the standard aspirate/dispense functions, and others offer universal capability for multiple well densities without extra hardware manipulation. In addition, third-party robotic arms or stackers may be seamlessly interfaced to the automated liquid handling system to further increase throughput.

Automated liquid handlers use the same pipette tips as manual pipettes. Some systems require specialized tips, while others are more flexible, allowing other manufacturers' tips to be used with similar performance. It is recom-



mended that BioTek's pipette tips be used on the Precision Microplate Pipetting System, however, many other manufacturers' tips and tip configurations may also be used, including sterile, non-sterile, wide-bore, aerosol barrier and low adhesion to suit many applications. Society for Biomolecular

> Screening (SBS)-compliant pipette tip racks fit comfortably on the deck, ensuring proper tip sealing, while those out of compliance may not fit on most automated liquid handling system decks. As with all new equipment, the instrument should be validated with the desired tips to ensure proper performance.

For more information, visit www.biotek.com

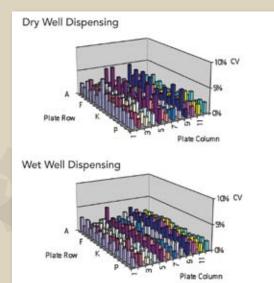


Figure 2. Dry- and wet-well dispensing using an 8-channel pipette and 200 µL tips. Per each, 10 µL of dye was pipetted into 192 wells of a 384well microplate; wet-well dispensing included 200 µL of previously dispensed DI water, while dry-well dispensing did not. Dry-well dispensing showed 3.83% CV precision and 98.76% accuracy, while wet-well dispensing showed 3.64% CV precision and 100.20% accuracy.

HOW IT WORKS O



Automated Purification of Nucleic Acids and Proteins

Problem: Until the mid-1980s, purification of nucleic acids was traditionally performed by phenol-chloroform extraction and alcohol precipitation, which involved tedious manual tasks with toxic substances. This approach was soon replaced by the introduction of spin-column technology, cutting the process down to a few simple steps: lysis of the starting material, binding of nucleic acids to a membrane in the spin column, washing and elution of the nucleic acids. The procedure cuts the processing time to less than an hour, but also standardizes the extraction process, making it the gold standard in all molecular biology laboratories. However, researchers continue to struggle with both time and resources. They need to stay focused on producing results and performing data analysis rather than carrying out repetitive manual workflow steps, such as processing multiple spin-column batches per day. The repetitive nature of these tasks can also make the procedure prone to human error.

Solution: An automated system, such as the QIAcube from QIAGEN, can do the same purification without all the manual steps. It is designed around spin-column technology and includes an integrated self-positioning centrifuge, a heatable shaker and a pipette system with a robotic column gripper. The robot mimics exactly the same procedure from lysis, binding and washing through to the elution without a change in the chemistry or protocol. This allows researchers to stick with well-established and reliable spin columns, but eliminates the need for tedious and repetitive manual steps.

The scientist simply provides the QIAcube with up to 12 samples and chooses the protocol of the integrated software. At this point, the automated instrument takes over. It adds the lysis buffer, pipettes the lysate onto the column and centrifuges the sample. After automatic washing, the sample is recovered with water or the appropriate buffer. The lysis of some samples requires heating, which is also fully automated, since the shaker can achieve and maintain sample temperatures of up to 70°C.

78

allows the automation of one to 12 samples at a time. It can be operated by anyone—from the novice to the expert—without the need for costly retraining of laboratory personnel.

More than 50 different manual spin column kits for the extraction of DNA, RNA and proteins can be automated with a variety of 100-plus standard protocols. The pure nucleic acids or proteins are ready to use in many downstream applications, such

> as RT-PCR, gene expression profiling or protein characterization studies.

For more information, visit www.qiagen.com

◆The QIAcube from OIAGEN.



By automating the purification process, hands-on time can be reduced by 80 percent or more, enabling scientists to direct more of their time

toward generating results and analyzing data, while at the same time offering standardization and virtually eliminating potential human errors.

The QIAcube is a benchtop system that is operated by an integrated touch screen and



Lab Manager January 2011 www.labmanager.com

TEN MOST

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PARTING POINTS

Takeaways from this month's issue:



MAXIMIZING ROI

By using metrics effectively, laboratory managers can better focus their R&D efforts and be more effective in improving their firms' sales and profitability. This is essential, now more than ever, given the slow recovery from the "Great Recession." Here are some guidelines for your lab:

- Suitable for applied research and technical service projects; difficult to apply to basic research
- Creation of a "partnership coordination council" is recommended at the start of a co-development project
- Be careful of having too many metrics and turning the process into an overly bureaucratic exercise



ROBOTS TO THE RESCUE

By making the transition from a manual to an automated process, Syngenta Biotechnology Inc. gained more than they hoped for. The robotic solution automated a tedious manual process, providing SBI scientists with a variety of advantages, such as:

- Many reactions could be run simultaneously between 12 and 72 hours without a scientist being present for sample collection
- Raw data flow increased by several thousand percent
- Scientists were able to take research in new directions without burdening the company with the high costs of additional personnel or expensive analytical tools

GOOD LEADERS, GOOD ACTORS

Good leaders need to be proficient in "situational leadership"having the skills and understanding to assess the scenarios they face and manage them with the right leadership style. Here are some tips on being a good leader:

- Situational leaders are believers in whatever leadership style they've chosen and exude extreme self-confidence
- · Consider the qualities of great leaders you know personally and adopt some of their ways to see what works
- Use 360-degree evaluation to discover how effective your leadership style is



HOW TO AUTOMATE YOUR LAB TO BEST FIT YOUR NEEDS

Marc Ferrer, Ph.D., Team Leader at the Chemical Genomics Center at the National Institutes of Health, stresses the need for using "fit for purpose" automation, while offering some tips for researchers and managers looking to automate their labs:

- · Define your goals, then talk to experts about the type of automation you need
- · Get opinions from different people, other than your usual vendors
- The do-it-yourself approach, without proper support and expertise, can lead to costly mistakes



DECIPHERING MSDS

Material Safety Data Sheets (MSDSs) inform chemical users of potential hazards associated with a chemical's use. Below are some important pieces of information MSDSs should include:

- Chemical abstract service (CAS) number: provides positive identification of each component
- · Physical and chemical properties, i.e. pH, vapor pressure, density and boiling point
- Conditions to avoid, i.e. temperature extremes and secondary containment
- Fire and explosive properties, along with proper extinguishing media

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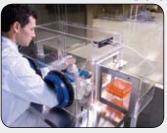


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