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BECKMAN COULTER

Life Sciences

death and taxes

Government regulations, like death and taxes, are an inescapable part of today's laboratories. Critical to personnel safety, sample quality assurance and control, and environmental protection, lab managers have a major responsibility to ensure that their labs stay compliant—whether it be OSHA, EPA, NELAC, ISO, NFPA, NIOSH standards or others. A very tall order, but one that, if neglected, can result in a failed inspection and subsequent damage to business and reputation. In this month's cover story, managers and others from a variety of disciplines share their insights into navigating the complex world of government regs.

HACCP is a specific set of guidelines that impact food and beverage industry laboratories. In this month's Business Management article, "Becoming a Productivity Partner," author Matt Grulke looks at how a LIMS can help managers keep those labs in compliance as well as improve productivity. "While labs fulfill a critical data management role when it comes to regulatory compliance, from ISO 22000 to HACCP, at the heart they are part of a production process where even small oversights or inefficiencies can lead to diminished productivity and profit loss," says Grulke.

As more businesses rely on global relationships for their growth and success, managing such far-flung teams remains a challenge. While improved online tools and resources make it simpler, technology alone cannot replace all aspects of effective management. Turn to this month's Leadership & Staffing article, "Managing from a Distance," (page 24) for tips on how to better facilitate laboratory operations and team communications remotely. One suggestion is to create a collaboration plan that "acts as a 'prenuptial agreement' with expectations on how often to meet, what communication tools to use, and other cooperative guidelines."

This month's Industry Insights articles look at two very timely topics. The first, "Insights on Next-Generation Sequencing," (page 34) looks at the role this technology is playing in the move toward medical diagnostics and personalized medicine. The second, "Insights on Trace Metal Analysis," (page 37) examines ICP-MS as the tool of choice for analyzing trace amounts of metals in a variety of environmental applications.

Speaking of environmental applications, our "Labs Less Ordinary" feature this month (page 16) introduces us to the Biotron Laboratory at the University of Wisconsin-Madison, where 45 environmentally controlled rooms can simulate almost any climate on Earth. "People are starting to realize that we need to know more about how the organisms—plants or animals—and materials will do going forward if we have different temperature-humidity scenarios," says Biotron director Hannah Carey.

Of the various technologies discussed in this issue, "GC Troubleshooting," (page 42) offers some particularly helpful tips for keeping your GC system up and running. From detectors to columns, manufacturers share their expertise in how best to maintain this important piece of laboratory equipment.

With winter behind us, I hope you are happily anticipating the promise of spring.

Best,

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Regulatory Compliance

Dedication, Resources, and Manpower Required

by Sara Goudarzi

On December 29, 2008, a young research assistant working at a University of California, Los Angeles (UCLA) lab used a syringe to transfer tert-Butyllithium from one container to another. The syringe came apart and the contents of the pyrophoric reagent, which spilled on the assistant, Sheharbano Sangji, combusted and instantly engulfed her in flames. Sangji suffered severe burns and died days later.

Many of those who examined the incident blamed it on lack of proper training and said it was one that could have been avoided if the victim were wearing protective gear. The California Division of Occupational Safety and Health considered the case a result of regulation violations.

"That was definitely one of the worst tragedies during my career that I could remember, and it had pretty severe consequences across the academic scene in terms of tightening up, making sure that we get everybody trained that we need to, especially when you're dealing with extremely hazardous substances like that," says Vince McLeod, a consultant who recently retired after 28 years as a senior industrial hygienist for the environmental health and safety division at the University of Florida, responsible for all Occupational Safety & Health Administration (OSHA) health and safety regulations in more than 3,500 laboratories at the university.

> "Laboratories are full of potentially hazardous minefields, and they don't include just chemicals."

Laboratories are full of potentially hazardous minefields, and they don't include just chemicals. Physical hazards are equally abundant. In 2011, a 22-year-old Yale University astronomy and physics student was working in a lab when she was killed after her hair was caught in a lathe.

Upon hearing of this and other incidents of students operating heavy machinery in laboratories and material engineering shops and sustaining serious physical injuries operating equipment without proper training, knowledge, and experience, McLeod and his team went on a mission to further ensure that such accidents are avoided at their facilities.

"We started a heavy emphasis on going through all our laboratories and finding those that had equipment like lathes, table saws, and other heavy machinery that can cause severe injury, making sure we had shields and guards in place and that operators were properly trained and that students did not work alone," he says.

OSHA is a federal agency that regulates safety and health in the workplace. The agency not only sets standards for workers to follow but also enforces them. These standards—which could be learned through training and education and are to be followed by personnel across the nation—help avoid risks. To that end, laboratory managers and employers should train their workers to deal with potential hazards and provide

protective gear along with chemical information and safety sheets for substances used.

"If you reviewed the safety data sheets associated with those [pyrophoric] substances, [they indicate] proper measures to protect against those types of hazards," says Kevin Slates, industrial hygiene laboratory director at the Indiana School of Public Health-Bloomington and former OSHA inspector, of the UCLA incident. "Accidents don't just happen, they're caused, and there's initial intervention that instructors or managers should have been aware of."

Staying compliant

The route to staying compliant differs for each institution and company laboratory, depending on the type of work and hazards specific to the setting.

For example, Sherrill Gelsomino, president of J&S Environmental Laboratories LLC in Union, New Jersey, runs a lab where the primary analyses consist of testing building materials and air samples for the presence of asbestos.

She's particularly aware of the five major federal asbestos statutes and regulations used by states for asbestos testing. These are OSHA's Construction Standards (OSHA 29 CFR 1928.58), the OSHA General Industry Standards (OSHA 29 CFR 2910), the Environmental Protection Agency's (EPA's) Worker Protection Rule (EPA 40 CFR 763), the EPA's National Emission Standard for Hazardous Air Pollutants (EPA 40 CFR 61), and the EPA's Asbestos Hazard Emergency Response Act and Asbestos School Hazard Abatement Reauthorization Act rules (EPA CFR 763).

J&S currently conducts the Environmental Laboratory Approval Program (ELAP) for the state of New York and the National Environmental Laboratory Accreditation Program (NELAP), developed by the NELAC Institute.

"The NELAC standards for laboratories are modeled after similar ISO standards that all laboratories accredited must adhere to," Gelsomino says. "Both the ELAP and NELAP accreditations require at least a biannual site assessment to ensure that the laboratory stays in compliance with the above regulations."

> "Both the ELAP and NELAP accreditations require at least a biannual site assessment."

As the industrial hygiene laboratory director, Slates is concerned with OSHA standards for laboratory safety, specifically the chemical hygiene plan under OSHA 29 CFR 1910.1450. Examples of what falls under that standard include personal protective equipment, storage of flammable and combustible chemicals, ventilation requirements for fume hoods, and hazard communication.

To ensure compliance, his university uses an institutional system. "We have a department of environmental health and safety, and they have safety specialists or inspectors [who] go out to assist in educational training whether or not they're conducting mock audits

and an assessment," Slates says. "They will [then] write up a technical report and send [it] to the department chair so there's accountability at the university and department levels to ensure that these laboratories are meeting requirements. They will also publish resources to graduate students, faculty, and lab instructors, and will provide resources for each laboratory to make those programs more site-specific based on what's done in the lab with regard to research or analytical work."

For J&S, strict quality assurance and control requirements are also in place and performed daily to ensure the integrity of the sample analytical testing and that it stays in compliance. Additionally, whenever there is an update with regard to regulations, employees are informed of pertinent information via either email or weekly meetings. Furthermore, courses and in-house training are provided to ensure that employees are kept up to date with the changing regulations. In-house standard operating procedures are also updated if necessary, explains Gelsomino, who oversees all compliance requirements.

Inspections

In order to ensure that laboratories are safe, government and sometimes health and safety entities within an organization routinely and randomly inspect laboratories.

At J&S, the agencies, ELAP, and NELAP conduct inspections at least twice a year. The agencies typically provide a one-month notice prior to a scheduled visit. Should the lab fail inspection, it could be subject to suspension and is given ten days to provide a rebuttal. "In my opinion," Gelsomino says, "ELAP is one of the most stringent accrediting authorities out there."

For the University of Florida labs that work with hazardous waste, it works a bit differently. Representatives from the Florida Department of Environmental Protection conduct large annual hazardous waste inspections. "They usually send out a team of inspectors [that includes] both state inspectors as well as at least one federal inspector," McLeod says.

For other types of labs at the university, inspectors from other agencies come in. For example, "There's an agency that inspects all your animal handling and animal care facilities, and [others, such as the DEA,] that come if you're dealing with controlled substances," McLeod says. "So there are a lot of agencies [involved], especially for a larger institution where you have a great diversity of research going on."

Although these agencies don't have to give the labs any warning and could show up unannounced, they often do notify them and will give labs about a week's notice. If they're planning a large inspection and intend to be present at a lab for several days, they usually let managers know a week ahead so they can plan accordingly.

Yet government inspectors never visit some labs. "I've been at Indiana University for ten years and the industrial hygiene laboratory director for eight of those years, and we have yet to have a government [inspection]," says Slates. "We haven't had a probable cause." Probable cause would be a programmed inspection, a catastrophic event that would initiate an inspection, or an employee complaint.

In industry, they often inspect labs randomly, Slates explains. However, many academic or university laboratories are considered lower priority in terms of risk and because there are "just so few inspectors available that it's not feasible for a university lab to expect a government representative to show up," says Slates. "That's why at [the] university level they'll conduct mock inspections to look at the same things that government inspectors look for."

Best practices

Staying compliant takes resources and manpower, but it pays back its weight in gold in terms of safety and efficiency. Managers each have their own take on what constitutes best practices for their lab or institution. For example, for Gelsomino, staying in compliance with quality assurance and quality control every step of the way means keeping abreast of compliance. "If [you are performing reviews] daily and complying with the checklists provided by the accrediting authorities, you are doing well as a testing facility," she says.

At the University of Florida, where there are many labs and it could be challenging to keep track of compliance, there's a designated person in each lab or division who handles all health and safety aspects. That person works with local environmental health and safety representatives to make sure the facility stays up to date.

It's important, McLeod says, to have a written program in place. The Department of Health and Safety provides a test bed for labs to use in light of their specific safety requirements based on a general template. "Also, we maintained and helped them keep up with their chemical inventories and things of that nature," he says. "You all have to work together, [and] looking at the lab standards that OSHA has—29 CFR 1910.1450—is a very good starting place in terms [of] helping your overall program."

Slates also recommends implementing OSHA's chemical hygiene plan, 29 CFR 1910.1450, within which other standards are integrated. "Examples," he explains, "would be fire protection plans, hazard communication, protective equipment hazard assessment, requirements for fume hoods, and even access to first-aid kits."

"Another recommendation that I'd make is to become members of professional organizations or societies," he says. "Within those societies, they'll have groups that will primarily focus on laboratory safety issues—it could be assessment, it could be program development or implementation—and from a management perspective you're managing programs, people, resources, and hazards. I think it's important that laboratory managers tie into existing associations, that way they're able to benchmark what other successful programs are doing and save time and resources in the process."

Such practices not only help avoid tragic accidents by protecting the health and safety of individuals and property, but could also increase lab productivity.

"[When] people feel as if their personal welfare is being considered and risks are reduced, they really focus on issues like quality in terms of what they're doing in the laboratory," Slates adds.

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

OPEN COMMUNICATION

By Donna Kridelbaugh

Lab managers are often so consumed with external communication (e.g., business development, reporting to sponsors) that communicating internally may be overlooked. It is important to stay in touch with the whole team—from lab technician to senior scientist—to ensure that everyone is working toward a shared vision and common goals. Additionally, open communication fosters a welcoming environment where team members feel respected and valued, leading to the sharing of new ideas that drive innovation and the collection of information for content needs.

Developing a culture of open communication within an organization begins with the onboarding process. The proper onboarding of new hires results in better prepared employees who are more quickly productive and, overall, more satisfied. Employees prefer to have a clear path to success, which includes discussing information about roles and responsibilities (e.g., communications expectations) from the start.

The prevalence of multi-institutional collaborations in science and industry is increasing due to factors such as outsourcing R&D capabilities and funding mechanisms, resulting in many benefits to the parties involved. However, more communication issues are introduced with remote teams, including the increased costs and time to communicate, lack of virtual tools that effectively simulate in-person interactions, and an overall disconnect.

Many of these challenges can be addressed with a well-designed communications plan that provides best practices (e.g., email etiquette, meeting rules) and outlines communications resources, along with access to training. While the onboarding process at collaborators' institutions may be beyond your direct control, a welcome packet can be developed and distributed to every team member with communications guidelines and other project-specific information that connects them with the resources required to perform optimally.

It is crucial to plan ahead for the onboarding of new hires. A well-structured onboarding program includes a carefully crafted training schedule with regular touch points and assessments, and is a competency-based curriculum that can be tailored to individual needs. A solid organizational structure will facilitate management of virtual teams and ensure proper onboarding of personnel at remote locations. For example, it is important to designate employees at each site whom you can rely on for specific tasks (e.g., training) and establish a regular communications schedule with them. Additionally, the appropriate support services (e.g., IT, facilities management) must be in place so that employees have continuous access to the tools and systems needed to work efficiently and safely.

While communications are key to a fully functioning team, the wrong communication style can easily destroy team dynamics and quickly disengage new employees. In most cases, micromanaging (i.e., exerting control over all aspects of a project) is unnecessary and counterproductive, especially for remote teams where communications may already be in excess. A micromanager inadvertently signals to employees that they are not to be trusted and also stifles creativity. Instead, managers must learn to trust first and delegate responsibilities to the most appropriately skilled team member—after all, the recruiting and onboarding process should be designed to identify and hire the best people.

Lab managers must value the significant role of open communications in effectively onboarding and managing teams. This includes setting clear guidelines and expectations on how and when to communicate and remaining flexible in the communication methods used, especially with virtual team members.

Donna Kridelbaugh *holds an advanced degree in microbiology and is a former lab manager. She is a strategic communications consultant who helps people, projects, and programs be successful through increasing visibility and online presence, securing funding, and developing effective outreach programs. Connect with her on Twitter (@science_mentor) and visit her website at ScienceMentor.Me.*

LABCAST Be sure to attend Donna Kridelbaugh's Lab Manager Academy webinar, "Virtual Onboarding" on April 6, or afterward at www.labmanager.com/virtualonboarding to watch the archived video.

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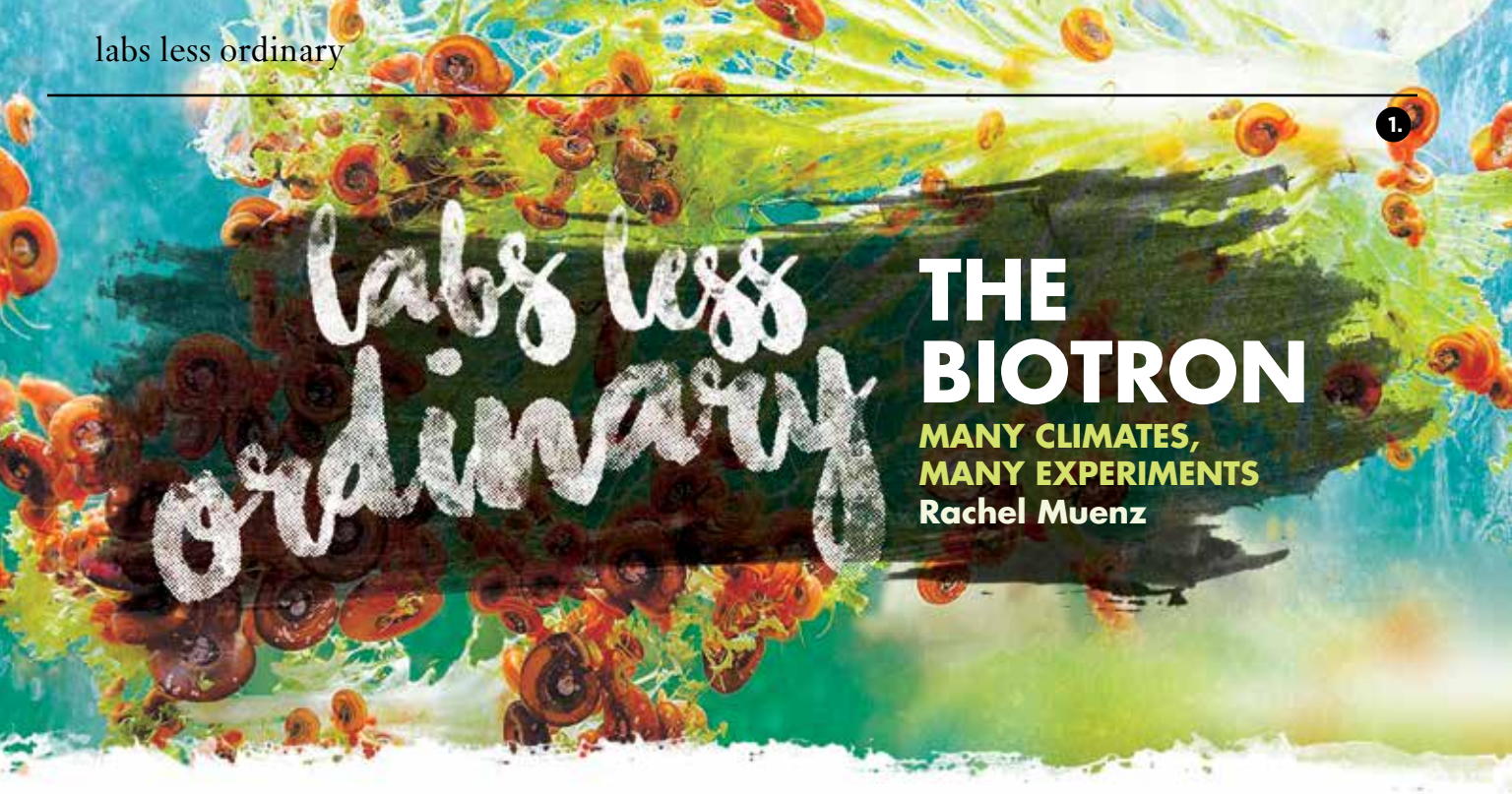

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THE BIOTRON

MANY CLIMATES, MANY EXPERIMENTS

Rachel Muenz

For most organizations, varying temperatures in the workplace are a source of many battles between staff over whether the heat or A/C should be set to high or low. But for the Biotron Laboratory at the University of Wisconsin-Madison, varying temperatures and humidity levels are a good thing. The facility offers 45 environmentally controlled rooms that are completely isolated from one another and can simulate almost any climate on Earth. That makes it perfect for a wide variety of plant, animal, and materials research.

"In the morning, when our staff does daily rounds, they travel from the tropical snail room to a hot summer on a potato farm to a cool Wisconsin golf course to a winter burrow on the prairie, all in ten minutes," says Biotron director Hannah Carey of the range of conditions the lab can simulate.

In terms of temperature, the lab can provide a range from -5°F to 110°F, and also offers humidity levels from "as dry as a desert to a moist tropical fog," she explains. The Biotron can also simulate lighting conditions up to half the power of full sunlight and provide automatic watering and equipment control by the minute.

Those capabilities mean there's always a huge variety of research going on at the Biotron, both academic and industrial, and it's the facility's goal to give researchers exactly what they need in terms of environmental conditions, whether they're studying *Schistosoma* parasitic worms in freshwater snails, how potatoes respond to heat stress, how long pesticides persist in turfgrass on golf courses, or Carey's own studies on hibernation in 13-lined ground squirrels.

1. Freshwater snails are seen feeding on lettuce in an aquarium tank in the Biotron. These snails are used in research conducted by Timothy Yoshino, professor of pathobiological sciences, to investigate the transition of the human blood parasite *Schistosoma mansoni*, one of four species that infects an estimated 240 million people worldwide. Photo by Bryce Richter / UW-Madison

"Our mission is to provide a unique environmental facility for researchers that they couldn't replicate in their regular buildings."

"Our mission is to provide a unique environmental facility for researchers that they couldn't replicate in their regular buildings," Carey says, adding that achieving that mission isn't without its challenges. For example, a recent project looked at the effect of freeze-thaw cycles on concrete and required going from temperatures of -5°F to 95°F every day, mimicking several years' worth of freeze-thaw cycles in only two months of research time.

"It was a load on the system, but we pulled it off," Carey says.

Another challenge comes from the fact that many of the experiments done in the Biotron require very precise conditions, and even the slightest deviation can cause disaster. With Carey's own research with ground squirrels, for instance, "temperature drops of only a few degrees

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2. Brooke Babler (left) and Robert Witherell (right), both researchers in the Wisconsin Seed Potato Certification Program (WSPCP), check on micro propagated potato plants used in research by WSPCP that are housed in test tubes inside an environmentally-controlled growth room at the Biotron Laboratory. **3.** Paul Bethke, associate professor of horticulture, checks on a variety of potato plants housed in wire cages inside a greenhouse at the Biotron. The plants are used to study resistance to heat stress-induced degradation of potato chip quality. **4.** A custom-designed Zero Zone direct expansion refrigeration rack provides cooling for room temperatures down to -20°C for a controlled environment room at the Biotron. **5.** Micropropagated potato plants used in research by the WSPCP are housed in jars inside an environmentally-controlled growth room. The goal of the WSPCP is to provide Wisconsin potato farmers with seed potato planting stock that is healthy and without varietal mixture. **6.** Graduate student Erin McMahan waters an assortment of alfalfa plants inside a greenhouse at the Biotron. The alfalfa plants are used as a control plant for a study seeking to find a cranberry plant that is resistant to the *sparganothis* fruit worm, a major pest of Wisconsin cranberries. Photos by Bryce Richter / UW-Madison

can be very dangerous, and higher temperatures can induce arousal," meaning the squirrels wake up before they are supposed to. To avoid such issues, the rooms have multiple alarms and are monitored 24/7, so that if something goes wrong, a staff member can respond right away.

"They have to get right on it, because the goal is to minimize any interruption in the researchers' experiments so they don't have to start all over," Carey says. "It's challenging, but it's so satisfying, especially for the staff [who] are doing this every day."

There are also backup rooms on hand if there's a breakdown or logistical issue with the particular room a researcher is using. And Carey and her staff of about nine are always working to identify vulnerabilities and to brainstorm plans to deal with potential contingencies down the road, such as power outages and other issues that could impact their clients' experiments.

"It's challenging, but it's so satisfying, especially for the staff [who] are doing this every day."

Carey adds that hearing researchers say that an experiment wouldn't have been possible without the Biotron is the main highlight of working there. Playing a part in so much important research isn't so bad either. Most recently, early studies done at the facility on the growth of food

plants under LED lights led to the International Space Station growing plants under LEDs.

Also recently, the Biotron has made a stronger push to get its name out there, as Carey admits they haven't done the best job in the past of letting people know they're there. She adds that while the facility was built in the heyday of environmental research in the late 1960s, opening in the early '70s, there was a lull in interest in the decade after.

"Now things are changing again," Carey says. "One part of it is just awareness of the environment, of urbanization and habitat change, and, of course, of warming. People are starting to realize that we need to know more about how the organisms—plants or animals—and materials will do going forward if we have different temperature-humidity scenarios."

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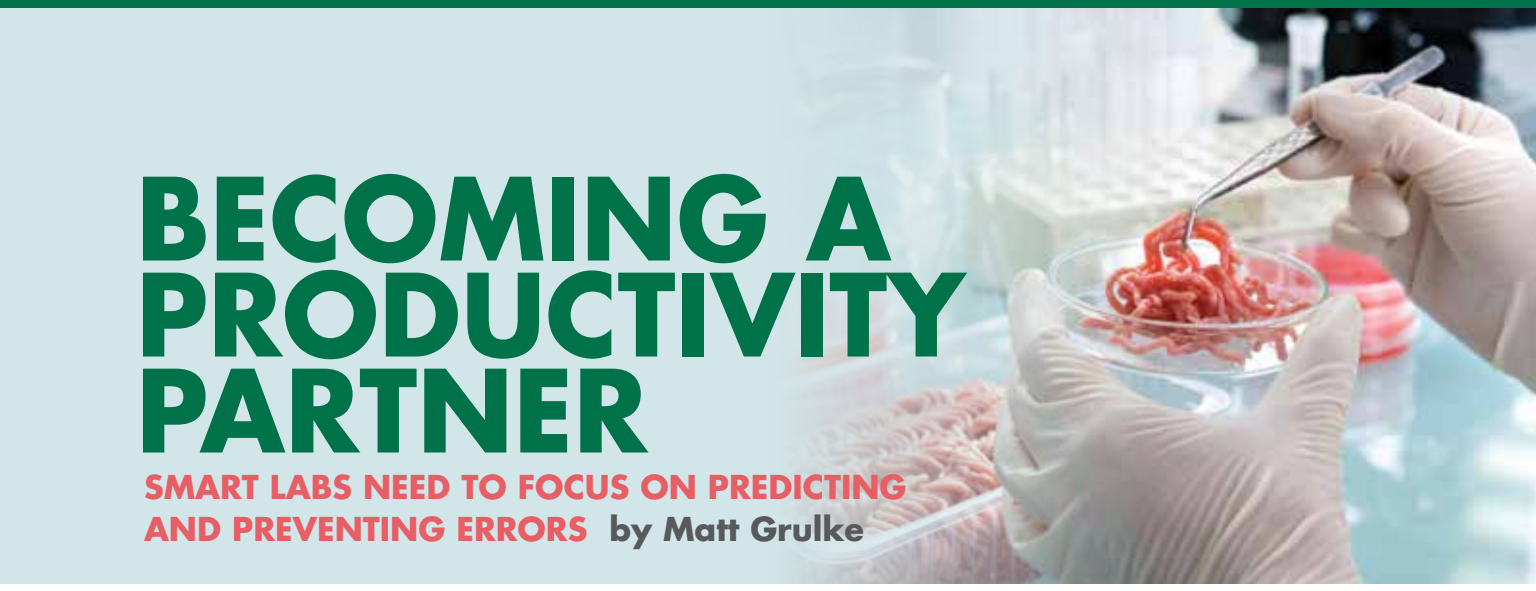

BECOMING A PRODUCTIVITY PARTNER

SMART LABS NEED TO FOCUS ON PREDICTING AND PREVENTING ERRORS

by Matt Grulke

Safety and quality are paramount to the food and beverage industry, but so is profitability. While no company would ever put profits ahead of the safety and satisfaction of its customers, tension does exist in some companies when labs are viewed as impediments to increased productivity. It doesn't have to be this way.

When a lab is responsible for product quality and safety, it fulfills a critical role, but it can also create bottlenecks: lab tests can stand in the way of the raw material acceptance, batch release, and mid- or post-production cleaning, for example. A lab is, in fact, part of a much larger, highly integrated process that includes enterprise resource planning (ERP) software, packaging systems, cold chain, and much more. With all these interdependencies, any inefficiency, from a laboratory informatics standpoint, is magnified.

> "Better budgeting and tracking are obvious remedies for inventory mismanagement."

While labs fulfill a critical data management role when it comes to regulatory compliance, from ISO 22000 to HACCP, at the heart they are part of a production process where even small oversights or inefficiencies can lead to diminished productivity and profit loss. So gaining control over these seemingly insignificant "everyday" problems can mean the difference between profit and loss for the company as a whole. The food and beverage industry is based on high volume, low cost, and small margins, making production efficiency high on the list of priorities alongside product quality and safety.

In the search for greater lab productivity and efficiency, many overlook the small, everyday issues. This is a mistake. By focusing on the common problems below, you'll have an opportunity to make immediate and demonstrative changes that position your lab as a productivity and profitability driver.

Poor inventory management

Expediting shipments of out-of-stock consumables to a lab—perhaps overpaying as a result—is sometimes called "hot shotting," and it's problematic. It's symptomatic of laboratory mismanagement. Inventory is fairly predictable within a single lab running certain tests and using consistent workflows, so failure to anticipate future need is unacceptable.

Consider a consumable such as vials for gas chromatography (GC). Because of high demand, technicians will store extra vials near their workstations. Because the item is no longer in inventory, a critical batch release may be delayed until a technician can hot-shot what's needed. Imagine a large dairy where a testing delay is a reason that milk with higher, more expensive fat content moves through production for hours. The lab would be responsible for loss of profit margin for that batch, and it could have been avoided.

Better budgeting and tracking are obvious remedies for inventory mismanagement. A laboratory information management system (LIMS) can enable labs to carefully track inventory as part of a comprehensive lab management program. It's even possible to create alerts about stock levels. The bottom line is that there is a bottom line: manage it better and you'll not only avoid waste, you'll avoid costly production delays that poorly position the lab within the overall enterprise.

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Inability to recognize analytical trends

Laboratory errors can be an early warning system. While many labs address errors *after* the fact, smart labs focus on predicting and preventing errors that mask QA/QC problems. But with analysts running hundreds of tests each week—many still using paper spreadsheets—this can be nearly impossible.

Today, more and more labs are turning to statistical quality control. The SampleManager LIMS, for example, includes this capability, enabling technicians to detect nonconformance trending before it reaches predefined thresholds. This gives labs real-time monitoring capability that relies on statistical algorithms: the lab is observing data trends WHILE the analysis is running, not weeks later.

One missed error can cost thousands or more in lost productivity, product recalls, consumable waste, and, much worse, contaminated batches that sicken customers. Finding minor errors as they occur—because a LIMS-enabled standard operating procedure (SOP) requires you to spot-check data at certain intervals—can mean the difference between profit and loss. And human beings alone simply cannot provide this analytical rigor.

Inconsistent procedures

Laboratories are at risk from inconsistent application of procedures, even "innovative workarounds" that show promise as time savers. There is only room for innovation in a lab if, *and only if,* it passes through the rigor of the SOP process.

Electronic SOPs (ESOPs) are the lab's defense against risk and the inevitable productivity declines that result from inconsistent procedures. With ESOPs defined in the LIMS, for example, there's a rigid workflow with clearly defined technical corrective actions to ensure consistency and adherence to protocol. Without this, it's too easy to make unintended errors.

Four considerations are important when developing ESOPs: thoroughness, standardization, distribution, and compliance. Lab performance, defensibility, and so much more depend on how successfully a lab addresses each of these imperatives. Fortunately, LIMSs have evolved to make management of SOPs easier and more efficient. This brings consistency that not only keeps productivity on track but also helps with compliance with ISO 17025 and other requirements.

Lack of traceability

A single laboratory may be responsible for hundreds of tests each week. And a test is not simply a test, it's the sum of many parts. Where did a sample originate? What is the maintenance history of the instrument used? What are the reagents and standards used for the test? When was the analyst last certified? Which vendor supplied the consumables? Answering these questions retrospectively can be time-consuming—and that time can sap productivity.

Analysts routinely spend a quarter of their productive time simply collecting data to defend a result. This can take away from time that should be spent contributing to productivity and profitability. But defending data isn't optional. And this is yet another area where data management software is about more than just data collection and reporting—it's about enabling productivity. It's about quickly returning to the job at hand—rapidly, efficiently, and accurately delivering results across the business that enable production to continue uninterrupted.

"Analysts routinely spend a quarter of their productive time simply collecting data to defend a result."

Today, a LIMS can reach across an enterprise: it still sits in the lab, but it integrates with data in materials requirement planning, ERP, and other enterprise systems in ways that directly impact defensibility. No more searching in multiple places, often a combination of handwritten notes, spreadsheets, and reports: everything required to defend a result is aggregated and organized for rapid analysis and reporting.

Missing maintenance

When many labs think of trend analysis, they don't often associate it with instrument maintenance, but that's a mistake. This reflects a misunderstanding of the importance of maintenance, especially preventive maintenance.

Data such as area counts, baseline conductivity, and retention time provide valuable evidence that, if trended and analyzed, can reveal much about the health of an instrument. Some LIMSs actually offer capabilities that

allow users to monitor instrument health so that work can be assigned more effectively on a regular maintenance schedule. Users are notified of upcoming maintenance—even of wear-part failure—so that maintenance can be scheduled before failure becomes an issue.

Analysts will tell you that they "get to know" their instruments, but sometimes signs are too subtle to sense the failure before it occurs and the instrument goes down. And with many new graduates, transfers, and others cycling through who are unfamiliar with various instrument types, there is simply too much margin for error. To understand what an instrument is telling them, it's much smarter for labs to rely on data; by simply setting a sample point and watching for deviation, labs can effectively give themselves an early warning system. And this can be easily done using a LIMS.

Does instrument downtime seem trivial? It better not, because when a GC goes down, for example, it can impact batch delivery and much more. And looking backward after a production stoppage or slowdown hardly solves the problem today. No, it's more important than ever for labs to demonstrate that they can play a proactive role in driving productivity and profitability. But it's hard to make that case when instruments are down or poorly calibrated and your lab is what stands between a business being fully operational and standing still.

Small steps create big changes

Labs are so important to productivity and profitability in the food and beverage industry. Yet too often, little problems—everyday problems that are often seen as trivial—are preventing them from reaching their full potential. And the pace of business today is more frenetic than ever, demanding more and more of managers and analysts who are already overworked.

Everyday problems have a tendency to fly below the radar and escape notice, especially in labs that still rely on paper to manage operations. This must not continue, as food and beverage companies and their labs face even greater scrutiny, exposing gaps that affect not only productivity and profitability, but also the ability to comply with increasingly more rigorous regulatory requirements.

A modern lab should be a productivity partner, capable of not only driving greater efficiency and profitability but also of mitigating future risk. Recalls are expensive, but better, more proactive management can help. Likewise, better data management can help with regulatory compliance, planning, R&D innovation, and so much more. In this regard, the LIMS should be seen as a catalyst for an entire enterprise, not simply a tool for managing a lab. Then the lab can be positioned in a totally different light, as a driver of—not an impediment to— productivity and profitability.

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MANAGING FROM A DISTANCE

A STRONG ORGANIZATIONAL STRUCTURE AND SUPPORT SERVICES ARE ESSENTIAL

By Donna Kridelbaugh

The ability to manage labs remotely is a necessity. All lab managers work remotely in some capacity—whether checking in with staff while attending a conference or working from home due to a sick child—and many are now tasked with the responsibility of working collaboratively as part of multi-institutional research teams or supervising an off-site location. As part of professional development and training programs, lab managers must be provided with opportunities to develop the skills required to effectively facilitate virtual collaborations.

The pros and cons

The complex scientific challenges being addressed in this century (e.g., climate change, precision medicine) require multidisciplinary approaches conducted by research teams comprising experts with academic, industry, and government affiliations. Federal funding agencies have encouraged the growth of team-based research with the advent of multiple principal investigator funding mechanisms that enable researchers to form cross-disciplinary teams and apply for "big grants."

Both the public and private sectors benefit financially from team science and virtual collaboration capabilities. Alice Marcy, in her role as scientific operations officer with Dynamis Therapeutics, Inc. (Jenkintown, PA), a small preclinical pharmaceutical company in the metabolic disease area, has managed more than ten research collaborations with academics, pharmaceutical companies, and contract research organizations in the past decade. As for the reason for this increasing trend toward public-private partnerships, she explains, "Pharmaceutical companies have decreased their internal research and development capabilities and have become more receptive to collaborative arrangements for drug discovery."

> "Pharmaceutical companies have ... become more receptive to collaborative arrangements for drug discovery."

Laboratories have been able to reduce expenses associated with business travel costs by using virtual communication platforms to connect with collaborators and clients around the world.[1] Meanwhile, the globalization of industry allows companies to capitalize on emerging and growing markets in other countries to develop products and solutions tailored for local regions.[2] Indirect benefits include the higher performance levels associated with teams that learn how to effectively collaborate, enabled by the use of electronic communication tools.[3]

Working remotely also provides numerous advantages for the lab manager, such as greater work flexibility, the ability to take time off for professional growth, and enhanced work performance. For example, Teesta Jain, vice president of clinical research at Sonostics Inc. (Binghamton, NY), finds that "working remotely gets that member of the team to have interactions with people in different areas, which often opens up new avenues with new ideas: more parameters in the study, what the results mean and future direction of these results, and also new products for the pipeline."

While technologies are advancing, there is still no substitute for direct, face-to-face interaction with research teams. Improvement is needed in the design of virtual communication tools that can simulate in-room interactions, which are essential for developing personal rapport and trusting relationships with individual team members. Jain, who primarily manages the clinical research lab for her company remotely, offers another difficulty in that "exchanging and bouncing off ideas to be more creative" is inhibited when working alone.

Other issues with geographically dispersed teams include the burden of constant electronic communication (i.e., communication overload) and a range of cultural and physical barriers (e.g., different time zones, ethics, and work styles). Additional challenges specifically related to laboratory work include staying updated on daily progress, troubleshooting lab experiments, and monitoring research data. However, the task of managing remotely is becoming more achievable with the collection of online tools and resources available to facilitate both laboratory operations and team communications.

Lab operations

There are a number of software tools that can assist in monitoring day-to-day activities to keep a lab running efficiently. These products, including electronic lab notebooks and inventory management systems, allow users to access experimental data and results, approve purchasing orders, and check inventory supplies without stepping foot inside the laboratory. *Lab Manager* offers a comprehensive selection of online resources to help managers choose the best products for informatics needs in their laboratories.[4] These resource guides also provide information on laboratory equipment that is capable of being brought online for remote monitoring purposes.

For example, Priyanka Bhattacharya, manager and head of the Chemical Science Division at Proton Power Inc. (Lenoir City, TN), has adapted her company's inventory management system to track chemical and laboratory supplies. This system helps her plan for experimentation when working remotely to check whether needed glassware or chemicals are in stock and to subsequently proceed with authorizing an experiment to be conducted while she is away. In Bhattacharya's lab, analytical instruments such as the GC-MS can be accessed remotely so she can review sample results and help troubleshoot protocols from outside the lab.

Team communication

Most employees will already be familiar with virtual collaboration tools in use for team communication, including options for videoconferencing (e.g., Skype), project management (e.g., SharePoint), and file sharing (e.g., Google Drive, Dropbox). While these tools are becoming commonplace, lab managers must focus on carefully selecting user-friendly tools that work best for the whole team. According to a National Research Council (NRC) report on team science, "When selecting technologies to support virtual science teams or larger groups, leaders should carefully evaluate the needs of the project and the ability of the individual participants to embrace new technologies. Organizations should promote human-centered collaboration technologies, provide technical staff, and encourage use of the technologies by providing ongoing training and technology support."[5]

Some online tools are better suited for virtual collaborations. For instance, Nancy Cooke, professor and program chair of Human Systems Engineering at Arizona State University and committee chair for the NRC report, suggests the use of videoconferencing software that has features to see who is online, allows team members to raise their hands to contribute to the discussion, and can easily be led by a moderator. There are also general best practices for holding virtual meetings, including distributing presentation slides and a premeeting agenda with call-in details in advance and promptly sending post-meeting summaries with action items. The NRC report details a suite of communication tools and guidelines for decision-making purposes.

Organizational structure

A strong organizational structure, along with support services, is essential for virtual lab management to work well. This structure should include a local point person authorized to deal with day-to-day issues. For example, Bhattacharya relies heavily on a research associate in her lab whom she can trust to manage the inventory and serve as the safety coordinator. The lab structure is supplemented by a solid IT department that provides access to remote computing functions (e.g., virtual private networks), a facilities division for safety and maintenance issues, and a purchasing office where she can forward orders. Overall, Bhattacharya comments, "Most of the time managing remotely works well as long as I have a phone to talk on, a laptop, and an Internet connection."

Smaller institutions and start-ups may not have the luxury of a dedicated person or unit to carry out routine lab duties, and in this case labs might consider outsourcing responsibilities. HappiLabs (Chicago, IL), is an example of a company that provides virtual lab management services, including strategic purchasing and inventory management, to save researchers time and money.[6] Additionally, when planning work breakdown structures across multi-institutional collaborations, Cooke suggests, "If tasks can break down into subtasks, then naturally group [them] by location where lots of interactions occur in one place, because a problem [with team science] is the overhead on communications."

"Most of the time managing remotely works well as long as I have a phone to talk on, a laptop, and an Internet connection."

Planning ahead

Cooke explains that there is an interdisciplinary community, called The Science of Team Science, dedicated to studying the science behind team-based research. These researchers are taking lessons from collaboration science and applying similar tools and techniques to help teams of scientists work better together. The Science of Team Science conference website contains a comprehensive list of resources to support the planning and management of large-scale collaborations with wide-reaching applicability.[7]

As an example of resources, the National Institutes of Health (NIH) has developed a field guide with a number of hands-on exercises (e.g., fostering trust, communicating science) for developing an effective team.[8] According to the guide, the first step is to prepare yourself (and team members) with the communication skills and "collaborative spirit" required for success. Cooke also finds that the top two characteristics needed in team science are a willingness to work across disciplines and lots of patience, because electronic communication just takes more time.

Another important aspect is the vetting of potential collaborators who have the same vision and values as your own team. Marcy recalls, "One of our best collaborations was with a partner that was highly engaged and thought

carefully about the best way to reach our company goals within budget limitations. It was like working with a company colleague rather than a contractor." She continues, "A good collaborator asks good questions during initial interviews to show they are thinking about the project, has lots of experience with what you want to accomplish, is rigorous and has high standards, complements your capabilities and can fill holes with their strengths, will be recommended by other groups, and has adequate time for your project."

As Cooke explains, it is essential to develop a collaboration plan in advance of starting a team-based project. The plan acts as a "prenuptial agreement" with expectations on how often to meet, what communication tools to use, and other cooperative guidelines. She emphasizes that it takes "start-up time" for the onboarding of all team members (e.g., developing a common vocabulary), and funding agencies should allow teams this time to get started. The aforementioned NIH field guide also contains a collaborative agreement template that can be used as a starting point. Whether managing a lab remotely on an intermittent basis or leading a major collaborative research effort, these team science tools and resources can help you direct highly effective teams from any location.

Donna Kridelbaugh *holds an advanced degree in microbiology and is a former lab manager. Connect with her on Twitter (@science_mentor) and visit her website at ScienceMentor.Me.*

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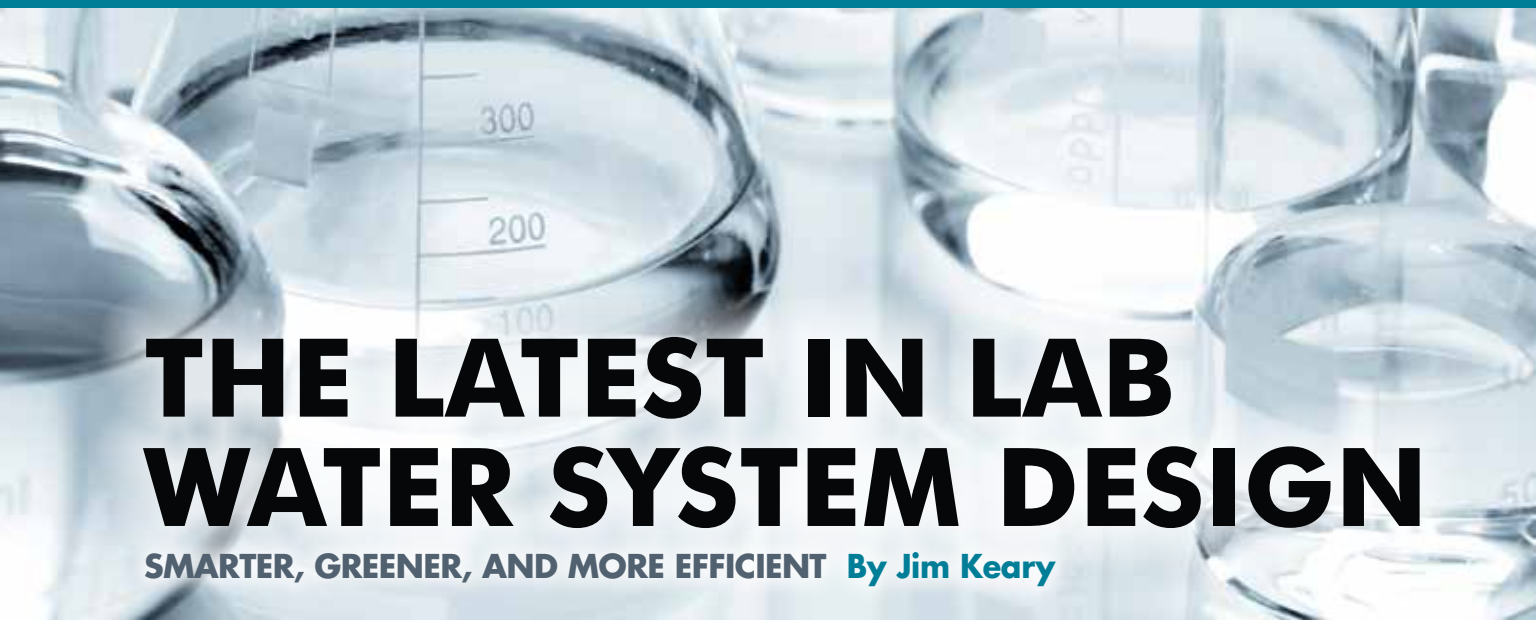


THE LATEST IN LAB WATER SYSTEM DESIGN

SMARTER, GREENER, AND MORE EFFICIENT

By Jim Keary

When you think of water purification technologies, you'd be forgiven for not immediately associating them with cutting-edge design. The pure water fueling the vast majority of your experiments can easily be taken for granted; your water purification system is likely out of sight and out of mind, diligently and humbly carrying out its job in the corner of the lab. However, if you look just a little bit closer, it quickly becomes apparent that the system's great design is precisely what has allowed you to overlook your water purifier—it runs efficiently, quietly, and consistently without hogging lab space, budget, or even energy.

"Lab managers usually err on the side of caution and oversupply the lab with pure water rather than risk running out."

Innovation

When it comes to removing impurities from water, there's no point in trying to reinvent the wheel. We all make use of powerful, tried, and tested techniques like reverse osmosis, deionization, UV treatment, and of course filtration. With these techniques, it's possible to produce some of the highest-quality pure water available.

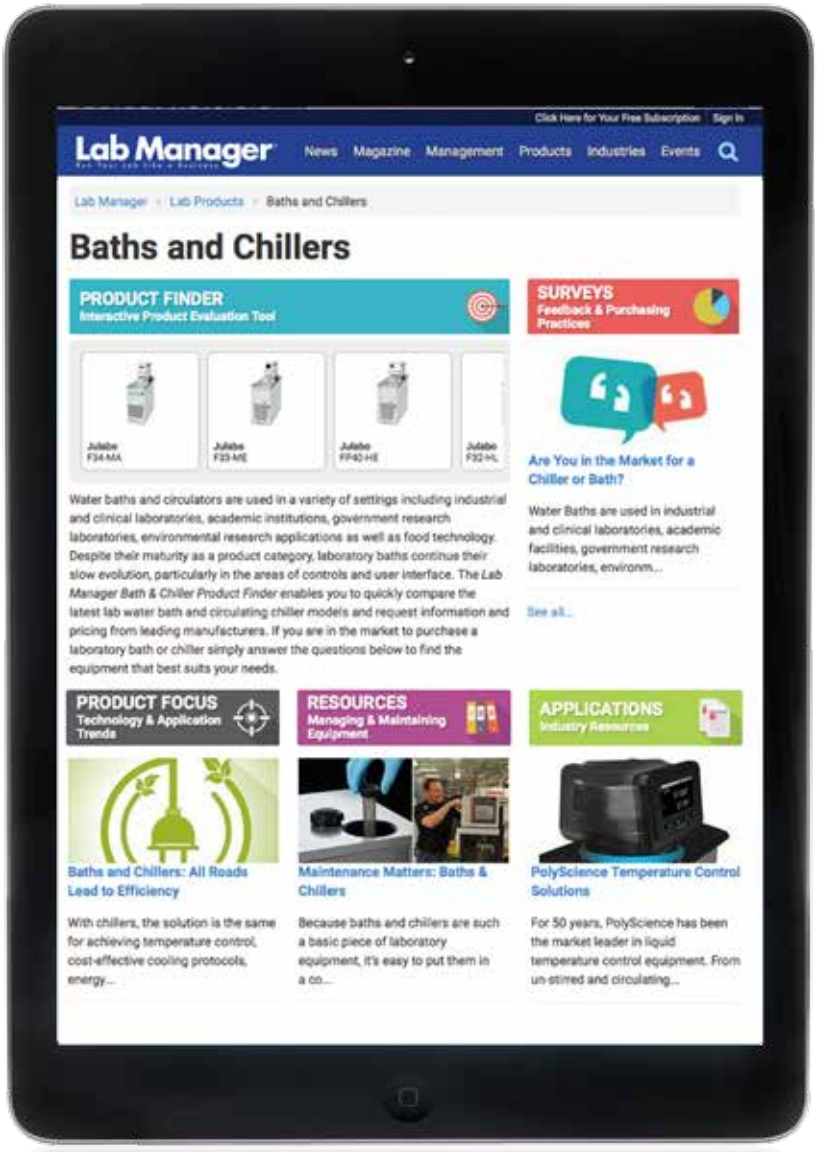
For this reason, innovation has had to happen in other areas of the design process. First up has been reevaluating the components of a purification system—tweaking its innards. Plastics often make up the bulk of a device's internal parts, as they offer a great combination of flexibility and performance while being economically efficient. In order to improve these, companies have been looking at the injection molding used to produce these plastic components. Adjustments here can lead to substantial design optimizations, resulting in the use of fewer pipework connections, for example, which in turn can result in reduced manufacturing costs. The icing on the design cake here is that better injection molding means smoother internal surfaces, and in the case of water tanks, this means not only fewer crevices for bacteria to hide, but also better mixing dynamics.

It isn't just plastics, though: There's a growing drive to incorporate innovative improvements for user interactions in the form of better display technology and even haptic feedback mechanisms. More information and feedback is always a good thing!

Form and function

Labs are dynamic and so is their need for water, utilizing variable volumes depending on the number of members or how productive those members are (or aren't!) feeling on a particular day. To cope with these changing demands, lab managers usually err on the side of caution and oversupply the lab with pure water rather than risk running out. This can mean large and costly purification systems, generating much more water than ever gets used. Suffice it to say, this is far from efficient.

Insightful manufacturers have realized this and have responded with modular water purification systems. With systems like these, it becomes possible to mix and match purification components and accessories, adding or removing additional dispensers, units, or even reservoirs as and when required.



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This is not only a great way to future-proof your lab, but it's also going to have less of an impact on what is already likely to be a tight budget, as there's no need to acquire the largest possible unit available. Whether you need ten or 100 liters of water, a modular system allows you to accommodate that without oversupplying.

Speaking of limiting aspects, there's also the space issue to consider. Lab space is always at a premium, and so investing in a modular system means that you make the most of the space you have available. Individual components can typically be stored in separate locations—maybe you have the dispenser on the bench and the reservoir underneath—so you don't need to sacrifice a great chunk of much-needed floor or bench space.

While it's not all about looking pretty, water purification systems should still be aesthetically pleasing, or at the very least unobtrusive. A sleek, quiet system that fits into the lab is much more preferable to a whirring behemoth of a machine—especially if you're the one working next to it all day!

Intuitive

This is a term that gets bandied about a lot nowadays, but it's worth mentioning just how important it really is. A good system should be intuitive; it should be self-explanatory. Your time in the lab needs to be spent doing science, not wading through an obtuse instruction manual when all you want to do is dispense half a liter of pure water! Great design will take this into account, allowing users to quickly understand what needs to be done in order to get what they need in the most expedient manner.

Going green

We're all much more environmentally aware these days. The manufacturing industry as a whole is slowly starting to accept the need to produce products that have been designed not only to reduce energy usage, but also their overall environmental impact.

This is why environmentally conscious manufacturers have been steadily making improvements, such as matching a purification system's power supply to a bespoke configuration and the power supply of its destination country. Others are helping reduce the amount of water that invariably goes down the drain during the purification process—something well worth investing time in when you consider that a typical lab may use up to 35 million liters of water every year.

Of course, aspects already mentioned here, like modularity and reduced internal components, mean that the environmental impact of the manufacturing process itself can be reduced. Some companies have gone a step further and obtained ISO 14001 accreditation, meaning that they have ensured that their environmental impact is being measured and improved. This means careful selection of materials, manufacturing processes, and the methods by which products are shipped.

The great design nestled in some of the more advanced water purification systems is clearly something that goes far beyond an aesthetically appealing unit. A great design can help you adapt to a lab's changing needs, address what are often tight space and budget demands, and even play a major role in reducing the overall environmental impact. You should therefore keep design in mind the next time you invest in a water purification system!

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BURNED OUT!

SAFE USE OF FLAMMABLE SOLVENTS IN THE LAB

by Vince McLeod

One event we constantly try to prevent is a laboratory fire. Unfortunately, they are all too common and even "small" ones can cause tremendous damage and adversely impact not only the immediate lab where the fire occurred but also most adjoining labs. And large fires can be devastating, destroying the source lab and sometimes the whole building. So, whenever we encounter the use of flammable solvents, our antennae go up and we take extra notice.

Flammable solvents are those that can easily catch fire and burn. This article will focus on liquids because, according to *Prudent Practices*, the most common fire hazard in the typical research lab is a flammable liquid or the vapor produced by one.[1] And the laboratory violation we hand out most often deals with use and storage of flammable liquids.

If we recall our safety training regarding flammable solvent use and the basic "fire triangle," three conditions must exist simultaneously for a fire to occur: an oxidizing atmosphere (usually air), a source of ignition, and a concentration of flammable gas or vapor within its flammability limits. If any one of these is absent, a fire will not occur. Controlling flammable vapors and gases and eliminating potential ignition sources are the best ways to reduce the fire hazard, since air is nearly always present.

Flammable and combustible substances—different physical properties

There are a few important concepts to understand at the outset. The first is the difference between flammable and combustible materials. The differentiation is based on flash point—the lowest temperature at which there will be enough flammable vapor to ignite when an ignition source is applied. Flammable liquids are more dangerous, because they have a flash point below 100°F (37.8°C). Combustible liquids have flash points between 100°F and 200°F (93°C). A closely related term is *vapor pressure*. Every liquid has a vapor pressure, which is a function of that liquid's temperature. As the temperature increases, the vapor pressure increases. As the vapor pressure increases, the concentration of flammable liquid vapor in the air increases. Therefore, temperature determines the concentration of vapor in the flammable liquid in the air. A certain concentration of vapor in the air is necessary to sustain combustion, and that concentration is different for each flammable liquid.

The next important concept is the *flammable range*—the range between the upper and lower *flammable limits*. Flammable limits are expressed as percent volume in air. Concentrations above the upper flammable limit (UFL) are too rich to burn (too much vapor) and concentrations below the lower flammable limit (LFL) are too lean to burn (not enough vapor). The most dangerous materials are those with the lowest flash point and widest flammable ranges.

The National Fire Protection Association's (NFPA) *Flammable and Combustible Liquids Code*, NFPA 30, is an excellent resource and introduction to the hazards of these materials.[2] And if you are interested in details, NFPA 30 further classifies flammables as Class I and divides them into Class IA, IB, and IC, while combustible materials are classified as Class II, IIA, and IIB, all based on flash points and boiling points. NFPA 30 also rates the fire hazard of flammable and combustible materials on a scale of 0 to 4 based on flash point. This rating helps you quickly assess the potential danger of a substance. Zero is the least hazardous and indicates the material will not burn. A rating of 1 is given to materials with flash points above 200°F and indicates the material needs to be preheated to burn, while flammables with flash points below 73°F are rated a 4 and are extremely flammable and the most dangerous.

Important guidelines for storage of flammable and combustible materials

The one issue we see cited most frequently is having excessive flammable solvents in the lab. NFPA 45, *Fire Protection for Laboratories Using Chemicals*, is the first reference we turn to as it provides universal guidelines for safe storage.[3] The maximum quantity of flammable and combustible materials that can be stored in the lab is set in NFPA 45, and this is how labs are classified. Chapter 4 of NFPA 45 classifies laboratories into four fire hazard categories based on the amount of flammable and combustible material in the lab. These are Class A (high fire hazard), Class B (moderate), Class C (low) and Class D (minimal). Examples of Class D are high school educational laboratories, while college level undergraduate labs are usually limited to Class C. Class A labs are allowed up to 10 gallons (38L) of Class I flammable liquid per 100 square feet or 20 gallons (76L) total of Class I, II, and III flammable and combustible liquid combined. These quantities can be doubled to 20 gallons of Class I liquid and 40 gallons (150L) of Class I, II, and III liquids, combined with the use of safety cans or storage cabinets.

"The most dangerous materials are those with the lowest flash point and widest flammable ranges."

NFPA 45 also addresses the maximum capacities for different storage container types. For example, for Class IA flammable liquids, the largest allowed container is one pint (500ml) for glass, one gallon (4L) for metal and approved plastic or polyethylene, and 2.6 gallons (10L) for safety cans. Safely storing flammable and combustible liquids in laboratories or stockrooms is risky business. However, by paying attention to the hazard class of the material, the largest container size, and the total quantities, you can minimize that risk. In addition, here are some general guidelines for safe flammable and combustible storage:

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

Resources

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Additional resources

NFPA 704: Standard System for the Identification of the Hazards of Materials for Emergency Response, National Fire Protection Association, Publication 704. www.nfpa.org/codes-and-standards/document-information-pages?mode=code&code=704

NIOSH Pocket Guide to Chemical Hazards. National Institute of Occupational Safety and Health. Publication 2005-149. www.cdc.gov/niosh/npg/

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INSIGHTS ON NEXT-GENERATION SEQUENCING

ENABLING TECHNOLOGY FOR DIAGNOSIS, PROGNOSIS, AND PERSONALIZED MEDICINE

by Angelo DePalma, PhD

Significantly higher speed, lower cost, smaller sample size, and higher accuracy compared with conventional Sanger sequencing make next-generation sequencing (NGS) an attractive platform for medical diagnostics. By practically eliminating cost and time barriers, NGS allows testing of virtually any gene or genetic mutation associated with diseases.

SCALABILITY AND SENSITIVITY

NGS brings scalability and sensitivity to diagnostics in ways that traditional DNA analysis could not. "NGS analyzes hundreds of gene variants or biomarkers simultaneously. Traditional sequencing is better suited for analysis of single genes or fewer than 100 variants," notes Joseph Bernardo, president of next-generation sequencing and oncology at Thermo Fisher Scientific (Waltham, MA).

Thermo Fisher's Oncomine Focus Assay for NGS, for example, analyzes close to 1,000 biomarkers associated with the 52-gene panel. These biomarkers constitute about 1,000 different locations on the 52 genes that correlate with the efficacy of certain drugs. The assay allows single-workflow concurrent analysis of DNA and RNA, enabling sequencing of 35 hot-spot genes, 19 genes associated with copy number gain, and 23 fusion genes.

NGS is also better suited to detect lower levels of variants present in heterogeneous material, such as tumor samples. And while both NGS and Sanger sequencing are versatile, NGS can analyze both DNA and RNA, including RNA fusions, at a much more cost-efficient price point.

"When interrogating a limited number of analytes, Sanger sequencing is the standard for many laboratory-developed tests, offering fast turnaround times and lower cost than NGS," Bernardo says. "We view the two methods as complementary."

Diagnostic NGS is moving inexorably toward targeted sequencing, particularly for tumor analysis. The targets are specific regions within a tumor's DNA or individual genes, or specific locations on single genes.

"Targeted sequencing lends itself to diagnostic testing, particularly in oncology, as the goal is to analyze multiple genes associated with cancer using a platform that offers high sensitivity, reliability, and rapid turnaround time," Bernardo tells *Lab Manager*. "It is simply more cost-effective."

That is why the National Cancer Institute (NCI) chose Thermo Fisher's Ion Torrent sequencing system and the Oncomine reagents for NCI-MATCH, the most ambitious trial to date of NGS oncology diagnostics.

NCI-MATCH will use a 143-gene panel to test submitted tumor samples at four centers (NCI, MD Anderson Cancer Center, Massachusetts General Hospital, and Yale University). The centers then provide sequencing data that helps direct appropriate treatments.

The NCI test protocol ensures consistency across multiple instruments and sites.

PERSONALIZED TREATMENTS

Another great opportunity for NGS-based diagnostics is in personalized or precision medicine for both new and existing drugs. Companion diagnostics—co-approved with the relevant drug—drive this entire business. "The only way personalized medicine can succeed commercially is if pharmaceutical companies incorporate a universal assay philosophy in their development programs instead of developing a unique assay for each new drug," Bernardo explains. For example, in late 2015, Thermo Fisher partnered with Pfizer and Novartis to develop a universal companion diagnostic with the goal of identifying personalized therapy selection from a menu of drugs targeting non-small-cell lung cancer, which annually causes more deaths than breast, colon, and prostate cancer combined.

While advances in sequencing have been remarkable in recent years, the eventual success of NGS-based diagnostics will not depend on instrumentation alone. "What [ensures] ease of use and commonality of results is the cohesiveness of the entire workflow, from sample prep to rapid sequencing systems and bioinformatics," Bernardo

says. "Those components working together will drive NGS into a realizable solution for the clinical market."

In addition to confirming a disease condition (diagnosis), NGS also provides valuable information on disease susceptibility, prognosis, and the potential effect of drugs on individual patients. The latter idea, known as precision medicine or personalized medicine, uses an individual's molecular profile to guide treatment. The idea is to differentiate diseases into subtypes based on molecular (usually genetic) characteristics and tailor therapies accordingly.

Precision medicine is still in its infancy, but dozens of pharmaceutical, diagnostics, and genetics firms have bought into the idea.

"We are just at the beginning of connecting genomic and genetic information to target specific therapies for patients," says T.J. Johnson, president and CEO of HTG Molecular Diagnostics (Tuscon, AZ). "Precision medicine will have a bright future as we gain better understanding of the root causes of disease."

In 2013, HTG commercialized its HTG Edge instrument platform and a portfolio of RNA assays, which fully automate the company's proprietary nuclease protection chemistry. This chemistry measures mRNA and miRNA gene expression levels from very small quantities of difficult-to-handle samples.

HTG entered the NGS market in 2014 with the launch of the first HTG EdgeSeq product, an assay that targets and digitally measures the expression of more than 2,000 microRNAs. The assay utilizes the HTG Edge for sample and library preparation, and it uses a suitable NGS instrument (from either Illumina or Thermo Fisher) for quantitation. The data is imported back into the HTG EdgeSeq instrument for analytics and reporting.

In 2015, the company launched four additional HTG EdgeSeq panels: immuno-oncology and pan-oncology biomarker panels, a lymphoma profiling panel, and a classifier for subtyping diffuse large B-cell lymphomas (DLBCL).

ELIMINATING BIOPSIES?

Traditional biopsies for tumor DNA analysis are invasive, risky, and often impossible to obtain, and they may not uncover the heterogeneity often present in tumors. It was recently discovered that dying tumor cells release small pieces of DNA into the bloodstream. This cell-free circulating tumor DNA (ctDNA) is detectable in samples through NGS.

In September 2015, Memorial Sloan Kettering Cancer Center (MSK) and NGS leader Illumina (San Diego, CA) entered a collaboration to study ctDNA for cancer diagnosis and monitoring. The aim is to establish ctDNA as a relevant cancer biomarker.

Heterogeneity as it pertains to cancer traditionally refers to multiple tissues located within a tumor, as determined histologically. A number of recent studies suggest that tumor heterogeneity occurs at the genetic level as well. "In particular, there appears to be a tremendous variety of sequence variants within the same tumor, even resulting in situations where one tumor can have multiple mutated genes that have been demonstrated to drive cancer," says John Leite, PhD, vice president, oncology—market development and product marketing at Illumina.

Heterogeneity challenges the search for treatments that target a specific gene product or pathway. Once the patient is treated, biopsies tell very little about how that patient is responding. "Our hope is that ctDNA provides clinicians with a real-time measure of the abundance of those mutated genes and that a decrease in the relative abundance is synonymous with a lower tumor burden," Leite adds.

Clinical trials are needed to demonstrate that patients whose therapy was selected using ctDNA versus traditional tissue biopsy testing had a significantly improved outcome or that the analysis might be informative for prognosis.

What about cancer cells that do not release DNA? "Studies show that tumors from different organs or tissues release more or less ctDNA into the peripheral blood," Leite explains, "but in general the possibility that some cells might not release ctDNA is an open area of research."

"The current bottleneck in personalized and precision medicine is the severe shortage of anticancer drugs."

For the MSK-Illumina collaboration, the cancer center will collect samples, and Illumina will apply its sequencing technology to detect ctDNA in those samples. The big draw here is the potential to reduce the number of invasive, expensive diagnostic and monitoring procedures with a simple blood test. This would not be possible without deep next-generation sequencing—the genomics vernacular for sequencing at great depths of coverage.

"Whereas sequencing to identify germline variants can be performed at a nominal depth of coverage—for example, reading a DNA strand 30 times—sequencing rare variants such as in ctDNA requires a much higher level of sensitivity, which is driven by increasing depth of coverage [as much] as 25,000 times," Leite tells *Lab Manager*.

In addition to the Illumina MSK collaboration and the work of Thermo Fisher Scientific described above, many more studies involving research consortia and pharmaceutical companies are under way.

"This is a really exciting time for oncology," Leite says.

REDUCING SAMPLE SIZE

Similarly, in November 2015, Circulogene Theranostics (Birmingham, AL) launched its cfDNA (cell-free DNA) liquid biopsy products for testing ten tumor types, including breast, lung, and colon cancers. The company claims the ability to enrich circulating cfDNA from a single drop of blood.

"While all liquid biopsy companies are focusing on the downstream novel technologies to selectively enrich or amplify tumor-specific cfDNA from a dominantly normal population, the upstream 40 to 90 percent material loss during cfDNA extraction leads to potential false negative results of cancer mutation detection," explains Chen Yeh, Circulogene's chief scientific officer. "This is why 10 to 20 mL of blood [are] generally required for conventional cfDNA liquid biopsies."

Released cfDNA fragments often complex with proteins and lipids, which shift their densities to values much lower than those of pure DNA or protein while protecting the corresponding cfDNA from attack by circulating nucleases. Circulogene's cfDNA breakthrough concentrates and enriches these genetic fragments through density fractionation followed by enzyme-based DNA modification and manipulation, eliminating extraction-associated loss. The technology ensures near-full recovery of both small-molecular-weight (apoptotic cell death) and high-molecular-weight (necrotic cell death) cell-free DNA species from droplet volumes of plasma, serum, or other body fluids.

"The 50-gene panel is our first offering," says Yeh. "We will continue to develop and cover more comprehensive, informative, and actionable genes and tests."

The current bottleneck in personalized and precision medicine is the severe shortage of anticancer drugs. Yeh provides perspective, saying, "We have about 60 FDA-approved drugs for cancer-targeted therapies on market, while there are approximately 150 cancer driver genes to aim for. If counting all mutations within these 150 genes, the numbers will be overwhelming."

Circulogene's cell-free DNA enrichment technology may be followed up with NGS, conventional Sanger sequencing, or any DNA assay based on PCR or mass spectrometry. However, the sensitivity of Sanger sequencing is insufficient for detecting variants with volumes below 15 percent. Moreover, the company's multiplex NGS liquid biopsy test captures and monitors real-time, longitudinal tumor heterogeneity or tumor clonal dynamic evolution, which goes well beyond testing of a single mutation on a single sample in traditional sequencing.

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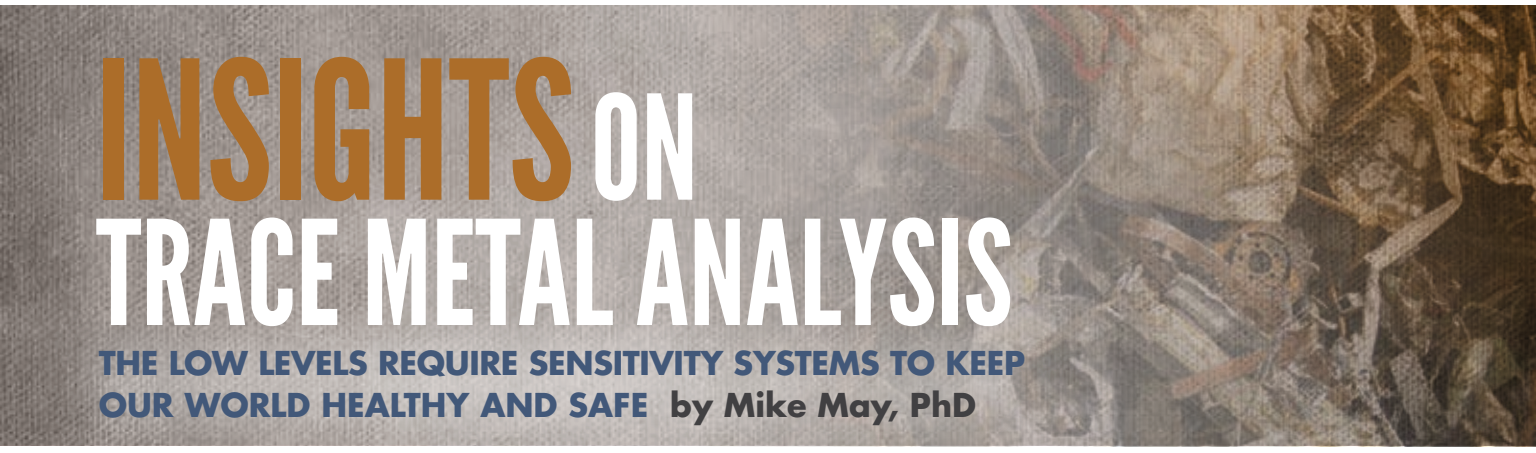


INSIGHTS ON TRACE METAL ANALYSIS

THE LOW LEVELS REQUIRE SENSITIVITY SYSTEMS TO KEEP OUR WORLD HEALTHY AND SAFE

by Mike May, PhD

In the 1970s in the United States, the Environmental Protection Agency started to ban the use of lead—specifically tetraethyl lead—in gasoline because of health risks, but aftereffects linger decades later. Although this additive made engines run more smoothly, its health dangers were documented as early as 1924. Lead, a potent neurotoxin, makes up just one example of how even trace amounts of metals can spawn environmental consequences that hurt humans and animals. "Some of the challenges of environmental analysis are detection of low concentrations of trace elements, especially for matrices such as seawater or soil and sediment digestions; controlling laboratory blanks, especially for mercury analysis; and getting good recovery of trace elements from soils and sediments using acid digestions," says Brian Jackson, director of the Trace Element Analysis Lab at Dartmouth College in Hanover, New Hampshire. Like many other experts in this field, Jackson and his colleagues rely largely on inductively coupled plasma-mass spectrometry (ICP-MS). In most cases, says Jackson, "ICP-MS gives the lowest detection limits with relative freedom from interferences through the use of collision and reaction cell ICP-MS instruments."

For example, Jackson's team recently analyzed trace-element concentrations in the feathers of songbirds in Pennsylvania to assess contamination from fracking. "The study authors found higher levels of strontium and barium in [the] feathers of birds from high fracking areas," Jackson says. "Feathers are challenging analytically because first it is necessary to clean the samples with surfactant and deionized water rinses, which is time-consuming and involves a lot of sample handling. Second, there is not a lot of biomass, so we used a scaled-down digestion with reduced volume of acid addition and final dilution volume." Moreover, the analyte levels were low parts per billion or even less. So, Jackson says, "we optimized the analysis to focus on this concentration range."

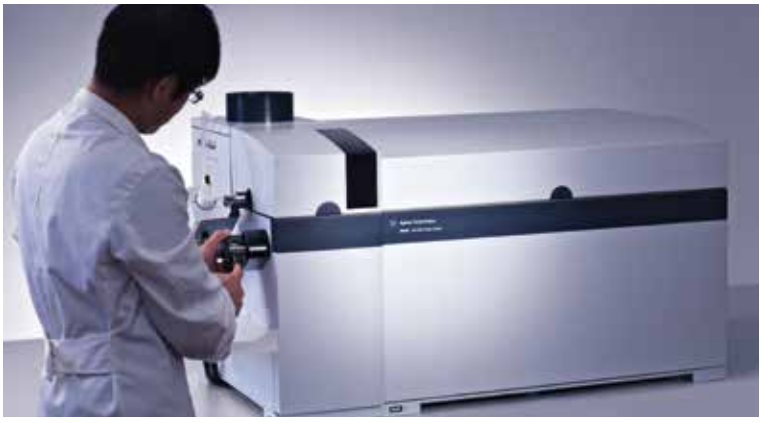
Beyond bird feathers, scientists use ICP-MS in many other environmental applications. Drinking water, rainwater, and even air can be analyzed for metal concentrations with ICP-MS. It can also be applied to more complex samples, including wastewater, sewage sludge, trade effluents, landfill leachates, soil and sediment digests, and biota. That variety of sample types reveals part of the challenge of analyzing environmental samples. As William Lipps, environmental/mining marketing manager at Shimadzu Scientific Instruments (Columbia, MD) says, "Environmental samples have highly variable matrices ranging from parts per million levels to parts per trillion (ppt) levels of analytes potentially in the presence of other components." He adds, "The various matrices of a sample can present different challenges depending on the element and the components of the matrix."

To get the most from this technology, scientists need ongoing improvements in the commercially available ICP-MS platforms. That allows even nonexperts access to this powerful tool.

EFFECTS OF INTERFERENCE

Various forms of quadrupole MS can reveal traces of metals in environmental samples, but this sample-technology combination poses some challenges. "The technique does suffer from some well-documented spectral and non-spectral interferences," says Craig Marvin, global environmental industry manager for Agilent Technologies (Santa Clara, CA). This comes from several main sources. One, says Marvin, is "direct overlap from a different element with an isotope at the same nominal mass—known as an isobaric interference, such as 114Sn overlap on 114Cd." Another is "overlap from a polyatomic ion formed from the combination of species derived from the plasma gas, sample solvent, and/or sample matrix—for example, 40Ca16O overlap on 56Fe."

To get accurate results, scientists need to correct the effects of interference. As Lipps says, "This requires a higher level of experience in the user compared with atomic absorption." He adds, "As samples and matrices change, new corrections and adjustments to the method



▲ *The right instrument, like this Agilent 8800 Triple Quadrupole ICP-MS, can reduce interference when analyzing environmental samples for trace-metal contamination. (Image courtesy of Agilent Technologies.)*

◀ *Inductively coupled plasma-mass spectrometry (ICP-MS) can be used to analyze many environmental samples, including drinking water, for trace metals. (Image courtesy of the author.)*

must be performed." In many cases, mathematical corrections resolve the interference problems, as long as the interference doesn't contribute too much to the MS peak of the analyte.

Technology also helps. "Most labs are switching to collision/reaction cell (CRC) instruments, as they are much simpler to use, provide unequivocal results, can be applied to unrelated interferences on multiple analytes, and provide better accuracy over a wide range of complex matrices," Marvin explains. For example, the Agilent 8800 Triple Quadrupole ICP-MS is a CRC instrument. Marvin says, "The Agilent 8800 controls the ions that enter the collision/reaction cell, providing consistent and predictable reaction conditions—even if the sample composition changes." He adds, "This enables reliable trace analysis for applications such as the low-level measurement of selenium and arsenic in soil, rock, and plant materials, where interferences often occur."

Being careful when using ICP-MS also improves the results. The high sensitivity of ICP-MS adds other challenges to getting accurate outcomes, and pushing this technology's limits increases those challenges. "Contamination becomes more problematic the lower you want to measure, and this problem includes reagent water, labware, and reagents used to prepare the samples," Lipps explains. "There may be a need for a cleanroom, and, certainly, there is a need to minimize all metal exposed near the instrument and where samples are processed."

Despite the challenges, ICP-MS offers many benefits in testing environmental samples for trace metals. For one thing, just one run analyzes a sample for many elements, including alkali and alkaline earth elements, transition and other metals, metalloids, rare-earth elements, most of the halogens, and some of the nonmetals. In addition, ICP-MS can analyze samples from a wide range of sources, and it can quickly detect analytes at concentrations down to ppt.

UPSTREAM ADDITIONS

To get more out of ICP-MS, some scientists add an upstream step. The interference, for instance, can sometimes be removed with chromatography before the MS. Depending on the sample, capillary electrophoresis, gas chromatography, or liquid chromatography (LC) can be used to improve the detection limits.

When combining ICP-MS and LC, in particular high-performance liquid chromatography (HPLC), scientists can separate and quantify metals in their different oxidation states. "Some very common elements measured in different oxidation states are arsenic, cadmium, selenium, and chromium," Lipps says. "These elements

occur naturally in the environment and their toxicity is dependent on their oxidation state." Lipps also points out that Shimadzu makes complete HPLC systems, including the software, and "this ensures [that] all pieces work together seamlessly as if they were one instrument."

Beyond those very common upstream tools, some scientists add others to ICP-MS. "For example, geochemists may be interested in a laser-induced breakdown or ablation system—LIBS," Lipps says. "Here, a laser is used to vaporize a sample and deliver it to the plasma for analysis." With this technique, solids can be directly analyzed with ICP-MS. Consequently, researchers don't need to use some of the aggressive chemicals, such as hydrofluoric acid, to dissolve the sample, as those chemicals can contaminate a sample. With LIBS, Lipps says, "Shimadzu uses an off-axis lens configuration to reduce the instrument background, thereby increasing sensitivity."

"Contamination becomes more problematic the lower you want to measure, and this problem includes reagent water, labware, and reagents used to prepare the samples."

ADVANCING APPLICATIONS

"One of the fastest-growing areas of ICP-MS is speciation measurement—the combination of chromatographic techniques with ICP-MS as a detector to determine the chemical form of elements in the sample," Marvin says. "These capabilities help explain the widespread acceptance of ICP-MS and confirm the status of ICP-MS as the premier technique for trace metals measurement."

Advances in materials also create new opportunities to use ICP-MS on environmental samples. In the December 2015 issue of the *International Journal of Environmental Research and Public Health*, researchers from the University of Vienna in Austria analyzed soil samples for copper nanoparticles, which are commonly used in engineered nanomaterials, including agricultural sprays. Moreover, many governments regulate these materials and it's hard to detect copper nanoparticles in soil. So this team tried ICP-MS. They concluded: "Overall, copper nanoparticles were successfully detected in the soil colloidal extracts."

In the field of analyzing environmental samples for traces of metals, ICP-MS is the primary tool that scientists use, but not the only one. For instance, Jackson and his colleagues rely almost exclusively on ICP-MS, but there is one exception: mercury in a solid sample when only that element is being analyzed. In those cases, Jackson says, "the direct mercury analyzer is a quicker and easier method." Also, for mercury in water, Jackson uses cold-vapor atomic fluorescence spectroscopy (AFS). He says, "Cold vapor AFS gives lower detection limits, mostly because of lower blanks."

ECONOMICS OF ANALYSIS

No matter how effective a technology might be, it must be affordable. When considering an ICP-MS system, the purchase price and cost of operation should be part of the decision-making process. For example, Lipps says, "the rate of argon use for an ICP-MS system can range from over 25 liters per minute to as low as 10 liters per minute." The required purity of the argon also impacts the economics, because the purer the gas is, the more expensive it is. "Some systems can operate without deleterious effect on purity as low as 99.9%, whereas some systems require 99.999% purity," he says.

The maintenance of an ICP-MS system also affects its lifetime economics, as well as its overall uptime. The parts that commonly need maintenance include the torch and the sampling and skimming cones. "Well-designed systems do not require any tools to access or remove parts for servicing," Lipps says.

This brief review provides only an introduction to a broad and critical field. The environment in which we live plays a fundamental role in our health, as well as the health of our world's environment. In many cases, metals can contaminate that environment, and scientists and public health workers depend on tools like ICP-MS that deliver fast and accurate analysis. Only then can we better identify and correct some of the dangers around us.

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Dr. Robert Linnen

ASK THE EXPERT

MINIATURIZATION IN SEM —TOOLS & ANALYSIS

by Rachel Muenz

Dr. Robert Linnen is a professor and the Robert Hodder Chair in Economic Geology in the Department of Earth Sciences at Western University in London, Ontario, Canada. His research focuses on the behavior of metals in magmatic-hydrothermal systems. Dr. Linnen's approach is to combine field and experimental studies in order to identify the mechanisms that are important for concentrating metals and controlling mineralization and then quantifying these processes in order to develop ore deposit models.

Q: Can you tell me a bit more about your work at Western University?

A: Largely, I study the origin of mineral deposits—if we understand how mineral deposits form, we can come up with better models to explore for new mineral deposits. In studying mineral deposits, there are a variety of tools. I'm a geochemist and a mineralogist, so I tend to use geochemical tools. One of the things that I look at is the compositions of minerals and how they help us understand ore-forming processes or just identify ore.

Q: I see you're using a benchtop scanning electron microscope [SEM] to look at problems in mineral exploration and mining. What are some of the specific problems you're looking at?

A: An example of where the JEOL NeoScope SEM comes in is with gold mines. In a typical gold mine, the ore, which is what you are recovering to make a profit out of the process, may only be a few ppm. It may be between 5 and 10 ppm. So when you look at the rock, you may not see any gold in it because the particles of gold are too small. We're dealing with very low concentrations that you're still making money off of. So I can have an assay of a rock that comes back at, say, 10 ppm, but I can't see any of the gold in it. The SEM allows me to go to a much, much lower scale—down to the 1µm or less than 1µm scale—and observe where the actual gold is in the rock. Is the gold in a particular mineral or is it by itself? There's pure gold, but there are also gold minerals like gold tellurides and things like that, so I can identify the minerology of the gold using the EDS [energy-dispersive X-ray spectroscopy] on the SEM. While a lot of my work involves understanding the genesis of ore deposits, I also spend some time on technique development. One of my current projects involves combining pXRF [portable X-ray fluorescence] and the benchtop SEM to map igneous stratigraphy [correlating different layers of rock], which is a key for platinum group element exploration. This is the first study of its kind, where the benchtop SEM is applied to either mineral exploration or studying mineral deposits or mines.

> "You don't have to send everything back to the lab now; you can start analyzing samples in the field."

Q: How have these technologies made things easier for geologists?

A: With pXRF, instead of having to take a rock and ship it to a lab, and then wait weeks to get an analysis back, you can just take one of these pXRF units in the field with you and start analyzing rocks. That's pretty cool. You don't have to send everything back to the lab now; you can start analyzing samples in the field. If you want to know chemical compositions of rocks and you want to do it quickly and do it in the field, this pXRF has revolutionized things; it's very widespread in the mining and mineral exploration industry. But for minerology, you can't really do that.

Q: What techniques have you had to use for the minerology side?

A: Historically, what we've done is bring a rock back, cut what's called a section of it, and then analyze it with the JEOL electron microprobe that we have in our department. I'm one of the principal investigators on that instrument. With the electron microprobe, you can analyze mineral compositions,

but it takes a long time. You have to bring the rock in from the field, cut up the rock, get the section prepared, and then do the analyses. That can take weeks to months.

Q: What does the miniaturized benchtop SEM allow you to do that you couldn't do before?

A: With the benchtop SEM, I don't even have to make one of these sections—I can just take a piece of rock and put it in the benchtop SEM and start analyzing my minerals. I can see whether there's gold or whether there are things like platinum group elements. I can see how the metals are distributed in the rock and the chemical compositions of the minerals that are associated with the metals. Benchtop SEMs have been around for a while, but nobody has really been doing this in geology. At our lab we're the first ones who are doing this, so we're developing new techniques as to how to use the benchtop SEM for mineral exploration and, for that matter, mineral processing as well. This is a new field of research. We haven't been bringing [the benchtop SEM] into the field with us, but there's no reason why we can't. We're doing analyses with it in my lab for gold, platinum, and other projects, and the EDS is the system that does the chemical analysis under the microscope. That's the real key part of the scanning electron microscope—the EDS on it. We use that to get mineral compositions. Everything that can be done with an electron microprobe, we're pretty much doing with the benchtop SEM at a much lower cost and with a much quicker turnaround.

Q: How has that work with the benchtop SEM gone so far?

A: Excellent. Most of my students use it, and they're applying it in what I call the "triage approach." In triage you look at what's most critical and you deal with what's most critical first and then what's less critical afterward. With rocks, we're not operating on them, but you do winnow things out—so you might collect 100 rocks in the field, and then of those 100 rocks in the field maybe 30 of them go for a particular kind of analysis, and then out of those 30 you're going to select three for another type of analysis. There's a hierarchy of decisions that you make on what you want to analyze. The benchtop SEM is not the highest precision or the highest accuracy, but it gives you an idea as to what's in the rock. So we use that philosophy in this triage method, and a lot of my students are using it as a first-pass evaluation of the rock to make the decision, for example, on which sample out of ten is the best one to select for further analysis, because that might be all I can afford. The benchtop SEM is very well suited to screen what samples go to the next stage of analysis.

> "With the benchtop SEM, because it's relatively low cost ... my students have instant access to it."

Q: What are the main ways that the miniaturization of SEM instrumentation has impacted your work?

A: With a regular SEM, and the electron microprobe is the same way, there are waiting times. So if I want to use the [regular laboratory] SEM, I might need to wait two or three weeks. Whereas with the benchtop SEM, because it's relatively low cost—an order of magnitude less than a full-scale laboratory SEM—my students have instant access to it. If I have something right in front of me and I want to answer that question, I can go down to the lab right now. I'm not booking an appointment. Obviously, different people from the department use it, but it's the accessibility as well—it's that all my students and students of others can use it without having to have a specific time booked.

Q: What, if any, are some of the challenges with the benchtop instrument?

A: If we had a wish list as to what the next generation is going to look like, then a larger sample size would be useful. But if you work with a larger sample size, then you need to make the entire piece of equipment bigger too, and then it becomes less portable. It's a trade-off between the small size of the benchtop SEM and the size of the samples that we'd like to analyze with it. The only other challenge will be making it truly portable. We haven't gotten around to designing a travel case for the SEM. That'll be something that'll have to come down the road. In coming up with a travel case, there are screws that have to come in and out of the machine, and that sort of stuff. That's an engineering thing that we haven't started looking at yet.

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GC TROUBLESHOOTING

TIPS FOR QUICKLY RETURNING TO NORMAL OPERATION

by Angelo DePalma, PhD

Although most chemists take classes in the theory of gas chromatography (GC), they learn operation and troubleshooting mostly through hands-on operation and laboratory lore. Thanks to the World Wide Web, online troubleshooting tips from vendors are available in seconds, without the need to find and dust off technical manuals.

Restek (Bellefonte, PA), for example, provides some of the best general-strategy rules for troubleshooting methodology:

- Change only one thing at a time.
- Carefully document all maintenance and troubleshooting activity.
- Check the obvious and routine things first: look at maintenance logs, check cables and connections, perform a leak check.
- Isolate system components and steps: confirm proper sample prep, perform a blank run, connect an alternate injector or detector, install a different column.

General and detector issues

Eric Denoyer, PhD, director of marketing, GC, and workflow automation solutions at Agilent Technologies (Santa Clara, CA), notes that GCs are complex but generally reliable systems. However, during a single GC analysis, a multiple-injection sequence, or an analysis of longer duration problems may arise in a number of areas, for example:

- Running out of a carrier or detector gases, or solvent in autosampler wash vials.
- Failure to draw sample due to syringe needle bending or other problem.
- Leaking septa.
- Inlet liner contamination.
- Flame ionization detector (FID) jet plugging.
- Thermal conductivity detector (TCD) signal noise or spikes due to ambient pressure fluctuations.

Denoyer notes that given all the possibilities for problems during a GC run or sequence, detectors generally contribute very few problems. However, two detector-related problems noted above stand out.

During the GC oven temperature program, the stationary phase on the column may slowly bleed off. "It may condense in the jet or actually burn, forming silicon dioxide, which slowly plugs the tip of the jet," Denoyer says. This leads to slowly increasing back pressure on the end of the column, resulting in gradually decreasing column flow and increasing peak retention times. Eventually, as the jet becomes sufficiently plugged, the flame can blow out on solvent elution. "The time frame for the plugging to happen can be months, years, or decades, depending on column bleed and maximum column temperatures," he says. The solution for this problem is regular FID jet maintenance. "Consider using a wider-bore jet for high-temperature applications or thick film columns," Denoyer adds.

TCD baseline noise and spiking occur because the detector itself is susceptible to ambient pressure changes, which couple onto the TCD signal baseline and result in corresponding noise. "Even opening and closing a laboratory door can cause a large spike," Denoyer notes. One strategy for overcoming this issue, at least on Agilent differential TCDs, is to install a small restrictor on the exit of the TCD, which isolates the internal TCD pressure from ambient pressure changes in the laboratory environment.

Diagnosing detector-related problems involves going through a series of steps:

- Running a no-injection system blank, solvent blank, or QC check standard.
- Executing a method-detection limit test.
- Performing a signal-to-noise check.
- Conducting a sample breakdown check.
- Executing a system precision test.
- Recalibrating the method.

Column issues

Column-related problems manifest themselves in retention time shifts (usually to shorter times) and improper peak shapes—tailing, split, small, or wide peaks. "My first question in supporting a customer with these issues is, what is the previous versus present column performance?" says Martin Smith, GC project engineer at Shimadzu Scientific Instruments (Columbia, MD). "Is the problem acute or chronic? Is this a sudden symptom or has column performance deteriorated over time?"

Since GC columns are expensive, labs should consider re-conditioning them until they no longer provide satisfactory performance. Periodic solvent washes or baking at high temperature are common regeneration methods that can add weeks or months to a column's usable life.

Baking out involves disconnecting from the detector, capping the detector inlet, stopping flammable support gases, and turning up the heat with column carrier flow. "You don't want to bake the dirty effluent into the detector," Smith says. Column vendors supply the specific column's bake-out parameters. "The double-edged sword of baking out is if you leave the column connected to the detector, you bake that dirty effluent into the detector, which doesn't win any prizes. Some detectors that contaminate easily, like an electron capture detector, are unforgiving toward the kind of contamination generated during a bake-out, with increased baseline noise as the result."

Solvent rinses take more effort but can sometimes provide superior results. Supelco (Bellefonte, PA), Restek, and other vendors supply kits for column rinsing. Solvents may be drawn into or pushed through columns, but Smith prefers the former. "Pressurizing a glass vessel can create a glass grenade." Column vendors also provide information on recommended pressures and solvents. Most stationary phases are cross-bonded and resistant to damage, but they may be compromised if the wrong solvent is used. Vendors will also specify volumes that will provide the cleanest possible column without removing the stationary phase.

Since the part of the column closest to the injector is by far the dirtiest, rinsing should always occur in reverse, from the detector end to the injector end, so as not to push contaminants through the cleaner region of the column. A bake-out with column carrier flow occurs after the solvent rinse to remove traces of solvent.

Innately dirty analyses abound. Smith mentions biodiesel and polychlorinated biphenyls in oil as common stock methods that can wreak havoc on a column. Note that some analytical methods specify solvents that are inherently unfriendly to stationary phases and essentially reduce column efficiency with each injection. In this case, solvent rinsing is unlikely to restore performance significantly.

"Miracles do happen, but typically rinsing and baking out amount to desperate measures to maintain a column in working order for a couple of weeks or months, but eventually you have to replace the column," Smith says. "Whatever you do, the column will never again work like new."

Smith notes that the common recommendation of clipping off one meter from both ends of a column may be too severe given the performance degradation resulting from shorter columns. "I lop off four inches at a time from the injector side instead, and keep injecting solvent to see if the contamination is gone. I'd rather keep column length as long as possible."

Angelo DePalma *is a freelance writer living in Newton, New Jersey. You can reach him at angelo@adepalma.com.*

FOR ADDITIONAL RESOURCES ON GC TROUBLESHOOTING, INCLUDING USEFUL ARTICLES AND A LIST OF MANUFACTURERS, VISIT WWW.LABMANAGER.COM/GC

ARE YOU IN THE MARKET FOR AN... HPLC SYSTEM?

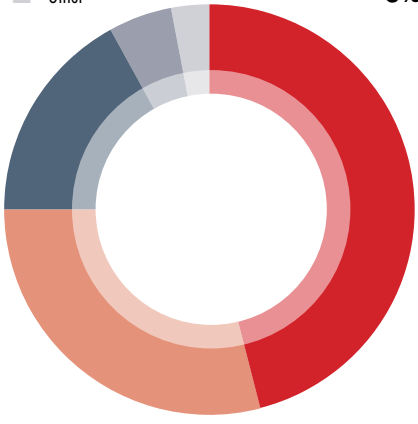
High-performance liquid chromatography (HPLC) is, for many scientists, an essential chromatographic technique. HPLC systems used for the separation, identification, purification, and quantification of various chemical and biochemical solutions are composed of a pump, a sample injector, a separation column, a detection unit, and a data-processor.

Types of HPLC systems used by survey respondents:	
Analytical HPLC	88%
UHPLC	28%
Ion Chromatograph	16%
Preparative HPLC	14%
GPC	9%
FPLC/Bio	3%

HPLC separation modes utilized by survey respondents:	
Reverse phase	80%
Normal phase	43%
Ion exchange	33%
Ultra-high performance (UHPLC)	24%
Ion chromatography	22%
Hydrophilic interaction (HILIC)	21%
Size exclusion (SEC)	18%
Chiral	13%
Gel filtration (GFC)	10%
Affinity	10%
Gel permeation (GPC)	8%
Ion exclusion	4%

Nearly 53% of respondents are engaged in purchasing HPLC instruments. The reasons for these purchases are as follows:

Replacement of an aging system	46%
Addition to existing systems, increase capacity	29%
Setting up a new lab	17%
First time purchase	5%
Other	3%



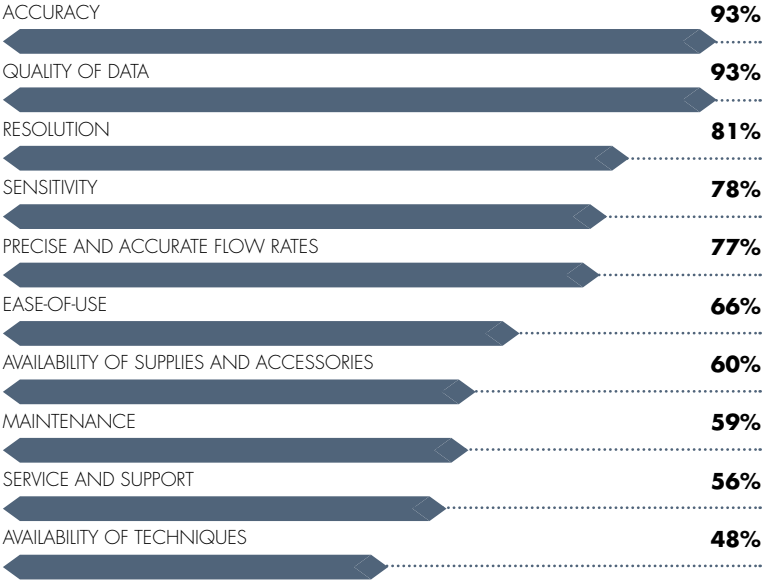
TOP 6 QUESTIONS

You Should Ask When Buying an HPLC System

1. How flexible is the system? Can the system be optimized to meet your laboratory requirements?
2. What tubes, vessels, and vials can it accommodate? Can components (such as additional detectors, valves, etc.) be upgraded in the future?
3. Is the software easy to use and operate? Can a demo version be put in place to get a feel for how the software functions for your laboratory's workflow?
4. How is the system (not just components) qualified during installation to meet manufacturer performance expectations?
5. Who provides the support and service for the product? Is it the manufacturer or a third party service group? If it is a third party service group, are they factory-trained?
6. Finally, ask about the total cost of the purchase—not just the price of the product being installed— but the total cost of ownership, which includes price, service expectations, warranty, etc.

TOP 10 FEATURES/FACTORS

Respondents Look for When Purchasing an HPLC system



For more information on HPLC systems, including useful articles and a list of manufacturers, visit www.labmanager.com/hplc-systems

Gary Siuzdak, PhD

ASK THE EXPERT

INNOVATIONS IN MASS SPECTROMETRY

by Tanuja Koppal, PhD

Gary Siuzdak, PhD, professor and director of the Scripps Center for Metabolomics at The Scripps Research Institute, talks to contributing editor Tanuja Koppal, PhD, about his work developing novel mass spectrometry-based (MS) approaches for metabolomics and nanostructure-based MS imaging. According to him, while innovations in instrumentation for MS are exciting, the next frontier lies in data analysis and integration using cloud-based computing.

Q: Can you share some details about the work being done at your center?

A: We are involved with a wide variety of research projects that are funded by the National Institutes of Health, the Department of Energy, and the Department of Defense. The topics range from bioremediation to studying cancer, microbiota, neurodegenerative diseases, and stem cells. There is also a component of the lab that is dedicated to doing routine types of analyses for clients. We are very diverse in what we do, and hence use many different types of LC, GC, and imaging MS for analysis. We have 25 different mass spectrometers in our lab, including multiple quadrupole time-of-flight (Q-TOF) MS, triple quadrupoles, ion traps, and TOF-TOF instruments. We are also developing new technologies, including nanostructure imaging mass spectrometry (NIMS), a matrix-free solution for tissue imaging, activity screening, and analyzing nanoarrays. However, our primary field of work is metabolomics, especially the bioinformatics side of metabolomics and its application.

Q: Why is MS such an important tool for metabolomic research?

A: MS is extremely valuable for metabolomics because of its high mass accuracy, sensitivity, and quantitative capabilities, and it's also very comprehensive in terms of the number of molecules it can analyze in a single run (thousands).

Q: How has MS improved over the years?

A: The sensitivity and reliability of MS have dramatically improved in the past decade, along with its ease of use. One of the interesting things about MS is that the technology has matured to such an extent that it has opened up all sorts of new applications. However, the one thing that still remains a challenge is the ability to share your data with your colleagues. Sharing data is still a challenge because the software being used on each end is often different. Hence, cloud computing is becoming very valuable.

> "Cloud computing is becoming very valuable."

Q: Can you tell us how you are using the cloud to help with your MS analysis?

A: We are using the cloud for XCMS, a widely used data analysis/bioinformatics platform we developed. With XCMS, all the MS data is available online and therefore immediately accessible to anyone with the appropriate permissions. Users can get direct access to their data via this cloud-based system without downloading any software programs. All they have to do is register online and they immediately will be able to see the data and the statistical analyses. There is a tremendous advantage to using this cloud-based system, an advantage that is reflected in the number of users, now approaching 10,000. Using the cloud is cheaper too; software redundancy is not needed when you are working in the cloud.

Q: What can you do using XCMS?

A: XCMS was the first platform designed to decipher metabolomic data. It was developed nearly 12 years ago as a downloadable software in our lab, and four years ago we turned this into a cloud-based system, XCMS Online (xcmsonline.scripps.edu). XCMS allows anyone to take MS-derived metabolomic data and perform statistical and comparative analyses. And while it was originally designed for biomarker discovery, we are now seeing it applied to forensics, the food industry, agriculture, cosmetics, and disease pathogenesis.

Q: Have you addressed the issues around data security when working in the cloud?

A: We have endured a number of [cyber] attacks in the past and have learned from our experiences; we believe we have a very secure system. However, there are labs and companies that do not want their data exposed in the cloud, so in designing our system we have simultaneously developed a personal cloud

where individuals or companies can set up a version of this XCMS software within the firewall of their own organizations. This is the commercial version called XCMS Plus.

Q: What are some of the limitations with working in the cloud?

A: One limitation is the amount of time it takes to upload the data, which is very location-dependent. If the connection is fast, it will take only a few minutes, but in some countries it can take hours to upload data. Now with XCMS Plus (the personal cloud), individuals can upload as much information as they want because they own the cloud.

Q: What are some of the recent innovations in MS that have transformed its use?

A: The ability to perform high-throughput, quantitative analysis as well as the ability to do imaging with high sensitivity has been transformative. Now you can image all types of tissues or arrays in a relatively short amount of time. However, the real breakthrough has been with the application of triple quadrupole technology, a technology that has become so sensitive and robust that it's being widely applied to many different areas, especially clinical studies. For example, over 50 million clinical analyses are performed each year using MS encompassing applications in neonatal screening, drug monitoring, hormonal testing, and more.

On the bioinformatics side, over the past two decades, new developments have allowed us to quickly identify and quantify proteins and metabolites. The identification of metabolites has been largely facilitated by the first metabolite database, METLIN, which is currently the largest in the world. XCMS coupled with METLIN gives people free access to a lot of comprehensive data and analysis tools.

Q: Can you describe your work with NIMS and how it's being used?

A: Details about Nanostructure Imaging MS were originally published in 1999 in *Nature*. Back then it was called desorption/ionization on porous silicon (DIOS). It was the first time that anyone had looked at these nanostructure porous silicon surfaces and seen such a prominent effect in terms of generating ions from them. Since then it has evolved, and now is one of the most sensitive MS technologies due to its efficiency in getting ions into the gas phase.

Q: What would you like to see change in MS?

A: MS is quite good as is, but having a dynamic range of 105 or 106 can be quite limiting. Biological fluids and tissues have molecules that can vary in concentration by 1010 to 1013, so having MS technology that would increase the dynamic range would really be quite beneficial for biological samples. Another big limitation for MS-based imaging technology is that it is typically limited to observing hundreds of molecules, therefore making it much less comprehensive than LC/MS-based technologies. What I would like to see is an imaging technology that would provide a much more comprehensive picture of biomolecules. The other area for improvement is informatics. There are lots of other problems that can be addressed with the right informatics tool, and those seem to be taking a while to come along.

Q: What would your advice be to new lab managers working with MS?

A: I would advise people to talk to their colleagues, attend the American Society for Mass Spectrometry (ASMS) conference, and listen to as many people as they can about their experiences. Only when you hear many different opinions can you make informed decisions. We have a local MS network, called SANDMAN (San Diego MS Analysis Network). In the past we typically had people come and give talks, but now we just meet at a brewery and interact with one another. It's working out quite well as a learning experience and networking opportunity, besides being an enjoyable event.

> "XCMS allows anyone to take MS-derived metabolomic data and perform statistical and comparative analyses."

Gary Siuzdak, PhD, is a professor and director of the Scripps Center for Metabolomics at The Scripps Research Institute in La Jolla, California (masspec.scripps.edu/) and an affiliate of the Lawrence Berkeley National Laboratory. Gary has also served as vice president of the American Society for Mass Spectrometry. His research includes developing novel mass spectrometry-based approaches in metabolomics, informatics, and nanostructure imaging mass spectrometry.

***Tanuja Koppal, PhD,** is a freelance science writer and consultant based in Randolph, New Jersey. She can be reached at tkoppal@gmail.com.*

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SUPER-RESOLUTION MICROSCOPY

NEARLY ANY BIOLOGIST CAN NOW USE SOME FORM OF THIS MICROSCOPY

by Mike May, PhD

On October 8, 2014, the world of microscopy moved closer to a major transition when the Nobel Prize in Chemistry for 2014 was awarded "for the development of super-resolved fluorescence microscopy" to Eric Betzig of the Janelia Research Campus, Stefan W. Hell of the Max Planck Institute for Biophysical Chemistry, and William E. Moerner of Stanford University. Super-resolution microscopy provides resolution that surpasses the diffraction limit—about 200 nanometers—of ordinary light microscopy. This form of microscopy comes in an alphabet of types: NSOM (near-field scanning optical microscopy), PALM (photoactivated localization microscopy), SIM (structured illumination microscopy), STED (stimulated emission depletion), STORM (stochastic optical reconstruction microscopy), and many more. Each version provides variations in capabilities, which can depend on changes in sample preparation, and only experts could make these work, until now.

When I ask Leanna Ferrand, product support leader for cell analysis at GE Healthcare's Life Sciences business (Issaquah, WA), if she is seeing more nonspecialists using super-resolution microscopy, she says, "Absolutely!" She adds, "We are getting to the transition place where maybe more nonspecialists than experts are using super-resolution."

At Cornell University's Biotechnology Resource Center, imaging director Rebecca Williams helps scientists use a range of super-resolution microscopes. For example, a Zeiss ELYRA provides PALM, super-resolution SIM (SR-SIM), and STORM modes. "SR-SIM is pretty straightforward," Williams says. "You can use any fluorophore that you want, and there's not a lot of limitations on the sample." She adds, "The sample can't be too thick, but SR-SIM will mostly work with anything that you'd use with normal imaging." Even while using traditional samples and preparation, SR-SIM increases resolution by a factor of two over standard light microscopy. "If you need to see just a little bit more," Williams says, "SR-SIM can make a huge difference." Perhaps even better, Williams and her colleagues can quickly teach scientists to use this technology themselves. "If you can run a confocal microscope, you can do SIM," Williams says.

Most nonspecialists, though, do need help using super-resolution microscopy. As Steve Ross, general manager, products and marketing, at Nikon Instruments (Melville, NY) says, "When it comes to nonspecialists, they primarily use super-resolution in core imaging facilities." He adds, "In the past few years, the majority of core facilities added different modalities of super-resolution."

> "If you can run a confocal microscope, you can do SIM."

Advanced systems

The super-resolution microscopes themselves allow this technology to move from expert to generalist. "The systems are just much more user-friendly than they used to be," Williams says. "The vendors have made complex processes—like programming tiled series or following selected regions—intuitive with just the touch of a few buttons."

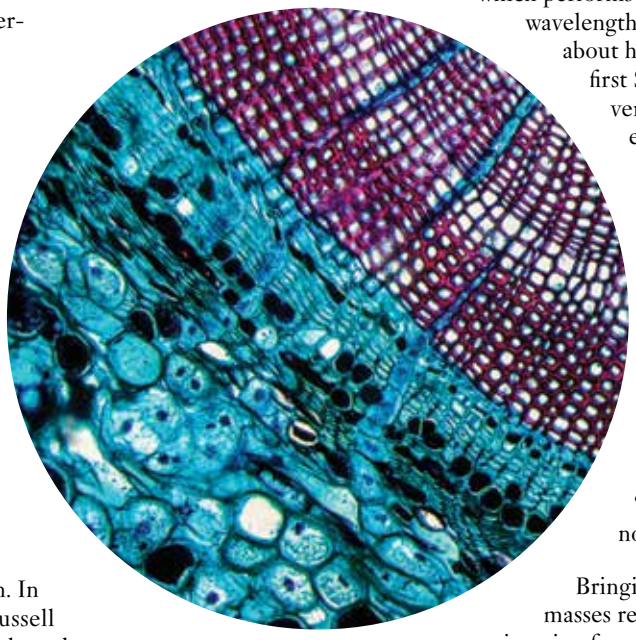
Also, today's super-resolution microscopes automate some features that produce excellent images. Focus feedback is one example. "If you take 20,000 images, and [they're] slowly going to go out of focus," Williams explains, "you are left with garbage." Focus feedback maintains the same focal plane. "It's a feature that works well now, and it didn't used to," Williams says.

In some cases, easier sample preparation also brings more biologists into super-resolution microscopy. "All microscopy takes a lot of sample preparation," Ferrand says, "and cutting any corners really shows in super-resolution." Nonetheless, she points out that SIM doesn't require special sample preparation, and those who

use standard fluorophores and mounting media on samples for other fluorescent microscopy techniques can start right away with those same samples.

> "The trend to get better images has always been there, and this is another step in the process."

Some platforms even deliver super-resolution-like imaging in more traditional technology. The Zeiss Airyscan detector, for instance, works with a confocal microscope, and with 488 nanometer laser light this detector gives 140-nanometer lateral resolution. Also, Nikon's A1-ER is similarly an extended-resolution confocal microscope.



A scientist can also purchase a system that provides confocal and super-resolution modes, such as the Olympus SD-OSR spinning disk super-resolution system. This microscope gives 120-nanometer lateral resolution. In talking about this microscope, Russell Ulbrich, product manager for high-end imaging systems at Olympus (Center Valley, PA), says, "People have explicitly stated their interest and then been surprised that they don't need to change their protocol to access super-resolution."

Despite the sophisticated imaging of the SD-OSR, it doesn't take much to run it. When I ask Ulbrich how much training is required, he says, "I'd show you one slider to move from 1x to 3.2x." He adds, "I'd also teach you about spherical aberration correction to optimize the signal-to-noise ratio of the system."

Besides those small bits of training, Ulbrich says, "If you already have a fluorescent sample, you can put it on this microscope and see more." In addition, you can see it at a pretty decent temporal rate—as much as three frames per second.

SIM-plicity

SIM provides a relatively painless transition from traditional to super-resolution microscopy. If you are a biologist who is familiar with confocal or widefield microscopy, Ferrand can train you to use the GE DeltaVision OMX SR in about three hours. This microscope provides localization microscopy and SIM. In addition, this microscope includes environmental control. "That means that you can use live cells and keep them healthy for hours and hours," Ferrand explains.

Some of today's SIM platforms are even designed for personal lab use. One example is Nikon's N-SIM E, which performs 3-D SIM and comes with three wavelengths for exciting fluorophores. It's about half the price of some of the first SIMs, and Ross says it has "a very streamlined user interface." It even includes GPU processing filters that let a user adjust the image in real time.

In addition, samples from other forms of microscopy often work fine with SIM. "If you set up your imaging on a confocal or widefield deconvolution system," Ferrand says, "then chances are you can use that sample for SIM." In the end, she says, "SIM will improve your science, not make you reinvent it."

Bringing super-resolution to biology's masses represents one more advance in imaging for everyone. "The trend to get better images has always been there, and this is another step in the process," says Ulbrich. Only a few years ago, most biologists probably didn't expect to get such easy access to super-resolution so soon, but having it surely pushes ahead many research projects.

***Mike May** is a freelance writer and editor living in Ohio. You may reach him at mikemay1959@gmail.com.*

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ARE YOU IN THE MARKET FOR AN...
AUTOMATED LIQUID HANDLING SYSTEM?

Automated liquid handling (ALH) systems span the range from semi-automated multichannel pipettors to room-sized systems. The industry is trending toward versatile, modular ALH systems—seemingly for every budget. Likewise, instrumentation, software, and methods have followed the trend toward greater user accessibility.

Types of liquid handling system used by survey respondents:

Individual benchtop workstations	59%
Stand-alone	52%
Self-contained multi instrument systems	27%
Other	2%

Automated liquid handling procedures performed by survey respondents:

Serial dilution	66%
PCR setup	45%
Plate replication	43%
Plate reformatting	32%
High-throughput screening	23%
Cell culture	14%
Array printing	9%
Whole genome amplification	7%
High-density array printing	5%
Other	18%

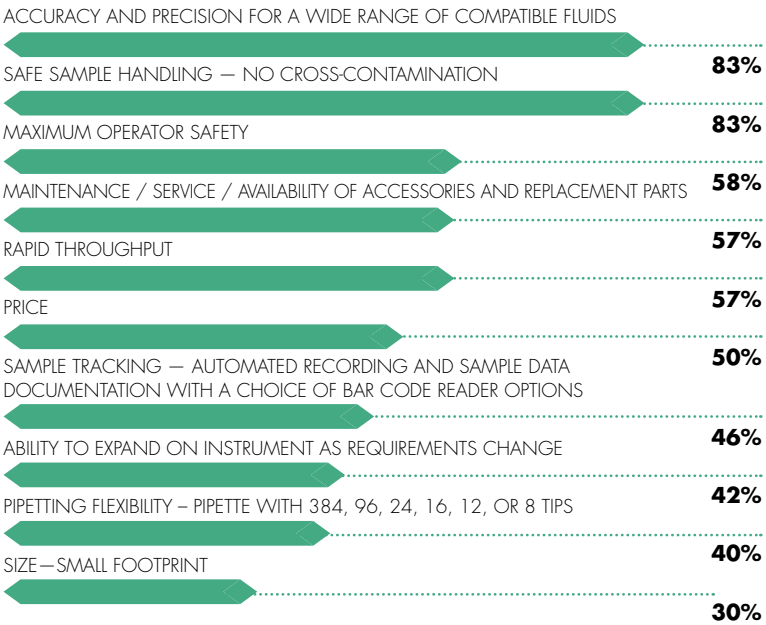
Nearly 56% of respondents are engaged in purchasing an automated liquid handling system. The reasons for these purchases are as follows:

- Addition to existing systems, increase capacity **55%**
- Replacement of an aging system **28%**
- First time purchase **10%**
- Setting up a new lab **7%**

TOP 7 QUESTIONS
You Should Ask When Buying an Automated Liquid Handler

1. What kind(s) of dispensing technology is used? Peristaltic pump dispensing offers low prime volumes and backflushing; microprocessor- controlled syringes have fast output and high precision. Hybrid detection systems combine both technologies in one and can even add washing functions.
2. Is plate handling automatable? Manual plate handling can slow productivity. Automating the process with a compatible microplate stacker increases throughput with walk-away operation.
3. Can it accommodate magnetic or plastic bead-based assays? If using bead-based assays, it should be equipped with appropriate magnets or vacuum filtration for critical wash steps.
4. What is the volume range, and how many different sample vessel types may be used?
5. Ask about the software—is it integrated and user-friendly? Does it allow for pre-programmed and custom protocols?
6. What is the flow rate spectrum? A wide flow rate spectrum allows use with sensitive cell-based assays to viscous liquids.
7. What assay validation data is available for this specific liquid handler? This provides proof that the instrument performs as indicated.

TOP 10 FEATURES/FACTORS
Respondents Look for When Purchasing an Automated Liquid Handling System



For more information on automated liquid handling systems, including useful articles and a list of manufacturers, visit www.labmanager.com/liquid-handling

STIRRERS

OVERHEAD OR MAGNETIC?: IT DEPENDS ON THE APPLICATION

by Angelo DePalma, PhD

For the first decade of my career as a synthetic organic chemist, the only stirring mechanism I ever used was the magnetic type, with or without a separate heating mantle, sometimes as a dual hot-plate stirrer. Then one day, while following a literature prep that called for an overhead stirrer, I decided that I knew more than the author and turned again to my trusty magnetic stirrer. Big mistake. When I returned from a coffee break, the stir bar had stopped doing its thing and the reaction vessel was nearly frozen solid. After carefully disposing of the reaction flask and stirrer, I followed the prep to the letter and got my product, but not before wasting nearly half a day.

Overhead stirrers are specified often when either reaction or mixing volumes are very large, typically above two liters, but even more frequently when the operation is initially viscous or expected to develop significant viscosity.

Creeping viscosity

As illustrated by the above example, viscosity can creep up without notice. Some reactions turn to thick slurries or form heavy precipitates as they progress. Similarly, syrup preparations begin as pure water and end as sludge-like products, particularly on cooling.

CAT Scientific (Paso Robles, CA) provides further examples for putting aside your magnetic stirrer and setting up an overhead mixing system: mixtures of water and organic solvents or of soluble and insoluble materials, suspensions, slurries, pastes, creams, and polymer processes that show a wide range of viscosities.

Magnetic stirrers, whether built into a hot plate design or not, will set a lab back anywhere from $200 to about $900. More features, stronger magnetics, more sophisticated controls, and greater robustness translate to higher prices.

The high end of the price range for magnetic stirrers is the price entry point for overhead stirrers, with the "sweet spot" for laboratories in the $1,000–$5,000 range. Overhead designs provide significantly higher mixing/stirring capability, greater volume capacities, and stronger agitation for processes involving highly viscous liquids.

What to look for

One consistent requirement for laboratory stirrers, be they magnetic or overhead, is a robust motor and protective motor housing. "Users need to be assured that stirrers will work reliably, accurately, and safely at all times," notes Nicole Kvasnicka, product marketing manager at Heidolph North America (Elk Grove Village, IL). "Regardless of the stirrer type, the motor must always be protected from the lab environment."

Magnetic stirrers have the advantage, she says, for rapid dissolution of small samples or "any simple application on the benchtop of a low viscosity."

For Refika Bilgic, managing director at IKA Works (Wilmington, NC), process consistency, reproducibility, and operational safety are the three primary things to look for in an overhead stirrer.

She explains the relationship between stirring or agitation forces for magnetic versus overhead stirrers, and how they relate to application: "The choice comes down to volume and viscosity, as well as the materials you're stirring. If a high level of sedimentation is expected, a magnetic stir bar will most likely get stuck and not run efficiently. In this situation an overhead stirrer is definitely the better alternative. In general, any sample processing smaller than 50mPa-s [milli Pascal-seconds] and one liter is suited for a magnetic stirrer; anything greater than both values should be processed by an overhead stirrer."

Selection of the stirring element—there are dozens of designs and sizes—also depends on the application, the viscosity, the desired speed range, and the samples. "Depending on which stirring element is used, a variety of effects can occur," Bilgic observes. "For example, a stirring element that is three-bladed or has an anchor shape creates different results in flow efficiency and direction. Stirrer designs can also result in different levels of shearing forces and homogeneity."

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MICROWAVE DIGESTION

INTERFACE AND SOFTWARE ADVANCES SIMPLIFY AND SUPERCHARGE THIS TECHNOLOGY

by Mike May, PhD

Add acid to a sample, apply microwave radiation, and you're ready for all sorts of further analyses, such as inductively coupled plasma mass spectrometry or atomic absorption. Microwave digestion can be applied to anything from foods and rocks to metals and pharmaceuticals, which can then be analyzed for components, such as heavy metals. To help scientists use this technology more easily, most vendors keep improving the user interface. Reynhardt Klopper, product specialist for microwave digestion and synthesis at Anton Paar USA (Ashland, VA), says, "The user interface on microwave digesters has changed quite significantly over the past few years. For example, most of them have full-color touchscreens." This simplifies how a scientist works with this technology and expands how it can be used.

For instance, scientists use the screen to control or modify the process on the fly. As Klopper says, "In our system, you can change many of the parameters—digestion temperature, the time of the experiment, microwave power output—in real time, while the experiment is running." He adds, "That was not possible with previous-generation controllers . . . You had to wait for the experiment to be completed."

Other experts also point out that today's microwave digesters let scientists keep better tabs on the entire process. "The graphic interface provides real-time digestion-related information during the whole procedure," says Alex Cooper, product specialist at Aurora Biomed (Vancouver, Canada). "So the user could check the actual status of the digesting samples instantly." That provides new capabilities in using microwave digestion, such as fine-tuning specific experiments or keeping better track of a process.

Dealing with data

"A microwave digester is more a preparation device than an analytical instrument," Klopper says. So scientists don't always want data from it, but today's platforms can often collect and export data through, say, a USB or Ethernet port. "This information is useful for method development or troubleshooting," Klopper explains.

The software on a microwave digester also offers other benefits. "Microwave digester vendors try to differentiate themselves with the intuitiveness of the software and unique features," Klopper continues. "We've included beneficial features in the software that are specific to particular industries." For example, Anton Paar's software is compatible with the U.S. Food and Drug Administration's Title 21 Code of Federal Regulations Part 11, which is required for electronic records in the drug industry. "It complies fully with this," Klopper says, "including how often you need to change the password or apply e-signatures to experiment results." He adds, "This is unique for microwave systems and appreciated by the pharmaceutical industry because they try to standardize how all the instruments in their labs handle data."

Like the rest of the world, labs also keep getting more connected. "A common request from users is for more connectivity options with lab instruments," Klopper says. "'Can it connect to your local network, and can I have remote access?'" So Anton Paar provides its microwave digesters with the ability to connect to a lab's network. "Via a built-in [virtual network computing] protocol, the user can connect to it with a laptop, tablet, or smartphone, and can remotely control the instrument," Klopper says. That's the role of some microwave digesters today, and of many more tomorrow.

In fact, the ongoing changes in today's microwave digesters make it possible for researchers to use these devices in more sophisticated ways, and that also allows for more uses ahead. As with nearly every device in today's labs, adding advanced interfaces and connectivity options gives scientists more opportunities to invent new uses for technology.

***Mike May** is a freelance writer and editor living in Ohio. You may reach him at mikemay1959@gmail.com.*

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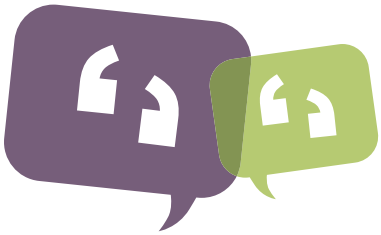
ARE YOU IN THE MARKET FOR A...
NEW GLOVE BOX?

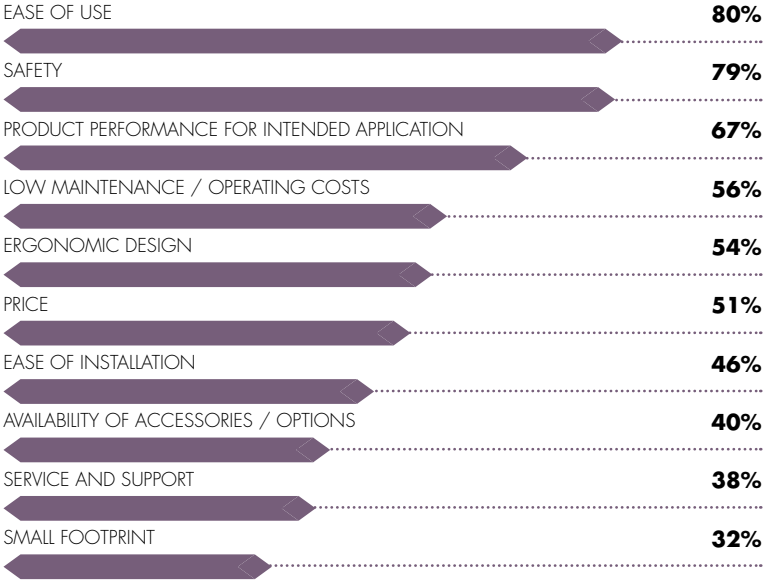


Glove boxes go by many different names and are used for many purposes. However, their essential attribute is the ability to maintain a completely separate environment from ambient. Glove boxes are completely closed compartments ranging in size from a few cubic feet to several hundred cubic feet and differ from other safety enclosures in two significant respects: users can introduce articles into glove boxes and manipulate them inside through ports fitted with gloves, and glove boxes typically use a specialized atmosphere.

TOP 5 QUESTIONS
You Should Ask When Buying a Glove Box

1. What applications are you using the glove box for? This will determine exactly what you will need in a glove box, such as an oxygen-free atmosphere, etc.
2. Are the incubation and processing separated in order to prevent contamination? This is important if you will be using the glove box for cell culture.
3. How much will the glove box cost to acquire and maintain? Are warranties offered? Custom glove boxes are the most expensive, so if a standard model can fit your needs that is probably the better way to go. Making small customizations to an off-the-shelf model is also another less costly option than a fully-custom unit.
4. What are your future needs? This will help determine if the smallest unit is really the best option or if a larger option which can accommodate future expansion would make more sense.
5. What sort of safety features does the glove box have? These are especially important if you are working with very hazardous materials.

TOP 10 FEATURES/FACTORS
Respondents Look for When Purchasing a Glove Box



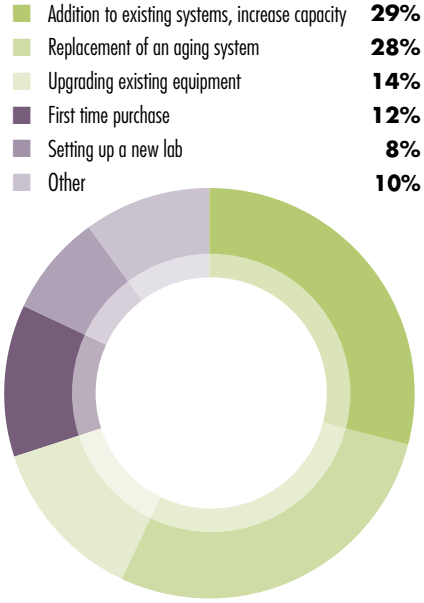
Primary purpose for glove boxes as reported by survey respondents:

Research	59%
Clinical	22%
Quality Control	20%
Production	8%
Other	10%

Applications for glove boxes as reported by survey respondents:

Manipulating dangerous, toxic, or moisture-sensitive substances	40%
Cell culture	29%
Storage and processing of chemicals, metals, calcium, etc.	22%
Air- or moisture-sensitive analyses	17%
Anaerobic bacterial growth	15%
Maintaining cleanliness for microchips or fabricated parts, sensor calibration	12%
Virus production	9%
Controlled-atmosphere welding	4%
Compounding pharmacy, vaccines	2%
Other	23%

Nearly 30% of respondents are engaged in purchasing a new glove box. The reasons for these purchases are as follows:



For more information on glove boxes, including useful articles and a list of manufacturers, visit www.labmanager.com/glove-boxes

ARE YOU IN THE MARKET FOR A... LABORATORY GLASSWARE WASHER?

Whether to employ central washing stations or point-of-use washers located under a lab bench or in a corner is something that has to be addressed with regards to laboratory glassware washers. The former provide an economy of scale and are popular with lab workers who, almost universally, hate to "wash the dishes." The downside for central washing stations is that glassware tends to disappear over time, due to breakage and operator error.

Types of glassware washer used by survey respondents:	
Medium Capacity Washer	54%
Small Capacity Washer	38%
Large Capacity Washer	15%
High Throughput Washer	5%
Other	1%

Lab washer components used by survey respondents:	
Lower baskets	79%
Upper baskets	74%
Direct injection (for beakers, pipettes, flasks)	58%
Test tube baskets	30%
Slides and Petri dish baskets	21%
Other	3%

Nearly 30% of respondents are engaged in purchasing a new glassware washer. The reasons for these purchases are as follows:

Replacement of an aging system	28%
First time purchase	25%
Addition to existing systems, increase capacity	22%
Setting up a new lab	22%
Other	3%

TOP 6 QUESTIONS

You Should Ask When Buying a Glassware Washer

1. How is the product manufactured? Ask about the quality of the materials used and the product life expectation based on manufacturing testing. Also find out about the product's warranty.
2. What differentiates the lab washer from others offered in terms of performance?
3. Does the company offer application support and technical phone support before and after product installation?
4. How sustainable is the product? Ask the company to provide details on energy and water consumption as well as the recycle ability of the product.
5. If the product is discontinued, for how many years does the company provide accessories and parts for the washer?
6. Finally, ask about the cost of the purchase—not just the price of the product being installed but the total cost of ownership, which includes price, service expectations, warranty, etc.

TOP 10 FEATURES/FACTORS

Respondents Look for When Purchasing a Glassware Washer

DURABILITY OF PRODUCT	84%
CONSISTENT WASHING AND DISINFECTION RESULTS	76%
LOW MAINTENANCE – EASY TO USE AND CLEAN	73%
SERVICE AND SUPPORT	58%
WARRANTY	55%
PRICE	54%
RELIABILITY OF VENDOR	53%
SAFETY FEATURES	51%
ABILITY TO CUSTOMIZE RACKS	44%
EASE OF INSTALLATION	44%

For more information on laboratory glassware washers, including useful articles and a list of manufacturers, visit www.labmanager.com/glassware-washers

WESTERN BLOTTING ANTIBODIES

Problem: Nearly 40 years after its introduction, western blotting continues to be a powerful method for protein quantitation. Arguably, finding the right antibody to detect the protein of interest is the technique's most critical and challenging step.

A recent Bio-Rad survey found nearly 60 percent of researchers blamed the primary antibody when their immunoblots failed. Even if the antibody does work, it may bind to other proteins in addition to the target protein or may not be sensitive enough to detect low abundance targets, complicating analysis of the results. Scientists using non-specific antibodies have gone on to unknowingly publish erroneous data. One reason this occurs is because vendors provide insufficient validation information, leaving researchers in the dark about the antibody's true binding efficiency and overall performance. Furthermore, manufacturing and quality control standards can be lax, which means there is no guarantee that buying different lots of the same antibody from the same supplier will produce the same results.

Solution: Vendors cannot realistically validate antibodies for every possible application and sample treatment or type. Validating for a broad range of antibody applications would be prohibitively expensive, driving up product prices. An alternative approach to ensure reliability is for vendors to narrow antibody selections. Bio-Rad, for example, is pioneering this approach with the introduction of its PrecisionAb™ Antibody product line, specifically validated for western blots. The new line is a targeted approach to overcoming many of the aforementioned industry challenges.

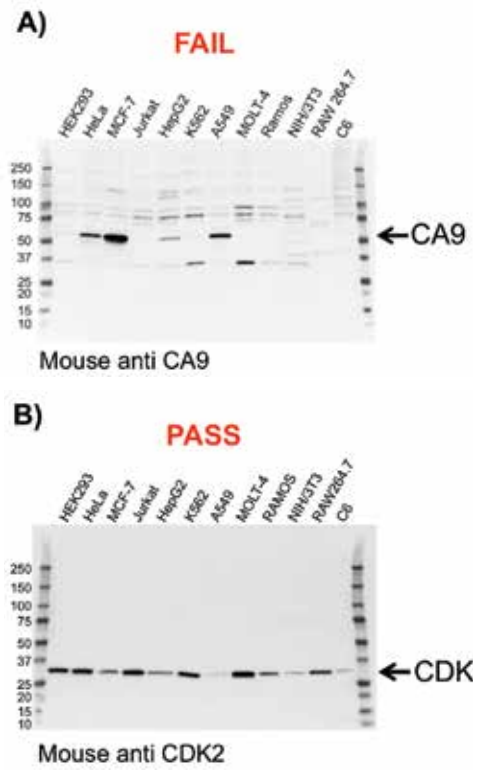
"As far as lot-to-lot variability is concerned, we're testing every lot that we bring in," says Mark Shulewitz, a senior scientist in the Content Business Development Team at Bio-Rad. "A new lot has to work or we don't accept it."

Additionally, while some vendors rely on over-expressing the target protein or concentrate the sample (preparing microsomes or nuclear fractions, for example) to show antibody binding, each PrecisionAb antibody is selected based on highly sensitive and specific detection of endogenous levels of target proteins without any special sample enrichment (Figure 1).

A second solution for improved reliability comes from greater transparency and information. Bio-Rad, for instance, has committed to presenting the full western blot image, including negative and low signals, to give a better indication of an antibody's overall performance across 12 different cell lines. This information is critical for investigators because a low or negative result "doesn't mean the protein isn't there, it's just—relatively speaking—much less abundant," Shulewitz explains.

To facilitate optimization and in-house validation by the researcher, the complete protocol used for the validation, along with a positive control lysate, is available for each PrecisionAb. This provides researchers increased confidence in assigning bands, as they can directly compare their western blots with the vendor's validation data—which uses the same protocol and positive control lysate. As a final move to empower researchers, trial sizes are available for all PrecisionAb antibody targets. This allows scientists to "try before they buy," experimenting with their own samples and study environments to confirm the product works before committing to a full vial.

For more information, please visit www.bio-rad.com/1PAb



➤ *Figure 1. Validation data for two PrecisionAb candidates. A) This carbonic anhydrase IX (CA9) mouse monoclonal antibody failed validation because it exhibits nonspecific binding and low signal-to-noise ratio. B) This cyclin-dependent kinase 2 (CDK2) mouse monoclonal antibody passed validation showing high specificity and sensitivity.*

TRANSFERRING VALIDATED HPLC METHODS WITHIN USP GUIDELINES

Problem: The topic of technology transfer raises caution with many laboratory managers of analytical laboratories. In routine analysis laboratories, such as QA/QC, the need for continued support of established high performance liquid chromatography (HPLC) methods can significantly outweigh the potential advantages of method modernization, making it exceptionally problematic or undesirable to adopt more modern liquid chromatography (LC) assays or instrumentation such as U(H)PLC ultra-high performance LC.

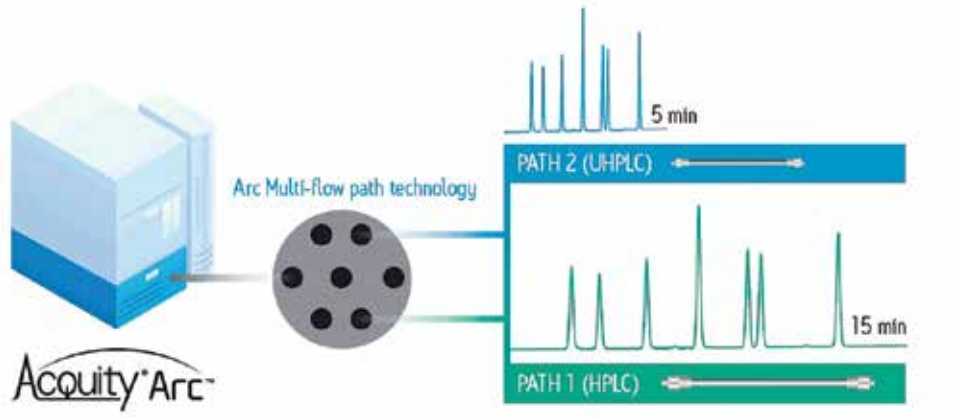
One of the key issues with transferring methods is the ability to replicate the result from one type of LC system to another. This is particularly challenging for gradient methods which requires the user to match not only the dwell volume of the system, but also the profile (or behavior) in which mobile phases are mixed. In addition, the ability to modernize these assays has been limited due to guidance described by the United States Pharmacopeia (USP), specifically outlined in Chapter 621 where making changes to the gradient methods are perceived as being risky and poorly understood.

Solution: Although the USP discourages making changes to gradient methods, guidance does allow for adjustments to be made to a validated HPLC method if necessary. As stated within USP Chapter <621>, "If adjustments are necessary, change in…the duration of an initial isocratic hold (when prescribed), and/or dwell volume adjustments are allowed." The ACQUITY Arc System was specifically designed to facilitate efficient technology transfer while strictly adhering to these method adjustment guidelines and regulations.

The ACQUITY Arc System, with Arc Multi-flow Path Technology was designed specifically to enable analysts to successfully transfer their established HPLC methods onto a modern LC platform, while providing the flexibility to further improve productivity in the future. By simply selecting between one of two fluidic paths in the system software, the user can reproduce the results created on their legacy HPLC systems in efforts to transfer their established HPLC methods from one LC platform to another. Alternatively, a second fluidic path can be selected to improve performance by pairing the system with more modern 2.x µm UHPLC columns. This novel technology essentially provides a selectable dwell volume to effortlessly enable the transfer of LC methods from any commercial LC system, mitigating the need to revalidate the assay by emulating both the dwell volume as well as behavior of which the mobile phases are mixed.

Having a choice of two fluidic paths provides a simple and easy way to emulate HPLC or UHPLC performance on a single LC system. It's like having two LC systems in one! Significant productivity gains can now be realized by deploying a single LC platform that allows the efficient transfer, adjustment, or improvement of methods from any LC platform without compromise.

For more information, please visit www.waters.com/arc



▲ *Simply select between HPLC mode and UHPLC mode with Arc Multi-flow Path Technology.*

TECHNOLOGYNEWS

AACR Annual Meeting 2016 • NEW ORLEANS

EB San Diego 2016 April 2 – 6

This month we highlight companies that will be exhibiting at **Experimental Biology 2016 (EB 2016)** and the **American Association for Cancer Research's Annual Meeting (AACR 2016)**. EB 2016 runs from April 2-6 in San Diego, CA, and is open to all members of the sponsoring and guest societies and non-members with interest in research and life sciences. AACR 2016 takes place April 16-20 in New Orleans, LA. This year's theme, "Delivering Cures Through Cancer Science," reinforces the inextricable link between research and advances in patient care. Remember that the new products shown here won't necessarily be at these shows, but the highlighted manufacturers will be on hand to answer questions.

ANALYTICAL

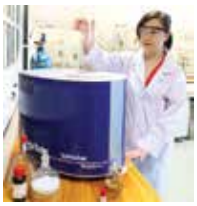
Gas Purifiers for Chromatography

- Self-regenerating purifiers are for hydrogen, helium, nitrogen, and air
- Allow the use of low grade feed gas to produce ultra-high purity gases for gas chromatography
- The high purity gases extend the life of disposable GC gas filters tenfold
- Simple to install
- Allow laboratories to improve and monitor gas quality

GasTrap www.GasTrap.com

Benchtop NMR Spectrometer

Spinsolve Phosphorus



- Phosphorous extends the line's high sensitivity and resolution to include the 31P nucleus
- High NMR sensitivity of 31P combined with its large chemical shift range, simple spectra, and absence of impurities in the background spectrum make 31P NMR ideal for routine purity assessment and tracking reactions
- Magnet design and thermal control, together with the internal lock, provide excellent long-term stability

Magritek www.magritek.com

Visible Light Spectrophotometer

LumaSpec LS800S

- Provides quantitative spectral power data, enabling users to characterize and monitor the illumination source of their microscope system
- Operates from 350 nm to 800 nm with 1.5 nm resolution
- Uses an illumination target slide mounted on the user's microscope to provide accurate and precise information about the illumination in the sample plane, leading to the most relevant information being obtained

Prior Scientific www.prior.com

Confocal Raman Microscope

inVia™ Qontor™

- Includes LiveTrack™, which enables users to analyze samples with uneven, curved, or rough surfaces
- Optimum focus is maintained in real time during spectral acquisitions and white light imaging, removing the need for time-consuming manual focusing, pre-scanning, or extensive sample preparation
- Microscope's technology reduces overall experiment times and makes it easy to use when analyzing even the most complex samples

Renishaw www.renishaw.com/Raman

ED-XRF Spectrometers

XEPOS

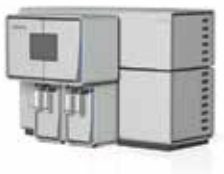
- Provide breakthrough advances in the multi-elemental analysis of major, minor, and trace element concentrations
- New developments in excitation and detection introduced with the new spectrometers deliver excellent sensitivity and detection limits and yield high gains in precision and accuracy
- Support precise product quality control at-line for a variety of applications

SPECTRO www.spectro.com

Ultra-High Resolution Isotope Ratio Mass Spectrometer

AACR 253

Booth 1530



- Designed to optimize the measurement of site-specific and clumped-isotope-ratio analysis of molecules
- Allows scientists to analyze new parameters including the formation temperatures of molecules, degradation processes of molecules, biochemical processes of nitrous oxide, photochemical processes in the atmosphere, and metabolic processes in biochemistry

Thermo Fisher Scientific www.thermoscientific.com

Glycoprotein BEH Amide 300Å 1.7-µm Column

AACR ACQUITY UPLC®

Booth 2512

- Enables biopharmaceutical companies to better understand where glycan molecules are located within the therapeutic proteins they are developing
- Novel, patent-pending ACQUITY BEH Amide technology assists scientists in obtaining reproducible glycan-related chromatographic and mass spec information at the intact protein, fragment, or peptide levels
- Designed to be used with Waters ACQUITY UPLC systems

Waters www.waters.com/glycans

IMS Q-Tof Mass Spectrometer

AACR Vion™

Booth 2512

- This high-resolution, benchtop Q-Tof mass spectrometer moves ion mobility mass spectrometry from research to routine
- With the selectivity that ion mobility delivers, scientists can identify and quantify analytes, confidently enabling faster method development and higher sample throughput

Waters www.waters.com/vion

BASIC LAB

Spiral Evaporator

DrySyn

- Enables scientists to evaporate tubes directly in DrySyn synthesis blocks up to 12 samples at a time
- Offers fast and effective parallel evaporation in tubes without solvent bumping
- Spiral air flow generated by this unique evaporation technology allows the evaporator to rapidly concentrate even high boiling solvents, such as DMSO, DMF, and water in tubes, without heating to high temperatures

Asynt www.asynt.com

Programmable Transmitter

AACR American Association for Cancer Research Open Source Bio™

AACR Booth 2641

- Enables conductivity, pH, dissolved oxygen, and temperature to be measured and controlled from one programmable device
- Transmitter allows for programmable functionality because the equipment is built around an Arduino™ compatible board
- Design allows the user to perform custom calculations, display custom values, graphs, or graphics on the LCD screen, control external equipment, and accept readings or inputs from external equipment

Boekel Scientific www.boekelsci.com

Mechanical Gel Strength Apparatus

Model 5265MG

- Directly measures gel strength development of well cement slurries under downhole conditions
- Allows oil service companies, operators, and their testing laboratories around the world to optimize cement slurries and to accurately determine the potential for annular gas and fluid migration
- Provides accurate simulation of dynamic slurry conditioning during placement phase, as well as the static gel phase of the operation

Chandler Engineering www.chandlereng.com

Media Preparation System

Demeter™

- Designed to streamline the media preparation process in commercial food testing labs
- Automates the traditionally manual, dehydrated media reagent preparation step in a lab for increased testing throughput and accuracy
- Records the precise volumetric amounts and temperatures (NIST traceable) used in a test, then feeds that information into a laboratory information management system, streamlining recordkeeping for regulatory compliance

Heateflex www.heateflex.com

Modular Clean Labs

- Feature a modular construction design that is cost-effective and time-efficient compared to traditional construction
- Entire laboratory workspace is pre-engineered, including the structure and the lab furniture/ fume hoods to outfit the interior
- Wall panels have a white fiberglass surface for chemical resistance and excellent light reflectivity

HEMCO www.hemcocorp.com/modrms.html

Class II, Type A2 Biological Safety Cabinet

EB LabGard AIR

AACR Booth 716 (EB 2016)

AACR Booth 630 (AACR 2016)

- Features a plenum under negative pressure at all times, reducing the risk of airborne leaks
- Includes three available opening sizes: 8-inch, 10-inch, and 12-inch
- Ergonomic features also include an armrest to reduce forearm and wrist strain while leaving the air flow system fully operational
- Cabinet is available in widths from 3 to 6 feet to suit a variety of lab layouts

NuAire www.nuaire.com

PRODUCT SPOTLIGHT

CHEAPER ANALYSIS, SAFER WATER

COD ANALYZER DESIGNED TO REDUCE COSTS FOR WASTEWATER TREATMENT PLANTS

AACR Booth 1530

Lab professionals at wastewater treatment plants recently got a new tool to monitor water quality and prevent environmental contamination when Thermo Fisher Scientific released its chemical oxygen demand (COD) analyzer, the Orion™ 3106.

Treatment plants use COD analysis to detect levels of organic pollutants in water, and early identification of these contaminants can indicate an issue in the treatment process of wastewater.

"By determining organic pollutants in surface water or wastewater, COD measurement can provide a useful indicator of water quality, something that is essential to the environmental monitoring industry," said Giovanni De Dona, global process business manager at Thermo Fisher Scientific, in a recent release. "By adding this new COD analyzer to our portfolio of portable and benchtop Orion water analysis instruments, we aim to provide environmental chemists with a complete solution to liquid analysis and measurement."

The new Orion instrument combines a digestion step with colorimetric analysis to measure the concentration of organic compounds that can affect water quality. Particularly high levels of COD may require additional treatment processes. The presence of high COD levels during the disinfection process will lead to additional hypochlorite dosing. This results in the formation of chloramines, which, if present in high levels, can be carcinogenic, Thermo Fisher Scientific stated in its product release.

Those concerned about the running costs of the instrument will be relieved to know that the analyzer is designed to reduce ongoing operating costs due to its low reagent consumption and maintenance. Also, by controlling the treatment process, users can reduce disinfection costs. The system shouldn't require much training as its interface simplifies navigation for a better operator experience.

For more information, visit http://www.thermoscientific.com/en/product/orion-3106-cod-analyzer.html

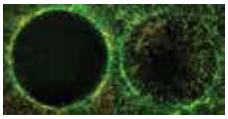
CELL CULTURE

3D Embedded Invasion Assay

Oris™

Booth 505 (EB 2016)

Booth 3042 (AACR 2016)



- Offers quantifiable real-time analysis of cell invasion
- Designed to enable cell movement through an extracellular matrix in three dimensions, thereby getting users as close as possible to an in vivo experiment using in vitro conditions
- No artificial membranes obscuring visualization of the cells
- Designed in an industry-standard 96-well plate format

AMSBIO www.amsbio.com

Cell Culture Chambers

lumox® x-well

Booth 929 (EB 2016)

Booth 1731 (AACR 2016)

- Feature a 50µm ultra-thin, gas-permeable film base that combines excellent imaging with strong cell growth
- Compared to plastic or glass bases, the gas-permeable lumox® film provides more effective gas exchange and homogeneous cell growth
- Available in 1-, 2-, 4-, and 8-well configurations with a standard adherent cell culture surface

Sarstedt www.sarstedt.com

Automated Cell Culture System

SelecT Mk5

- Designed for the routine production of high quality complex cell lines
- Has been extensively redesigned to upgrade its flask handling and pipetting capabilities
- Now comes with an integrated Vi-CELL® cell viability analyzer and a new low volume reagent dispensing module
- Provides an established method of continuous, unattended large-scale culturing of reproducible assay-ready multiwell plates

Sartorius (TAP Biosystems) www.tapbiosystems.com

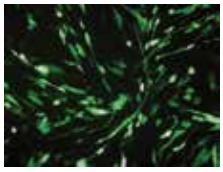
CHEMICALS, KITS, & REAGENTS

Transfection Reagent

DNA-In® CRISPR

Booth 505 (EB 2016)

Booth 3042 (AACR 2016)



- Simplifies and accelerates genome editing using large plasmids and difficult-to-transfect cells for life science researchers generating disease models
- Specially formulated to enable highly efficient transfection of large plasmids (containing CAS9, guide-RNAs, and reporter cassettes) particularly when using hard-to-transfect cell types
- Fully chemically-defined and animal component-free, leading to increased reliability and low cell toxicity

AMSBIO www.amsbio.com

VEGF ELISA Kit

Booth 1649

- Vascular endothelial growth factor (VEGF), originally known as vascular permeability factor (VPF), is a family of proteins that stimulate vasculogenesis and angiogenesis
- Provides a quantitative, competitive detection method for measuring melatonin in serum, plasma, and cell culture supernatants
- Ultra-sensitive assay measures as little as 4 pg / ml of VEGF and provides fully quantitative results

Enzo Life Sciences www.enzolifesciences.com

ATHAP MALDI Matrix Kits

Booth 535 (EB 2016)

- Improve the detection of hydrophobic proteins or peptides containing transmembrane domains
- Alkylated trihydroxyacetophenone (ATHAP) has demonstrated superior detection capabilities over conventional MALDI matrices for membrane proteins/peptides containing hydrophobic regions
- Increase detection sensitivity, unlocking a better understanding of the structure and function of vital hydrophobic molecules

Shimadzu www.ssi.shimadzu.com

Kits for Large Molecule Quantification

ProteinWorks

Booth 2512

- For laboratories doing protein bioanalysis
- Includes a family of five sample preparation kits
- Facilitate a simplified, standardized, and reproducible path to LC-MS protein quantification in serum and plasma samples via the surrogate peptide approach

Waters www.waters.com/proteinworks

LAB AUTOMATION

Automated Incubator

BioSpa 8

Booth 702 (EB 2016)

Booth 2251 (AACR 2016)

- Links microplate washers and dispensers with readers and imaging systems for unattended workflow automation
- Real time temperature and CO_2/O_2 control and monitoring, plus humidity level monitoring and plate lid handling provide an ideal environment for cell-based and other assays, with minimal manual intervention
- Robotic arm moves microplates, cell culture dishes, and flasks between its environment-controlled drawers and integrated instruments

BioTek www.biotek.com

Sample Storage Tubes

- The first commercial sample storage tubes incorporating p-Chip® tracking technology
- p-Chip, a unique electronic microtransponder ID tagging technology, is 100 times smaller, far less expensive, and more reliable than RFID technology
- Ensure reliable sample information, tracking, and security in challenging cold conditions down to cryogenic (-196°C) temperatures

Brooks Automation www.brooks.com

Automated Storage System

SampleStore™ III AC

- The first sample storage solution to incorporate acoustic tube technology that provides higher throughput and storage density
- Acoustic tube technology allows tubes to be picked, re-arrayed, and delivered as complete orders inside the automated store versus traditional plate-based systems that require extensive post-storage processing
- Creates a new, higher-efficiency workflow

Brooks Automation www.brooks.com

Switching Technology for Automated Decapper

LabElite™ AutoSwap™

Booth 732 (Hamilton Company)

- Adds new functionality to the LabElite automated tube decapper
- Enables fast and easy switching of labware-specific decapper adapters on the fly without manual intervention, allowing workflows to proceed with different types of tubes
- Switches between any two sets of Hamilton adapters, which include options compatible with tubes from all major manufacturers, in 96- or 48-well formats

Hamilton Storage www.hamilton-storage.com

Screening System

AACR iQue Screener PLUS

Booth 2424

- This integrated instrument, software, and reagent system enhances the screening workflow, from sample preparation to results
- Enables rapid, high-content, multiplexed analysis of cells and beads in suspension in 96-, 384-, and 1536-well plates
- System's patented sample delivery system enables rapid plate processing (less than five minutes for 96 wells), and assays can be miniaturized to conserve precious sample and reduce reagent use

IntelliCyt www.intellicyt.com

Automated Incubator

AACR Cytomat 10 C450

Booth 1530

- For automated incubation and storage
- Provides high- capacity cell growth and assay incubation laboratories with fast plate accessibility, enabling access to cells in less than ten seconds
- Flexible design ensures that the incubator integrates easily into existing lab space, while advanced controls decrease contamination and assay variability risks

Thermo Fisher Scientific www.thermoscientific.com

LIFE SCIENCE

Agrigenomics Genotyping Solution

Eureka™

Booth 512 (EB 2016)

Booth 722 (AACR 2016)

- Designed for low-cost, low-plex genotyping by sequencing (GBS)
- Delivers high throughput sample processing with low cost per sample
- Overcomes the challenges associated with current GBS technologies which are susceptible to variability in genomic reads and missing SNP information, high cost, and have complex informatics analysis
- Assay can be accessed as a service or kit-based product

Affymetrix www.affymetrix.com

Multi-Mode HTS Microplate Reader

AACR PHERAstar® FSX

Booth 2232

- Combines high sensitivity, high speed, and excellent flexibility in plate formats up to 3456 wells
- Performs all leading non-isotopic detection technologies with ease and speed
- Offers an ultrahigh dynamic range in luminescence, enabling a higher flexibility and more precise measurement results
- Implements Simultaneous Dual Emission detection for AlphaPlex™, increasing throughput significantly by cutting read times in half

BMG LABTECH www.bmglabtech.com

UV Sterilization Cabinets

CleanView

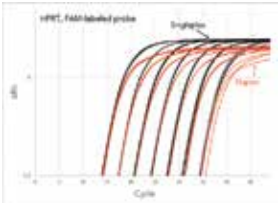
- Provide a sterile contained environment for the preparation and manipulation of sensitive biological samples
- A low cost alternative to a clean room
- Powerful UV lights in the cabinet are used to denature nucleic acids in five to 30 minutes, making them unsuitable for amplification
- Incorporate safety features to prevent user exposure to UV light

Cleaver Scientific www.cleaverscientific.com

Gene Expression Master Mix

AACR American Association for Cancer Research PrimeTime®

Booth 543



- This optimized enzyme mix is designed for probe-based qPCR
- Enhances the IDT PrimeTime qPCR product line, as researchers can economically obtain both assays and a master mix that are optimized and validated to work together
- Integrates into new and existing experimental workflows, because it is also compatible with all commercially available 5′ nuclease gene expression assays

Integrated DNA Technologies www.idtdna.com

Automated Micro Bioreactor System

Ambr® 15 fermentation

- Designed to enhance microbial strain screening with advanced capabilities supporting fed-batch microbial cultures
- Comprises 24 single-use stirred micro bioreactors (each with an 8-12mL working volume) integrated to a user-friendly, automated workstation
- Offers parallel processing and walk-away control of 24 micro bioreactors, providing fermentation scientists with efficient, consistent results from an enhanced early stage screening platform

Sartorius Stedim Biotech www.sartorius.com

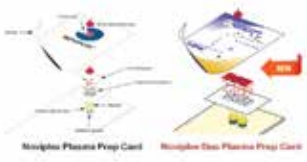
Plasma Prep Card

EB 2016

Noviplex™ Duo

Booth 535 (EB 2016)

- Designed for preparing two plasma samples from a single application of blood
- Prepares a blood sample anytime and anywhere without the need for a power source
- Allows users to prepare a precise volume of plasma from a variable amount of blood, and stabilize the plasma samples in minutes for shipment worldwide without the need for dry ice
- Suited for use with LC-MS/MS analysis



Shimadzu www.ssi.shimadzu.com

SUPPLIES & CONSUMABLES

Laboratory Labels

CILS-8100X

- Stay secure during typical lab processes such as freeze/thaw cycles, water baths, autoclaving, and sterilization
- Resist temperatures of -80°C to +135°C to ensure samples are easy to identify, reducing the risk of error

CILS International www.cils-international.com

Sleeve Protector

Kimtech Pure A4

- Helps keep workers and the workplace safe from hazardous chemicals and biologics
- Features reinforced seams and advanced barrier fabric to provide enhanced protection against dangerous liquids
- Easy to don and doff
- Include thumb loops for full wrist coverage
- Available in a range of sizes and are bulk packaged and recyclable

Kimberly-Clark Professional www.kimtech.com

Sample Storage Starter Packs

- Enable labs to start securely sealing and storing up to 4,000 samples
- Contain everything needed to start using 2D coded sample storage tubes
- Precisely manufactured in a certified Class 7 clean room production environment, a choice of RNase / DNase-free 0.75ml, 1.40ml, 3.00ml, or 4.00ml sample storage tubes provides the versatility to suit almost any sample storage requirement

Micronic www.micronic.com

Glycol Solutions

- Glycol based solutions in both ethylene and propylene are now available for immediate shipment
- Recommended for use in all closed primary and secondary heating, cooling, and refrigeration systems
- Are fully inhibited glycol based solutions designed for applications where no incidental contact with humans, food, or beverage products could occur

Mokon www.mokon.com

Microplates

AntiBIND™

- Reduce protein binding and adsorption, factors that until now could hamper researchers working with rare proteins
- Employ a newly-patented technology that changes the surface of polypropylene plates from hydrophobic to hydrophilic, resulting in protein recovery increases of as much as 100 percent compared with competitive low binding plates

WHEATON www.wheaton.com

CHEMICAL SAFETY MEETS ENERGY EFFICIENCY: PROTECTOR® AIRO™ FILTERED FUME HOODS

Labconco has combined its patented, fully-featured Protector Hood design with GreenFumeHood* (GFH) Technology from Erlab* to create the Protector Airo. Like its big brother, the Protector Echo™, the Airo requires no ducting or infrastructure redesign to install, and it requires no make-up air since it returns its filtered exhaust back to the laboratory. This allows the Airo extremely low energy consumption compared with ducted hoods.

The Airo's lower height allows placement in spaces with ceiling heights as low as eight feet. It's available in 3' and 4' widths and two depths (for a larger Filtered Fume Hood, see the Protector Echo).

- No Ducting Required
- No Infrastructure Redesign
- No Make-Up Air Required
- Fast, Easy Installation
- Low Cost of Ownership

The Airo offers the safety, comfort and familiarity of a traditional ducted hood, while demanding zero make-up air, greatly reducing one of the laboratory's highest operating costs: Energy. Rising energy costs and environmental concerns drive the demand for filtered fume hoods to constantly increase.

- Fully Featured Filtered Fume Hood
- GreenFumeHood (GFH) Technology
- Proven, Versatile Neutrodine* Filters

Safety and Versatility

Neutrodine filters capture a far greater range of chemical fumes than traditional carbon filters, so the Protector Airo Filtered Fume Hood can handle many applications that DH III ductless hoods cannot.

Safety benefits of the Airo include:

- Comprehensive Sensor Package
- Redundant Filtration
- Controlled Access via Radio Frequency Identification (RFID) Cards
- Optional gGuard* Communication Software

The comprehensive sensor package monitors more than just a filter breakthrough. Temperature, acid, solvent, and laboratory air quality sensors are included. This package allows the hood to be used with a broader range of chemicals than other filtered hoods, and if the lab air quality sensor detects a spill inside the lab and outside the hood, it will raise an alarm.

Safety is of utmost importance, so the Airo has secondary filters located above the sensor package in case of filter breakthrough. These redundant, secondary filters are identical to the primary ones so the user can continue their process without concern about chemical breakthrough while waiting to receive replacement filters.

gGuard Communication Software

The gGuard communication software is a powerful accessory that pairs with the Airo to provide monitoring statistics for the laboratory building management personnel. This software gives access to the following safety information and updates:

- Filter Saturation Detection
- Filter Identification (Using The RFID Tags on the Filters)
- Sash Position
- Blower Speed
- Pollution of Laboratory Air
- Temperature Inside Fume Hood
- Usage Authorization

The Protector Airo is a safe, energy-efficient solution for a broad range of general chemistry fume hood applications. To request a chemical assessment for compatibility with your applications, please visit labconco.com.

** Registered trademark of Erlab*

Protecting your laboratory environment
LABCONCO®

by Beth Mankameyer, LEED Green Assoc., CSI, CDT
Labconco Corporation
816.822.3718
bmankameyer@labconco.com

RAPIDLY BUILD DNA FRAGMENTS AND CLONES HANDS-FREE WITH THE BIOXP™ SYSTEM

What if you could focus on the science of discovery instead of worrying about acquiring the DNA needed for analysis? In the era of DNA cloning in the 21st Century, the BioXp™ System allows you to say goodbye to phosphorylating DNA, long ligation incubations, the inherent limitations of relying on template DNA, and labor-intensive manual cloning.

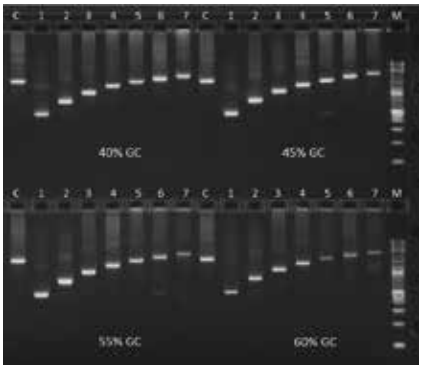
▲ Figure 1. The BioXp System delivers speed, convenience, and greater experimental control.

Automated DNA Cloning

The BioXp System is a laboratory benchtop instrument that builds linear double-stranded DNA fragments (BioXp Tiles) or clones in an overnight run starting from digital nucleic acid sequences. Because the BioXp System does not rely on a DNA template to build BioXp Tiles and clones, building novel synthetic genes and genetic elements is a reality. Additionally, placement of the instrument in the research laboratory or core facility setting brings you convenience and greater control of experimental workflows (Figure 1).

Reliable Results across a Range of DNA Fragments

Up to 31 BioXp Tiles or 23 DNA BioXp Tiles cloned into a pUC-derived vector (pUCGA 1.0 clones) can be built simultaneously in a single run on the instrument. In Figure 2, electrophoresis of DNA fragments built on the instrument, ranging in size from 430 bp (Lane 1) to 1810 bp (Lane 7), with GC contents of 40 to 60%, is shown.



▲ Figure 2. The BioXp System reliably builds DNA across a wide range of the complexity continuum.

High Cloning Efficiency of BioXp Clones

BioXp Tiles and pUCGA 1.0 clones undergo error correction on the instrument deck and are immediately ready for downstream analysis. BioXp Tiles are compatible with common cloning workflows, and pUCGA 1.0 clones are compatible with both chemical transformation and electroporation. The overall cloning efficiency of full-length pUCGA 1.0 clones is 83%. As expected, highest cloning efficiencies are observed from the transformation of smallest clones; the cloning efficiency of pUCGA 1.0 clones containing inserts <900 bp is >90%. Following transformation, typical downstream steps include sequence verification and error-free clone identification.

Summary

Advantages of the BioXp System include:

- The ability to acquire DNA fragments and clones hands-free
- Faster turn-around time than conventional methods
- Access to synthetic biology at your laboratory workbench
- High cloning efficiencies of pUCGA 1.0 clones

To learn more about the BioXp System and to discover our complete offering of services, reagents, instruments, and software, visit www.sgidna.com/bioxp.

SGIDNA
A Synthetic Genomics, Inc. Company

www.sgidna.com

No Limits: How SRC Technology is Changing the Game for Metals Prep

A revolutionary advance in benchtop microwave digestion, the UltraWAVE features patented Single Reaction Chamber (SRC) technology.

BENEFITS

Convenient

- No assembly or disassembly of vessels is required
- Uses simple and inexpensive disposable vials
- Eliminates method development, using the same method for almost every sample type

Efficient

- Offers high sample throughput, 2x traditional microwave systems
- Disposable vessels eliminate the need for cleaning between sample runs
- Digests any combination of samples simultaneously, no batching required

Productive

- Stainless steel chamber construction can heat to extremely high temperatures and withstand pressures greater than 2.5x that of any other closed-vessel microwave digestion system
- Digests even the most difficult sample types
- Maximizes sample size to address homogeneity and/or detection needs

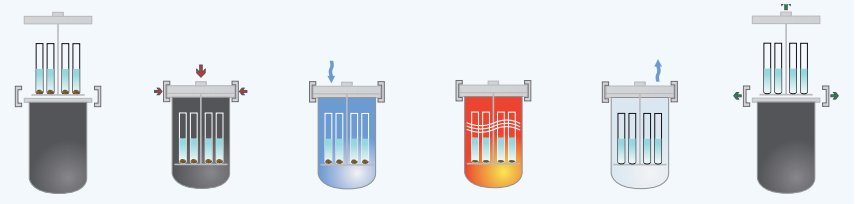
Cost-Effective

- Lowest cost per sample
- Lower labor costs
- Significantly reduced consumables costs

WHAT IT IS

The superior alternative to traditional closed and open vessel digestion, the UltraWAVE offers industrial and research labs greater digestion capability, at least double the sample throughput, improved workflow and significantly lower operating costs—all with a single, easy-to-use instrument.

HOW IT WORKS



1. Sample rack is lowered automatically into microwave chamber
2. Chamber clamp is secured by the operator. Interlocks prevent operation without clamp in place
3. Chamber is pre-pressurized with inert gas to prevent sample boiling. Cross contamination is eliminated
4. Microwave energy is applied. All samples under same temperature and pressure conditions
5. Very fast cooling step due to water cooling of chamber. Chamber is vented and acid vapors extracted
6. Clamp is released and sample rack automatically rises from chamber

ABOUT MILESTONE

With over 50 patents and more than 18,000 instruments installed in laboratories around the world, Milestone has been widely recognized as the global leader in metals prep technology for the past 26 years. Committed to providing safe, reliable and flexible platforms to enhance your lab's productivity, customers worldwide look to Milestone for their metals digestion, organic extractions, mercury analysis and clean chemistry processing needs.

MILESTONE

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The new range of Eclipse precision and analytical balances from Adam Equipment aligns precision and performance. All models of Eclipse combine a brilliant LCD, capacitive touch keypad and both RS-232 and USB interfaces to provide a unique weighing experience for lab professionals. The Eclipse series includes analytical and precision models offering capacities up to 32,000g, with readabilities starting at 0.0001g (0.1mg).

Contact: Adam Equipment Inc.
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MARKETPLACE

LAB MANAGER ONLINE

We look back at our web content since the January/February issue and look forward to what's in store for the upcoming April issue.

1 Celebrating the Scientific Achievements of Five African-American Women

With Black History Month in full swing last month, we took a brief look at the key contributions of five African-American women to their scientific fields. Our picks covered important figures from the 1800s up to the present day, including those who worked in the fields of medicine, chemistry, space, and engineering.

Read more at **LabManager.com/BHM-scientists**

2 Trending on Social Media: SNOLAB: Doing Science in an Active Mine

As of February 18, *Lab Manager*'s top January/February issue article posted to Facebook and Twitter was our first Labs Less Ordinary profile on SNOLAB in Sudbury, Ontario, Canada. In this article, we shared the challenges of working 2 km underground and how the lab deals with those issues, as well as its plans for the future.

Read more at **LabManager.com/SNOLAB**

3 Most Popular Webinar

Last month's top webinar on LabManager.com with 842 registrants was "Speaking with Poise and Confidence—An Introvert's Roadmap to Success," presented by Rick Parmely. This presentation shared techniques to motivate introverted persons to speak up at team meetings and other group venues. Though it ran Jan. 19, you can still catch it on demand at the link below.

Read more at **LabManager.com/webinar-introverts**

LabManager.com

NEXT ISSUE ➡

Rethinking Green Lab Practices

Our April issue looks at the latest developments in green laboratory practices and technologies. Topics will include the push toward eliminating plastics in the lab and increased recycling; breakthroughs in water usage and conservation efforts; and initiatives to increase shared laboratory equipment. Find out how your lab stacks up against these new best practices.

Get *Lab Manager* on the go.
Download a pdf at LabManager.com

Envelope pushed.
Game changed.

- Improved workflow
- At least 2X the throughput
- No batching required
- Lower operating costs

You'll never look at metals prep the same way again.

The Milestone UltraWAVE isn't just an evolution; it's a revolution—changing how industrial and research laboratories around the world prep samples for analysis.

Patented UltraWAVE Single Reaction Chamber (SRC) technology goes beyond traditional closed and open vessel digestion, offering significantly greater digestion capabilities for even the most difficult sample types.

High-performance stainless steel construction allows for higher pressures and temperatures, while disposable vessels eliminate the need to assemble, disassemble or clean between processing. Just as important, dissimilar samples can be processed simultaneously, saving time and money. The bottom line? The UltraWAVE is changing the game for metals prep.


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UltraWAVE


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at milestonesci.com/gamechanger

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