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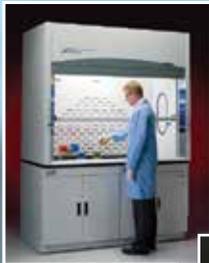
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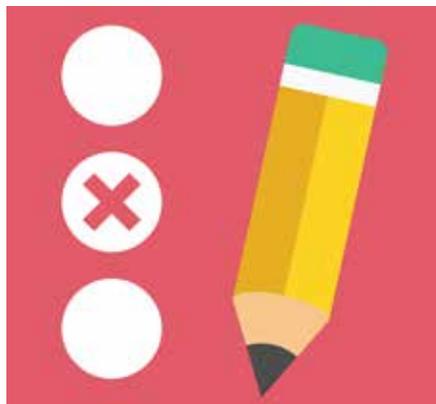


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## SEPTEMBER SATISFACTION

If you're curious to know how satisfied your peers are with their jobs and a rough idea of what they're earning, you're in luck! Coming up in our September issue, you'll find the results of our 9th Annual Salary & Employee Satisfaction Survey where you'll learn how those in the laboratory environment feel about their responsibilities, their bonus and benefits plans, whether or not they receive adequate training and education, and more. You'll also find charts and tables showing how salaries compare based on job title, degree or degrees held, geographic location, industry, and research specialization.

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# off course

Last month I took a mini vacation to Northern New Mexico, a place I fell in love with years ago when I drove from my home state of California to New York after college. Taos and the surrounding area offer some of the most enchanting landscapes I've ever seen. Flying into Albuquerque, I normally rent a car and head straight north. But on this last visit my husband suggested we take a side trip to Los Alamos. Tucked away in the Jemez mountains and scattered across four mesas, Los Alamos is remarkable for its abundance of scientists and gorgeous landscape, but most notable for its role in the development of the atomic bomb. (Their bus line is called "Atomic City Transit.") Visiting the Los Alamos Historical Museum, I was fascinated by the stories, artifacts, and photos related to the Manhattan Project. One photo that caught my eye was of various objects used in the lab in 1945, including a pair of "safety glasses"—round metal frames with large glass lenses. Thankfully we've made some progress in the area of laboratory safety since then. But perhaps not as much as we would like.

This month's cover story presents statistics comparing the safety records of industry with those of laboratories, and the numbers aren't good. "Occupational Safety & Health Administration statistics demonstrate that researchers are 11 times more likely to get hurt in an academic lab than in an industrial lab. There have been serious accidents in academic labs in recent years—including fatalities—that could have been prevented with the proper use of protective equipment and safer

laboratory procedures." Turn to page 10 to find out what you can do to improve these statistics and guarantee that all of your employees subscribe to the highest safety standards.

Last month we looked at the increasing acceptance and usefulness of laboratory apps and how that technology is changing the way laboratory work is carried out. This month we look at another technological trend—smaller and more portable analytical instruments. Like apps, these latest field instruments get researchers out of the lab and directly to their sample sources. Turn to page 32 to find out what's new in this exciting field, including the use of dongles and drones.

Insights articles this month look at developments in metabolomics research (page 46) and neuroimaging (page 56). Our product focuses look at UHPLC systems for biopharma workflows, homogenizers for cell disruption, what to consider when choosing a fume hood, and deciding between a viscometer and rheometer. All good information.

Whether it's mini or maxi, I hope you have some wonderful vacation plans for this summer.

Best,

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## CLOSING THE GAP BETWEEN INDUSTRIAL AND LABORATORY SAFETY PRACTICES

by Vince Mcleod

There is a widening gulf between how safety is practiced in industry compared to how it is practiced in research laboratories, especially in academic settings. A rash of serious incidents has brought the reality of this gulf to light in a tragic way. Issues span a variety of gaps, including organizational buy-in and accountability, oversight of safety programs, and weak or incomplete hazard evaluations. This article will take an in-depth look into these and other issues and discuss how you can avoid potentially serious shortfalls in your lab safety programs.

An unexplained upsurge of research laboratory accidents during the past few years has spotlighted a dangerous phenomenon: a seeming lack of adequate safety programs in these settings, particularly in nonindustrial research laboratories. In brief, we have had fatal fires (UCLA researcher Sheri Sangji<sup>1</sup>), serious explosions (Texas Tech<sup>2</sup>), and horrific deadly accidents (Yale Physics Lab Shop<sup>3</sup>). Why is this? Why are we lacking a strong safety culture in these settings? What do we do to improve it? Are there better ways to instill a culture of safety where it is missing?

The huge disparity between safety cultures and practices in industrial versus nonindustrial settings is indisputable. In a recent letter published in *Chemical & Engineering News*, the chief technology officer at Dow Chemical, the senior vice president of Corning Global Research, and the vice president of Dupont's Global Research and Development, all members of the American Chemical Society's Presidential Commission on Graduate Education in the Chemical Sciences, had this to say about the wide gulf in safety cultures:

*"The facts are unequivocal. Occupational Safety & Health Administration statistics demonstrate that researchers are 11 times more likely to get hurt in an academic lab than in an industrial lab. There have been serious accidents in academic labs in recent years—including fatalities—that could have been prevented with the proper use of protective equipment and safer laboratory procedures."*

We have to agree wholeheartedly with that last statement. All incidents and injuries can be prevented, even when performing cutting-edge research. The questions are: How much prevention is the right amount and what do those preventive measures look like?

### Recent groundbreaking work

A great place to start is the Chemical Safety Board's report on the Texas Tech explosion. The CSB case report found systemic deficiencies that contributed to that incident, including a lack of safety management accountability and oversight; poor assessment of all hazards, particularly the physical hazards; and a lack of documentation, investigation, and communication of previous incidents.

In another significant report last year, the National Research Council, an independent, nonprofit organization of experts dedicated to improving government decision-making and public policy in all matters of science, engineering, technology, and health, published a treatise on the subject titled "Safe Science."<sup>5</sup> The goal of their report is to promote a better safety culture in nonindustrial research laboratories. Their suggested approach begins by looking at methodologies used in industries such as airlines, healthcare, and manufacturing/production.



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We will take a closer look at those two breakthrough publications, but to be fair, when we start to think about how to close the gaps and build a better culture of safety in these nonindustrial research laboratories, we must keep in mind the unique and dynamic nature of the settings. There typically are large flows of new and inexperienced researchers through these labs, resulting in high turnover and a wide range of experience from young researchers just beginning work to seasoned laboratory veterans, something not seen in your average industrial laboratory setting. This same problem is also encountered by the changing of principal investigators and scientists as researchers visit from other institutions and some pursue the quest for tenure. All this turnover and varying lengths of stay impact training and make maintaining a strong safety culture a challenge. And finally, the most sacred expectancy of all, well-known leading researchers expect a high degree of autonomy and little, if any, infringement on their intellectual and academic freedoms. When

you combine high turnover and a resistance to shackling freedoms with an all-too-prevalent attitude of knowledge superiority, you have a very tough nut to crack.

### Telling survey statistics

In 2012, the University of California Center for Laboratory Safety teamed with the Nature Publishing Group and BioRAFT, a developer of university laboratory management software, and conducted one of the largest surveys of lab safety culture to date.<sup>6</sup> Almost 2,400 respondents participated; 62 percent were from the US and another 21 percent were from the UK and EU, 90 percent of which were from academic research laboratories. Although a great majority of respondents (85 percent) agreed with this statement—"appropriate safety measures in my lab have been taken to protect employees from injury"—a deeper look hints this may not be the case. Here are a few examples.

A basic tenant of lab research is "never work alone." Yet the survey showed that only 7 percent of respondents reported this never happens in their lab. Thirty-five percent said it occurred daily and 80 percent said it was at least a weekly occurrence. The primary piece of personal protective equipment is the lab coat. Yet less than half (46 percent) said that they wear one even though their work requires one at all times. Forty percent disagreed with the statement that their supervisor, lab manager, or PI regularly checks for safe performance of lab duties and proper use of safety equipment. Finally, almost half of all respondents (45 percent)—and 55 percent of those working in large labs (20 to 100 workers)—agreed that "overall safety could be improved in their workplace."

### What to do?

We have shown that changing the safety culture in nonindustrial research settings presents unique challenges. These have been clearly identified and well documented due to recent severe and deadly accidents. If you want to be the impetus of change or perhaps begin to elevate the safety culture in your facility, we encourage you to start by becoming familiar with the current knowledge base. The Chemical Safety Board's Texas Tech report identified six key lessons learned from that incident. We have stated them here for you in terms of action items:

1. You must go beyond OSHA's Laboratory Standard (29CFR 1910.1450) and ensure your safety management plan addresses all hazards, especially physical hazards and physical hazards of chemicals.

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2. Your institutional chemical hygiene plan and standard operating procedures must verify that all research-specific hazards are fully evaluated and mitigated.
3. You must recognize the lack of current standards and guidance on hazard evaluation and mitigation and risk assessment addressing the unique issues in nonindustrial research labs. Most are specific to industrial settings and not fully transferrable to your environment.
4. Written protocols and training specific to the research are absolutely necessary.

5. Your institution's organizational structure must ensure direct reporting from the safety inspector/auditor to an individual/office with "authority to implement safety improvements."
6. Previous incidents and near-misses must be documented, tracked, and communicated in order to provide education and improvement to safety programs.

The National Research Council's *Safe Science* goes even deeper into what safety entails and how we shift from mere compliance to promoting a strong and positive culture of safety. This report discusses the different safety systems and cultures and looks at the knowledge base, including those from aviation, healthcare, and nuclear industries. The characteristics of nonindustrial organizations and their roles, responsibilities, and accountabilities are examined. The knowledge gaps for these settings are explored and ideas to address safety dynamics are presented.

*Safe Science* is a comprehensive and excellent review of safety culture and a must read for laboratory managers and principal investigators alike. It concluded with 15 findings, nine conclusions, and nine recommendations. We'll summarize the recommendations for you.

1. Leadership. Top management must actively demonstrate and show ongoing commitment that safety is a core value of the institution.
2. Performance Linked. Promoting a strong, positive safety culture should be one of the criteria for promotions, tenure, and salary decisions.
3. Resource Based. Identify and design research that can be done safely based on limited and constrained resources.
4. Risk Management. Develop risk management plans with input from all stakeholders. Direct resources and establish policies to maximize a strong safety culture.
5. Teamwork. Use support organizations (e.g., Environmental Health and Safety), teams, and groups to build a safety culture.
6. Teamwork 2. Provide means and encourage collaboration between researchers, principal investigators, and EH&S personnel.

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7. Review. Establish and require incident and near-miss reporting. Document and centralize information. Communicate lessons learned.
8. Evaluate. Establish and require research-specific hazard analyses.
9. Training. Develop and implement initial, ongoing, and periodic training to ensure understanding of associated hazards and risks. Ensure the ability to use proper protective measures and mitigate potential harm.

What is more important than ensuring research is performed in a safe manner and that workers leave at day's end as healthy as when they arrived that morning? We have a duty to instill the mind-set that if you cannot do the research using the best safety practices, then you shouldn't do it at all. We all need to share the best ideas and best practices when it comes to safety. And, we should always strive to ensure that all our employees embrace the very best safety practices.

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**S**tyle. Not what color shoes to wear with blue pants. The style I'm referring to is behavioral style. Yes, we all have a behavioral style and understanding this will help you realize why that person down the hall makes you crazy and more importantly, what you can do about it.

Simply put, behavioral styles reflect how we are wired and how we, of course, behave. The good thing about behavior is that you can temporarily adapt it whenever you need to in order to match another person's style. It's like a stereo synthesizer where the levers on the volume, base, treble, etc. can be moved up and down for your listening pleasure. If you are mostly bass but the person you are working with is not, you can lower your bass for a few minutes to have an effective conversation and raise it back up as you exit their office.

Each person has a dominant and secondary style that can be determined by observing their outward behavior.

There are four behavioral styles: Dominance (Go-Getter), Influence (Promoter), Steadiness (Nurturer), and Conscientiousness (Examiner), commonly referred to as DISC™ styles.

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# ARE YOU IN STYLE?

by **Patty Kreamer, CPO, ACC**

When you fine tune your observation skills, you'll begin to notice the pace at which someone goes through life and if their attention is more focused towards people or tasks. Do they talk, walk, or eat fast or slow? Do they care about others' weekend, family, or life or are they more task or goal oriented?

Once you observe these behaviors, you can determine the style you are encountering. Then you can begin to understand how to best communicate with that person.

### Here's how it breaks down:

- **(D) Go-Getter** = Fast Pace / Task Oriented
- **Promoter** = Fast Pace / People Oriented
- **(S) Nurturer** = Slow Pace / People Oriented
- **(C) Examiner** = Slow Pace / Task Oriented

**Go-Getter** - You want to be direct and fast paced with your conversation. They don't really care about what you did at the family picnic, but they want to hear that you completed a project.

**Promoter** - Ask them about their friends and family, compliment them on their bold wardrobe and make them laugh any time you can. Talk faster or you may lose them.

**Nurturer** - Cares about you and those close to them. Be genuine with a Nurturer or they will dismiss you

as being disingenuous. Don't make sudden changes and expect them to be happy about it.

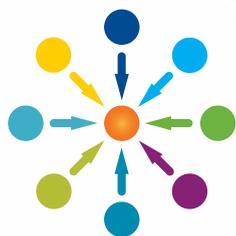
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Knowing someone's style makes it easier to effectively interact with that style in order to positively impact the relationship. So, remember that person that makes you crazy down the hall? It's very possible that their style is the opposite of yours.

*Patty Kreamer is a Certified Professional Organizer, productivity coach, partner/co-owner at Referral Institute of Western PA, LLC speaker, and author of But I Might Need It Someday, The Power of Simplicity, and Success Simplified. She works with financial advisors to help them develop strategic practice management processes in order to become more productive and perform better. [www.referralinstituteofpittsburgh.com](http://www.referralinstituteofpittsburgh.com)*

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## LATEST TRENDS SHAPING THE SCIENTIFIC WORKFORCE

# THE POWER OF QUIET LEADERSHIP

by Mark Lanfear, BS, MS, CCBA

**B**eing involved in workforce solutions, I've always been fascinated by the dynamics of leadership in the workplace. Over the years, I've noticed that casual observers often believe extroverted personalities make the best leaders and managers. Being outgoing myself, I'd like to think that's true. But look more closely and you'll find that many of the best, most effective leaders are introverts by nature, schoolyard nerds who grew up to be outstanding at drawing out the best in the people who work for them.

Think about Warren Buffett, Bill Gates, or Steven Spielberg, self-described introverts whose success is legendary. Or Abraham Lincoln and Eleanor Roosevelt, neither exactly known as the extrovert of the party but two of the most recognizable symbols of leadership. Quiet, strong leaders often have amazing influence on the world around us. (Even the coolest fictional character out there, Marvel's Tony Stark, is an introvert at heart, happiest when creating the next Iron Man suit alone in his lab.)

So what is an introvert, anyway? Not necessarily a shy person, as psychologist Carl Jung first described, but defined now as a more reserved type who prefers solitary activities to social encounters. An introvert gains energy through reflection and quiet time as opposed to drawing energy from crowds and applause as an extrovert does.

That's hardly a bad thing, especially for professional and technical talent in fields like life sciences. If you're in this business, you want all the deep thinking you can get, right? (And if you're reading this column, you probably fit this description.)

**“An introvert gains energy through reflection and quiet time.”**

Understanding personality types is important in modern talent supply chain management. For example, if you're an extroverted manager looking for talent, try to channel your inner geek and look at the potential of the introverted people within your organization or candidates that you're recruiting. By understanding their inner strengths and what motivates them, you'll have a greater opportunity to connect. But be aware that you might have to dig deeper to find the hidden gems who don't have an extrovert's natural ability to self-promote.

From a 180-degree standpoint, introverts who manage introverted talent need to realize that communicating with and motivating employees who fit this personality type might not be their strong suits. But doing so effectively may simply be a matter of looking within. In other

words, what works for the managers probably will work for the talent who report to them too.

Given that introverts tend to look more for a result than a response in what they do, managers of introverts should try to provide talent like this with goals to achieve and yardsticks for measurement. Defining assignments and then providing the space to work out the answers rather than constantly supervising or interrupting their problem-solution navigation time is a smart approach.

In my experience, STEM-oriented people do their best work when they feel it's providing value in some way. Reinforcing that sense within tasks and goals is a strong way to harness the passion and energy of a managed workforce without a lot of rah-rah needed.

On another note, from the talent perspective, if you're a loner at the workplace hoping to advance your career, don't be afraid to leave your comfort zone to get noticed. Seek out others in the organization who can provide some balance on the extroverted side if possible, and use their energy as an example of how to shine a light on yourself. A little of that goes a long way in raising your profile and enhancing your prospects for promotion.

Brian Grazer, the highly acclaimed producer of some of the best movies and TV shows of the past couple

of decades (*Apollo 13*, *A Beautiful Mind*, *24*), recently posted a blog about his management style. Instead of telling people who work for him what to do, he asks questions.

“Understanding personality types is important in modern talent supply chain management.”

“Asking questions creates a space for people to raise issues they are worried about, or to give the boss information he or she might not know and might not be expecting,” he writes. “Most important, asking questions gives people the chance to make the case for the way they want a decision to go. And vice versa.” This seems like a great way to manage people in any business, period—but particularly

in life sciences, where finding solutions using personal initiative is so important and introverts abound. ([www.linkedin.com/pulse/when-youre-boss-questions-better-than-orders-brian-grazer](http://www.linkedin.com/pulse/when-youre-boss-questions-better-than-orders-brian-grazer))

So embrace the introverts’ qualities that get things done without the need for a standing ovation. Hug your inner geek and celebrate your Tony Stark-ness. People like you can move mountains. Introvert or extrovert, I’d love to hear about ways you’ve successfully navigated and managed your workforce, so get in touch at [@marklanfear1](https://twitter.com/marklanfear1).

*Mark Lanfear is a global practice leader for the life science vertical at Kelly Services, a leader in providing workforce consulting. He has operated clinical trials around the world for almost two decades. In addition, Mark is a featured speaker at many life science industry conferences and a writer for life science periodicals. He can be reached at [mark.lanfear@kellyservices.com](mailto:mark.lanfear@kellyservices.com) or 248-244-4361.*

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# THE SMART LAB

## A FRAMEWORK FOR SPECIFIC, MEASUREABLE, ACHIEVABLE, RELEVANT, AND TIME-BASED PERFORMANCE GOALS by Kurt Headrick, PhD

Many organizations encourage the use of SMART goals. There are many guides readily available, but they tend to be general, with no laboratory-specific examples.<sup>1,2</sup> Some contain a sample laboratory SMART goal but are otherwise general.<sup>3</sup> A guide exists to help lab managers use SMART goals to manage their own time,<sup>4</sup> but not their lab or their direct reports. Preliminary work on lab-specific SMART goals is not widely available.<sup>5,6</sup>

SMART goals are goals that are Specific, Measurable, Achievable, Relevant, and Time-Based.

**Specific**—What is measured? Is there a single key output?

**Measurable**—Is the goal quantitative? How is it measured? What are the units?

**Achievable**—Is the goal challenging? Is it attainable? Are sufficient resources available?

**Relevant**—Is the goal meaningful to the employees' role? Is it aligned with the organization's strategic objectives?

**Time-Based**—When will results occur? What is the timeline?

The SMART acronym gives managers a useful framework for developing goals. Considerable thought and effort are required, however, to develop goals that achieve their purpose of motivating desired, organization-critical behaviors. Poorly crafted or improperly executed goals may not succeed in motivating desired behavior and can even motivate undesirable or counterproductive behaviors. Managers need to carefully consider:

- Does the goal encourage the desired behavior?
- How could the goal be misunderstood?
- Could the goal encourage any undesired behaviors?
- How and when will employees know how they are

doing or when the objective is fully achieved?

- Do the goal and associated metrics discriminate between top performers, average performers, and underperformers?

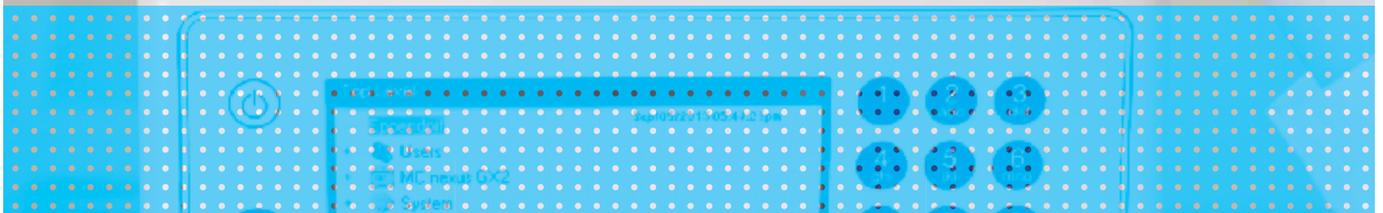
Harris discussed requirements for motivating desired behaviors in analytical chemistry teaching laboratories.<sup>7</sup> The concept of discrimination is central to motivating desired behaviors. Harris defined discrimination as a measure of the difference between the best and worst performers, and found that discrimination correlated with student morale. Where discrimination is high, there is a strong correlation between achievement and assessment. Where goal discrimination is low, there is little apparent difference between top and bottom performers, leading to poor morale and underachievement.

Harris also discussed the importance of a rational and effective scale for evaluating the goal. Harris found that a five-point scale worked well, although in practice he extended this to include a possible score of zero. In the context of goal setting and evaluation, such a scale could be expressed as follows:

- 5—Exceeds all objectives
- 4—Exceeds most objectives
- 3—Meets performance objectives
- 2—Meets most objectives
- 1—Meets some objectives
- 0—Does not meet any objectives

### QC-based SMART goals

Laboratories traditionally use customer satisfaction surveys to assess laboratory performance, with individual goals developed based on desired survey responses.



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There are a number of shortcomings with goals based on customer satisfaction surveys. Customer survey goals are more qualitative than quantitative, because the quality of the survey results depends on completion rates and timeliness of responses; this can be problematic even with supposedly mandatory surveys. Customer survey goals are subjective, with some customers evaluating the lab based on their ideal lab performance rather than agreed-upon service targets. Customer survey goals show poor discrimination, in that some customers are easily satisfied, whereas other customers are never satisfied. It is difficult to quantify individual contributions from customer satisfaction surveys. Finally, goals based on customer satisfaction surveys are reactive rather than proactive; it can take one year or more for the manager to get feedback and take appropriate action.

Laboratory managers can use data the lab already generates to develop SMART goals. QC (quality control) data is used to validate assay and laboratory performance, so goals based on QC data are obviously relevant. Goals based on QC data are proactive; analysts always know exactly how they are doing. Analysts can thus take immediate steps to improve, and there are no surprises or disagreements over progress, status, or assessment. Managers can track individual and group progress and proactively intervene as required.

Analytical laboratory key performance indicators typically include accuracy, precision, and turnaround time. Neglecting any of these three may lead to undesired behavior (e.g., increased turnaround at the expense of accuracy). Targets are based on external (to the laboratory), scientifically justifiable criteria. Supervisors' individual goals are a composite of their personal scores for the above three goals with those of their direct reports, so supervisors are motivated to maximize team performance.

### SMART accuracy goal

The accuracy goal is shown in Table 1. The key laboratory assay used PTC-1a<sup>8</sup> CRM as a QC sample. Samples were assayed by aqua regia digestion with inductively coupled plasma (ICP) spectrometry finish. Although a suite of elements was typically reported, only Ni and Cu were used for the goal, as these were the key customer analytes. A competent, diligent analyst cannot do better than the 95 percent confidence interval for the CRM. A linear progression of the CRM 95 percent confidence interval was used. This is a stricter criterion than Harris used, and is also stricter than the ISO 17025

criterion of  $100 \pm 10$  percent recovery. Harris discussed that optimal discrimination is not necessarily obtained from a Gaussian distribution of scores, and that skewing the distribution may improve discrimination. In this case, one additional 95 percent confidence interval is added on the low side for Ni to account for mafic, nickel-bearing silicates incompletely decomposed by aqua regia that are present in the CRM but not present in the samples. Analysts were assessed daily on the average of the Ni and Cu scores for that day, with the annual score being an average of the daily scores. Each error the analyst authorized in the LIMS (laboratory information management system) resulted in a one-fifth penalty on their annual accuracy goal score.

SCORE ↓	% NI	% CU
PTC-1a Certified Values >	10.03 ± 0.07	13.51 ± 0.11
5	9.89 – 10.10	13.40 – 13.62
4	9.82 – 10.17	13.29 – 13.73
3	9.75 – 10.25	13.18 – 13.84
2	9.68 – 10.32	13.07 – 13.95
1	9.61 – 10.39	12.96 – 14.06
0	Outside above range	Outside above range

▲ Table 1—SMART Accuracy Goal

**Specific**—Based on QC samples' agreement with CRM certificate of analysis.

**Measurable**—Percent of relative error.

**Achievable**—QC data combined with the above external, scientifically justifiable criteria were used to verify that the goal was suitably challenging (discriminating); the goal was modified (skewed) to account for a known, small negative bias for Ni, as discussed above.

**Relevant**—Customer assays are validated using this QC data.

**Timely**—Measured daily, with annual assessment.

### SMART precision goal

The precision goal is shown in Table 2. Justification for the intervals in Table 2 was taken from Skoog, Holler, and Crouch,<sup>9</sup> where they state for ICP that “under ideal conditions, reproducibilities of the order of 1% relative have been demonstrated ... such high precision is not often achieved in the overall measurement process.” This statement referred to multichannel ICP, whereas the ICP

used was sequential, so is likely to be of lower precision, especially considering the nature of the geochemical samples being determined and that analysts also prepared the samples they assayed.

Each batch of samples included one assay duplicate. Customers typically submitted samples consisting of nine different streams with varying concentrations/ratios of Ni, Cu, and other elements. When developing this goal, precision was evaluated for each of the nine streams as well as overall. It was found that most imprecision was related to four of nine of the streams where Ni and/or Cu were present at low concentrations.

Over the course of the year, analysts' large number of assay duplicates will average out between the low- and high-precision sample streams. Because supervisors assay a relatively small number of batches, it is possible that they may assay a disproportionate number of low-concentration assay duplicates. Supervisors' individual annual scores were thus weighted to 4/9 if their ratio for these imprecise duplicate streams was outside the

range of 1:2 to 5:4 to prevent them from being unfairly penalized if they happened to have a disproportionate number of low-concentration assay duplicates.

SCORE	NI AND CU AVERAGE % RSD
5	≤ 1
4	1 – 1.5
3	1.5 – 2
2	2 – 2.5
1	2.5 – 3
0	> 3

▲ Table 2—SMART Precision Goal

**Specific**—Based on agreement of assay duplicates.

**Measurable**—Percent of RSD.

**Achievable**—QC data combined with the above external, scientifically justifiable criteria were used to verify that



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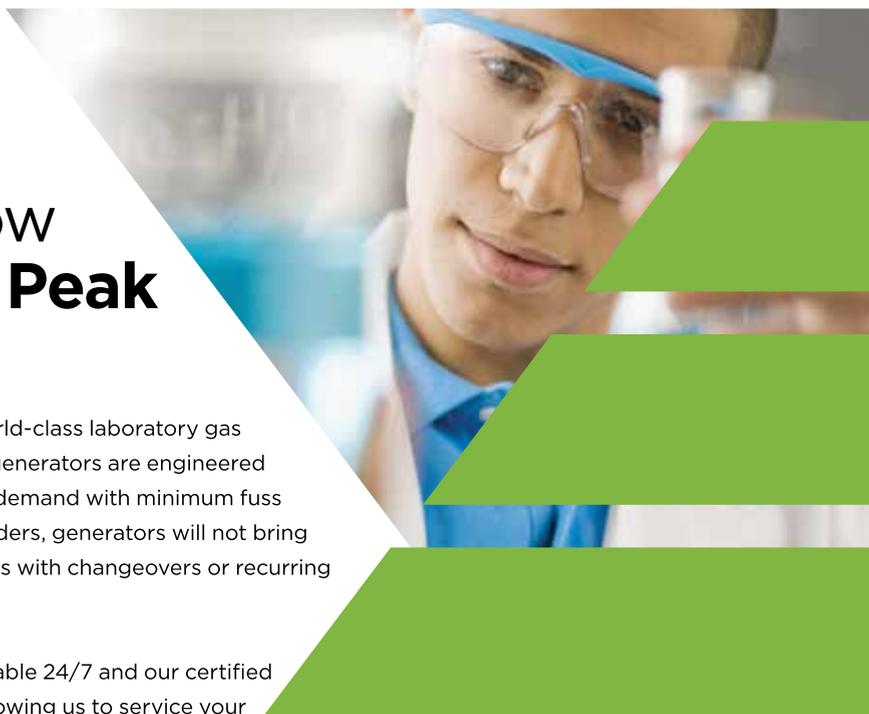
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the goal was suitably challenging (discriminating). Provision was made for the goal to be modified (skewed) for supervisors, as discussed above.

**Relevant**—Successful labs minimize variability.

**Timely**—Measured daily, with annual assessment.

**SMART turnaround goal**

The turnaround goal is shown in Table 3. Customer requirement for turnaround time was four hours from delivery to the lab. Turnaround time can be tracked in LIMS for each analyst.

Exceptions to meeting the required turnaround time were specified in the goal. Crew change-outs where no other analyst or supervisor was present to complete the work were exempted. Mandatory training and meetings that could not be rescheduled were exempted; otherwise, analysts would have to choose between a lower assessment or risk disciplinary action for missing meetings and training. Alarms when the building must be evacuated, as well as safety incidents, may make it impossible to assay the samples within four hours and were thus exempted; otherwise, analysts might be tempted to ignore alarms and safety incidents. Many analysts and one supervisor were members

of the emergency response team (ERT) and were required to immediately respond to any alarm anywhere on the site. ERT callout within four hours of samples receipt was also exempt for ERT members; otherwise, lab staff would be motivated to quit the ERT.

Instrument malfunction and servicing were NOT exempted from the turnaround goal. Analysts were thus motivated to keep instruments well maintained to minimize downtime. Supervisors were motivated to ensure analysts were diligent with assigned maintenance, and to schedule maintenance and servicing to minimize customer impact.

SCORE	COMPLIANCE
5	95%
4	90%
3	85%
2	75%
1	50%
0	< 50%

▲ Table 3—SMART Turnaround Goal

**Specific**—Based on time from sample receipt at the lab to the time the samples are authorized in LIMS.

**Measurable**—Time in hours, recorded in LIMS.

**Achievable**—Various exemptions, as well as what is specifically not exempted in order to motivate all desired behaviors, were detailed in the goal, and based on external criteria.

**Relevant**—Based on customer business requirement.

**Timely**—Measured daily, and assessed annually.

**SMART goal concerns**

Limit the number of goals. Focus, primacy, and impact decrease as the number of goals increases. Use the minimum number of goals required to motivate all organization-critical behaviors. If this results in more than a couple of goals, limit the number of target behaviors or use other means to motivate those desired behaviors.

Involve staff in goal development. They will be more than happy to tell you what they think is realistic and achievable, identify ways in which the goal may

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be misunderstood, and suggest negative behaviors that may be unintentionally motivated. Consulting staff during goal development decreases potential resistance to and resentment of the new goals and improves morale and engagement.

Use of laboratory data is not a panacea for developing SMART goals. Projects and nontechnical behaviors (e.g., safety) may not be amenable to the use of laboratory data. Other SMART metrics must be developed in such cases.

Not all desired behavior can be captured in a couple of SMART goals. SMART goals are just one tool to attain the organization's goals. Other mechanisms—such as salary increases, recognition and awards, professional development, special assignments, promotions, gifts, praise, etc.—exist for motivating desired behaviors.

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# THE INTROVERTED MANAGER

**FIND A MANAGEMENT STYLE THAT IS TRUE TO YOUR TEMPERAMENT AND NATURAL STRENGTHS**

by Lina Genovesi, PhD, JD



**T**he business world is a web of interactions revolving around social events, social media, open office environments, work teams, and group activities. Extroverts dominate the business world and strive in that environment.

If you are a lab manager, there is a good chance that you are an introvert, and there is a good chance that management may not view your introverted tendencies as positive contributors to your management skills.

You may feel pressured to fit in, and you learn quickly that it pays to conform and act extroverted. However, no matter how hard you try to act extroverted, you may still end up facing challenges stemming from your introverted tendencies.

Below is a road map that you can follow to utilize your introverted tendencies to thrive in an extroverted business world.

## The introverted temperament

There are misconceptions that introverts are shy, poor public speakers, or less happy than extroverts. In fact, introversion and extroversion do not define personality types, but generally refer to personality traits relating to utilization of energy.

Extroverts are stimulated and recharge their energy by being with people and participating in high-energy events, while introverts draw energy from within and tend to embrace solitude. Introverts may suffer from people exhaustion and may react strongly to stimulus, and therefore need much less of it or they become overstimulated.

In her books *The Introverted Leader: Building on Your Quiet Strength* and *Quiet Influence: The Introvert's Guide to Making a Difference*, Jennifer B. Kahnweiler, PhD, lists and compares the natural tendencies of introverts and extroverts.

Because of the differences in these natural tendencies, introverted managers have different management styles than extroverted managers.

For example, an introverted manager can lead by example, focusing on the mission at hand and listening

more intently to employees; an extroverted manager brings a different skill set and motivates people with his or her enthusiasm and talkative demeanor.

EXTROVERTS	INTROVERTS
Energized by people	Energized by time alone
Talk first, think later	Think first, talk later
Talk out their thoughts	Process their thoughts in their heads
Enthusiastic	Reserved
Transparent and easy to read	Less demonstrative emotion in facial expression
Freely share personal data	Share personal data with a select few
Prefer talking to writing	Prefer writing to talking
Focus on breadth	Focus on depth

In terms of completing projects, an introverted manager can be analytical to a fault, constantly trying to figure out whether something is working, and an extroverted manager can start something, pump it up, and then let it fail quickly and decisively.

## Your challenges

Because of your introverted tendencies, you may encounter challenges—stress, perception gaps, career detractors, and invisibility—which may erode your ability to manage and achieve your career goals.

## Stress

Stress can be a result of work overload and people exhaustion, and can translate into physical symptoms. Work overload can affect introverted and extroverted managers alike. However, introverted managers will be more prone to people exhaustion when forced to be with people constantly.

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## Perception gaps

Perception gaps are a result of key differences between how the introverted manager thinks his co-workers see him and how they actually do. Because of these perception gaps, the introverted manager has to face negative impressions such as being labeled a slow thinker and devoid of backbone.

“Interpersonal skills are key when an introverted manager takes a leadership role.”

## Career detractors

It generally requires more than technical expertise to get people motivated, and interpersonal skills are key when an introverted manager takes a leadership role.

When you are achieving results for your company and developing relationships, career possibilities open up. If you do not attend to developing relationships, you inevitably hit a wall.

## Invisibility

Invisibility can cause problems for introverted managers, and the key impacts of this invisibility are lost opportunities, ideas not heard, and lost personal power.

## Dealing with your challenges

These challenges may appear daunting, and you can deal with them by first developing awareness of your natural tendencies and then taking action to use your natural tendencies to make an impact.

## Developing awareness

Kahnweiler has identified areas of strengths—quiet time, focus on depth, focused listening, focused conversation, and writing—of which you should become aware.

## Quiet time

Since introverts suffer from people exhaustion, they need quiet time to replenish their energy.

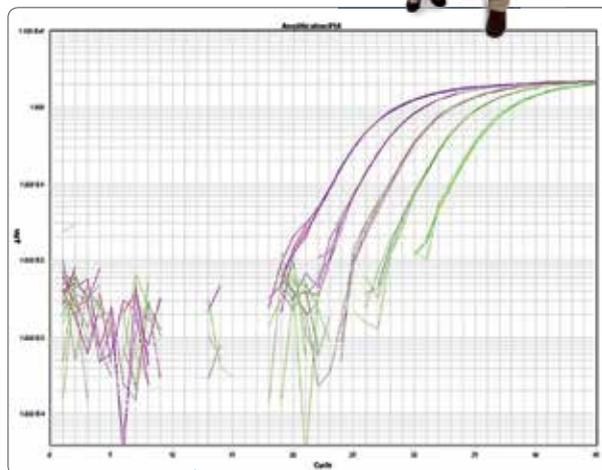
Although from an extroverted viewpoint taking quiet time seems like a waste of time, from an



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introverted standpoint it is time much needed to provide yourself with the energy needed to unleash your creativity and maintain your focus.

Therefore, you should make it a priority to schedule quiet time and protect it by reducing stimuli and going within yourself.

### Focus on depth

Since you tend to focus on depth, one of your strengths is your

ability to be well-prepared. The right amount of preparation sets you apart and increases your self-confidence.

Therefore, you should enhance this strength by putting together well-thought-out presentations and showcasing your expertise. This will help you make a strong case and prove the value of your proposal.

Few introverts achieve their goal alone, and most realize that they magnify their ability to make a difference when they strategize with others. Therefore, you should enhance your preparation by enlisting others to achieve your goals.

### Focused listening

Since you tend to listen first and then talk, you will maximize your ability to manage when you maximize focused listening. Focused listening engenders empathy, establishes credibility, and builds engagement, all of which help form the relationships that are necessary for managers.

Preparation feeds the strength of focused listening and involves creating the right conditions to slow down and really listen so others will feel heard and verbalizing your idea or proposal so people know how to engage with you.

Focused listening can deplete your energy, and when it happens, you need to schedule your quiet time to recharge.

### Focused conversation

Since you tend to feel more in your element in one-on-one conversations, having focused conversation maximizes your ability to manage. Focused conversations give you the opportunity to provide support and encouragement, spark learning, solve problems, and work through conflicts.

Preparation feeds the strength of focused conversation. It involves setting up space and time to talk, preparing questions ahead of time for more productive conversations, carving out opportunities for random conversations, and remaining authentic and flexible.

Focused conversations can also deplete your energy, so you need to schedule your quiet time to recharge.

### Writing

Introverts tend to be skillful writers and use all kinds of writings to motivate others, advocate

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their positions, and connect with audiences.

Being well-prepared feeds your writing strength, and involves studying your audiences and adapting your style of writing to make your case.

Since practice makes perfect, continuous honing of your writing skills will improve your preparation and increase your persuasiveness.

Introverted managers can use their writing skills in a social media context to increase visibility and to develop and grow relationships.

### Taking action

Kahnweiler proposes a four-step process—preparation, presence, pushing, and practice—to take action by leveraging your natural strengths in this process and closing the perception gap.

### Preparation

Preparation involves getting yourself ready for a tough meeting and relying on your strength to focus on depth. Careful preparation increases your knowledge, and anticipating questions and being prepared to answer them will give you the confidence you need to handle yourself in the meeting.

To prepare, pull together what you know, conduct your due diligence, and strategize. Use your natural strength from taking quiet time to manage yourself. Give yourself some positive self-talk, and practice by rehearsing the questions and possible answers.

### Presence

Being present is how you position yourself to close the perception gap with your listeners and show them that you are engaged in the here and now. It relies on your natural strengths of focused listening and conversation.

### Pushing

After you have prepared and learned ways to be present, pushing involves stepping out of your comfort zone and developing and solidifying your skills.

### Practice

Practice involves seizing and practicing new behaviors that may seem strange and unnatural at first, but you will become proficient at them. With repetition and practice, new behaviors will help you close the perception gap.

### Getting along

The tendencies of introverted managers affect how they deal with their extroverted colleagues. In order to get along, you need to develop an awareness that your extroverted

colleagues have an essential need to speak and that they have important things to say. You may want to test what you hear them say by asking questions and giving them face time.

In terms of managing your lab, you need to develop an awareness of each lab member's personality type. Based on this awareness, you need to delegate tasks in such a way as to highlight their strengths and mitigate their weaknesses.

In the event that you have introverts and extroverts on your team, it will be helpful to actively facilitate conversations from introverts and limit talking by extroverts so they do not dominate any group action.

### Finally ...

At the end of the day, it is important to remember that staying true to your temperament while utilizing your natural strengths is key to your credibility and to being an effective manager in a business world dominated by extroverts.

*Lina Genovesi, PhD, JD, can be reached via email at [lina.genovesi@gmail.com](mailto:lina.genovesi@gmail.com) or by phone at 609-462-4337.*

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# WELL IN HAND

## DEVELOPMENTS IN FIELD INSTRUMENTATION

by Trevor Henderson



For a variety of applications, the ability to quickly and precisely detect various elements and compounds at the sample source is essential. Such applications include environmental monitoring, forensic identification, military operations, and drug detection. Industrial applications, including identification of specific chemicals and carcinogens in a variety of durable goods from children's toys to plumbing supplies, require frequent screening to avoid possible risks to human health. Further, the increasing globalization of our food supply has led to the need for portable instrumentation to quickly, accurately, and affordably detect pesticides, veterinary drugs, and adulterants at all points in the supply chain.

For maximum effectiveness, portable analytical instrumentation must be lightweight, fast, and durable, with simple and intuitive interfaces. While portable units often lack the dynamic range, sampling capabilities, and overall selectivity and sensitivity of their benchtop counterparts, recent advances in miniaturization and microfabrication have resulted in handheld and portable instruments that are increasingly rapid and reliable.

### Health, safety, and emergency response

When assessing emergency exposure situations, first responders often have limited knowledge of the situation, and therefore require rapid assessments to respond quickly and



▲ Portable GC/MS offers fast and accurate analytical results for field workers.  
Source: Torion Technologies Inc.

appropriately. Historically, when a suspected exposure occurred, field analysts would collect samples and send them to a central lab for analysis, and perhaps days later the lab would return the results. With portable on-site analysis, first responders can make actionable decisions and share results in near-real time in an effort to mitigate potential risks and exposures.

For many field analysts, the top analytical tool has been, and continues to be, the gas chromatograph (GC). When coupled with mass spectroscopy (MS), the ability to detect, identify, and quantitate potential toxic threats in near-real time offers considerable benefits, as any health and safety concerns can be addressed immediately.

“Advances in miniaturization and microfabrication have resulted in handheld and portable instruments that are increasingly rapid and reliable.”

Among the industry leaders in portable GC/MS technology is Torion Technologies Inc. (American Fork, UT). Torion boasts the world's smallest and most portable capillary gas chromatograph—toroidal ion trap mass spectrometer in its TRIDION®-9 fully portable

GC-MS. Designed to deliver fast results (typically in less than five minutes) and weighing in at less than 32 pounds, it is both battery and line operable, with an onboard helium GC carrier gas cartridge.



▲ TRIDION®-9 fully portable GC/MS.  
Source: Torion Technologies Inc.

Although not new to the market, the TRIDION®-9 has undergone several recent improvements to both the hardware and software designed to improve speed, reliability, and sensitivity. Further, new sampling devices such as the CUSTODION™-NT (needle trap) for quantitative air sampling, and the SPS™-3 Sample Prep Station for sample desorption and transfer, have been added to complete the suite of available tools.

### Infrared and Raman

Over the past decades, the market for infrared and Raman spectrometry has grown in response to increased demand for improved border security and threat assessment. These devices have been shown to be infinitely useful for the detection of a variety of chemicals in industrial, security, and military applications.

Fourier transformation infrared (FTIR) spectroscopy offers several advantages for field technicians: rapid results (typically in seconds); mechanical simplicity, which offers little possibility of mechanical failure; and internal calibration, which means it never needs to be calibrated by the user. These advantages, in combination with several others, make this tool an invaluable resource for obtaining field results that are both accurate and reproducible.

Portable FTIR spectrometers are often the go-to devices for on-site analysis of various incoming materials and outgoing finished products in many industrial, chemical, and food industries. In many industries, the need to rapidly identify potential hazardous substances, including known carcinogens, is critical. Agilent Technologies (Santa Clara, CA) recently released a new portable FTIR package to rapidly identify polymers and measure total phthalates.

Phthalates represent a class of compounds present in PVC and have been implicated as both endocrine disruptors and carcinogens. The system can nondestructively determine the chemical composition of a polymer in seconds; if the identified polymer is PVC, the 4500 will accurately measure the amount of phthalate present.



◀ Agilent Technologies 4500 series portable FTIR.  
Source: Agilent Technologies.

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“There is critical need to both identify polymers and rapidly screen them for banned or restricted chemicals,” according to Phil Binns, managing director of spectroscopy at Agilent. Agilent’s polymer package is one of many packages available for Agilent’s battery-powered 4500 FTIR spectrometry system.

An ideal complement to infrared absorption technologies is Raman scattering. Raman technologies offer the advantage of being able to accurately detect many unknown substances accurately, as well as being able to measure aqueous solutions and take measurements through transparent or semitransparent containers. Such technology is ideal for counterfeit screening, material identification, hazardous material detection, and threat defense.

Common materials that fluoresce often cause unwanted interference for Raman instruments; however, new devices such as Rigaku Raman Technologies’ (Wilmington, MA) Progeny handheld device eliminates issues of fluorescence interference with the use of a 1064nm excitation laser and also allows the use of a handheld Raman to measure materials through colored bottles.



◀ *Rigaku Raman Technologies Progeny handheld Raman analyzer. Source: Rigaku Raman Technology.*

### Merging technologies

For Thermo Fisher Scientific, customer demand for an instrument that combines both FTIR and Raman technologies has led to the release of the Thermo Scientific™ Gemini™ Analyzer, the world’s first and only handheld integrated FTIR and Raman instrument.



◀ *Thermo Scientific™ Gemini™ analyzer. Source: Thermo Fisher Scientific.*

“Leveraging ten years of customer feedback and the state of the art of what is available in technology today, we were able to create a powerful tool for handheld, field-based, chemical identification.” This according to Chris Langford, production manager for safety and security at Thermo Fisher Scientific (Tewkesbury, MA).

The Gemini analyzer, designed with military and first-responder applications in mind, offers comprehensive and confirmatory results in a device that is lightweight, rugged, and easy to operate. To support field users, Thermo Scientific also offers comprehensive field support. According to Langford, Thermo Scientific’s reach-back support allows 24/7 support from PhD chemists in situations where spectra are not in the database or require additional analysis. “In critical situations, analysis and response to reachback requests can be performed in less than an hour,” says Langford. “In addition, technicians can provide hardware and software support to field personnel.”



▲ *Gemini™ analyzer represents the first and only combined FTIR and Raman analyzer. Source: Thermo Fisher Scientific.*

With a simple, intuitive interface and a comprehensive onboard library of over 16,000 common substances and the ability to add user libraries and custom spectra, the Gemini analyzer is well positioned to be an instrument of choice for many applications.

### Getting better than lab results

Arguably, field instruments often lack the robustness and sensitivity of their laboratory counterparts. This, however, does not mean that the quality of field analysis cannot be as good as, or better than, that in the traditional laboratory.

When assessing sources of potential error, the first consideration is often one of sample integrity. By analyzing a sample close to its source, one greatly minimizes the risk of sample contamination or degradation, damage during sample delivery, and issues surrounding chain of custody. Further, if an investigator suspects that there is an issue with the sample, or results are inconclusive, another

sample can simply be taken without having to return to the field. The field investigator also has the opportunity to adjust the parameters immediately to ensure that good samples are obtained and results are of superior quality.

Having the ability to choose the appropriate methods and instruments to meet the requirements of the field experiment gives the operator the means to best meet the requirements of a specific site, an ability that is not often possible in the typical laboratory, where samples must simply fit into the regular workflow.

Field sampling also has the benefit of representative sample collection. Real-time results mean that you can focus on areas of interest, rather than collecting a large series of samples over a wide area—many of which may turn out to be unnecessary. By identifying an area of concern early, efforts can be focused on relevant samples, improving overall data quality and reducing time in the field.

## The future of field science

In a society driven by the need for fast, accurate, and available data, field instrumentation will continue to find its way into the hands of a great number of individuals for a wide variety of purposes. We will continue to see innovation in instrumentation, whether it be in securing our food chain, protecting our nations, or securing our personal health and well-being. Beyond advancements in traditional markets, we are also seeing an increase in instrumentation coupled with consumer electronics.

As an example, earlier this year biomedical engineers at Columbia University developed a dongle, a piece of hardware that attaches to the headphone jack of iPhones and other smartphones, and in this case serves the purpose of a do-it-yourself STD test. This dongle contains a one-time-use cassette that screens blood for markers of HIV and syphilis using an enzyme-linked immunosorbent assay (ELISA). According to Samuel K. Sia, associate professor of biomedical engineering at Columbia University, “Coupling microfluidics with recent advances in consumer electronics can make lab-based diagnostics available to almost any population with access to smartphones.” Sia estimates the dongle will have a manufacturing cost of \$34, much lower than the \$18,450 that typical ELISA equipment runs. While security concerns remain over health-record confidentiality, such technologies will undoubtedly lead to a revolution of new “citizen scientists” able to collect, analyze, and share data with their smartphone.



▲ *Smartphone dongles provide point-of-care STD testing from finger prick whole blood in 15 minutes. Source: Samiksha Nayak for Columbia Engineering.*

Field researchers can also look forward to instruments with increased flexibility and adaptability, such as the recent release of Ocean Optics’ (Dunedin, FL) STS (stimulus + transducer + signal) Developers Kit. This new set of sensing tools brings together its powerful STS spectrophotometer, a Raspberry Pi microcomputer, customizable software, and remarkable wireless capabilities. Allowing extremely flexible configurations and control via smartphone or tablet, the unit is lightweight enough to be drone-mounted, allowing remote sensing in areas not accessible by field personnel.



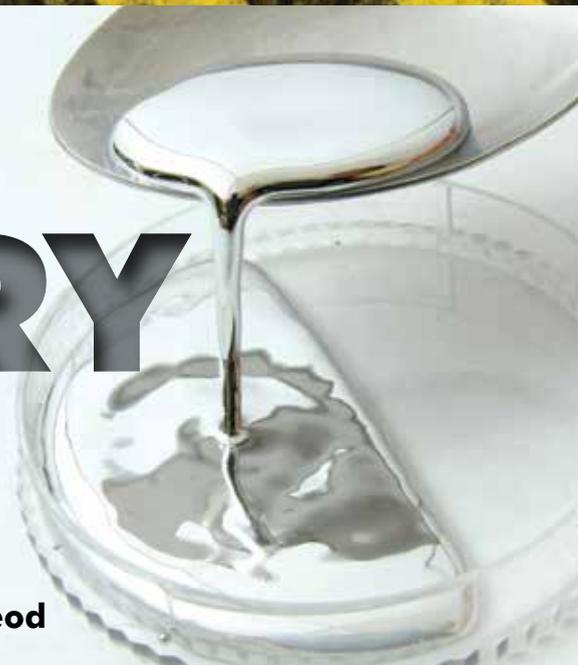
◀ *Ocean Optics STS Spectrophotometer Development Kit offers new opportunities for research method development. Source: Ocean Optics.*

Through coupling with consumer electronics, we are beginning to see analytical technologies that were previously limited to the lab now in the hands of a new generation of citizen scientists. Armed with smartphone-driven devices, such individuals could yield vast amounts of previously unattainable research data. When this is combined with the introduction of new flexible, open-source platforms and instruments, we can expect to see the emergence of new and innovative applications as these devices become increasingly affordable and available.

*Trevor Henderson, technology editor for Lab Manager, can be reached at [thenderson@labmanager.com](mailto:thenderson@labmanager.com) or by phone at 888-781-0328 x 291.*

# MERCURY RISING

**ELEMENTAL AND MERCURY COMPOUNDS AND THEIR ASSOCIATED HEALTH RISKS** by Vince McLeod



No, this is not an article about anger management. Nor is it about climate change or the T-1000 Terminator returning. If you have spent much time in a laboratory, you have most likely dealt with it though. We are talking about the 80th element of the chemical periodic table. Mercury—aka quicksilver—the one with the symbol Hg and atomic weight of 200. Turns out this stuff takes many forms and can be hazardous to your health. We are going to look at the three different forms (elemental, organic compounds, and inorganic compounds), their properties, hazards, and symptoms of exposure. Then we'll turn to safe handling, providing tips on everything from managing waste to cleaning up spills.

The most common form encountered in the lab is elemental mercury, found in thermometers, barometers, manometers, and sphygmomanometers, to name a few instruments inhabiting laboratories. But you may have noticed fewer of these recently, as the potential hazards have led to the phasing out of mercury thermometers and sphygmomanometers, especially in healthcare and clinical settings, for the more friendly alternatives such as alcohol-filled thermometers and solid-state or infrared electronic instruments. In addition,—and you might want to pass this article to your facility managers, physical plant personnel, and maintenance workers—mercury is found in batteries, float valves, mercury switches and relays, and fluorescent lamps, among other building items.

Inorganic mercury compounds are formed when mercury combines with elements such as chlorine, sulfur, or oxygen. In the past, these compounds were found in laxatives and latex paints. However, EPA canceled registration for mercury in interior paints in 1990 and this use was discontinued in 1991.<sup>1</sup> In addition, most agricultural

and pharmaceutical uses have also been discontinued in the United States. One exception is mercuric chloride, which is still used in disinfectants and some pesticides.

Organic mercury compounds have little industrial value and few uses but are the most toxic, as we will see. They are usually classed with the generic term “methylmercury” and form primarily in nature through a metabolic process called biomethylation. Organomercury compounds most often present as environmental pollution from contaminated fish or polluted waters, but may also be used in chemical and research laboratories.

## Health hazards—symptoms and effects

Elemental (metallic) mercury is the most common form encountered in labs and typical work environments. It is a silvery, odorless liquid at normal temperatures and a major source of occupational exposures, primarily from inhalation of vapors following a spill or inadequate cleanup of one. Acute (short-term) exposure affects the central nervous system (CNS), producing tremors, mood changes and reduced cognitive, sensory, and motor nerve functions. The kidneys are also affected, with renal failure at extremely high doses. Chronic (long-term) low-level exposure can cause the same CNS effects with increased irritability, insomnia, memory loss, and headaches. The kidneys are also affected, leading to development of proteinuria.<sup>2</sup>

Exposure to inorganic mercury compounds occurs usually through ingestion, with some potential for dermal absorption. Acute exposure causes a metallic taste in the mouth and leads to nausea, vomiting, and severe abdominal pain. As little as 1 to 4 grams can be lethal for the average 150-pound person. For chronic exposure to these compounds, the major effect is kidney damage,

similar to that produced by metallic mercury vapors.

Organic mercury compounds can produce severe effects. Exposure occurs primarily from both inhalation and ingestion, but dermal absorption is also possible. Acute inhalation exposure is rare, but leads to major

**“Organic mercury compounds have little industrial value and few uses but are the most toxic.”**

CNS effects such as blindness, deafness, and impaired consciousness. Oral ingestion produces severe reproductive and developmental effects such as mental retardation, ataxia, blindness, and cerebral palsy. Chronic inhalation or ingestion damages the central nervous system with the earliest symptoms showing as blurred vision, malaise, and speech difficulties. Dermal exposure can be very dangerous as it is easy to receive toxic doses. Low levels produce all the symptoms above, but a high dose (as little as 200 mg) can lead to death.<sup>3</sup> Recall the Dartmouth researcher who tragically received a fatal dose through protective gloves (albeit the wrong type).<sup>4</sup>

### Avoiding problems—safe handling and proper cleanup

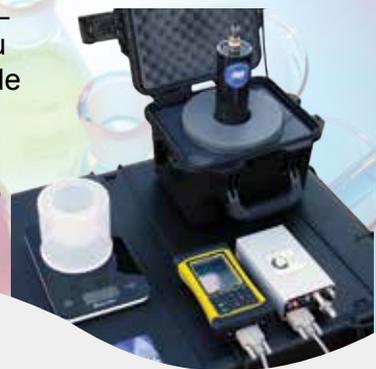
Knowing the facts, we can see that mercury and its associated hazards are serious business. Although OSHA does not have a specific standard covering its use in the workplace, there are established permissible exposure limits for mercury compounds. These are contained in the air contaminates table (29CFR1910.1000, Table Z-2).<sup>5</sup> If any mercury compound is used in your workplace, an exposure assessment and hazard evaluation is required for those employees handling the material. The OSHA permissible exposure limit is 0.01 mg/M<sup>3</sup> as an 8-hour time-weighted average for organic (alkyl) mercury compounds with a ceiling of 0.1 mg/M<sup>3</sup> for all other mercury-containing materials. A ceiling limit is an exposure limit that must not be exceeded during any part of the workday. The graphic below contains additional recommended exposure limits and health limits from other agencies and professional groups. LOAEL refers to the lowest observable adverse effect level and RfC is the reference concentration most likely to result in no observable adverse effects as a lifetime risk.

As far as handling mercury compounds, if you are not performing specialized research with an organic mercury compound, the most probable exposures will be from dealing with metallic mercury cleanups from accidental spills or broken equipment (thermometers, switches, etc.). If you are working with the methylmercury compounds, then you must have those employees thoroughly review and understand the safety data sheets. Develop and follow detailed safety protocols and standard operating procedures (SOPs). Perform all work in a fume hood and ensure that employees are using the right personal protective equipment. Finally, have a qualified industrial hygienist review the SOPs and conduct the exposure assessments.

A few final words on mercury spill cleanups are in order, as spills are the most likely scenario where mercury would be encountered. First, secure the area and prevent any unnecessary foot traffic. Use a mercury-binding sulfur powder (or commercially prepared mix) to dust the

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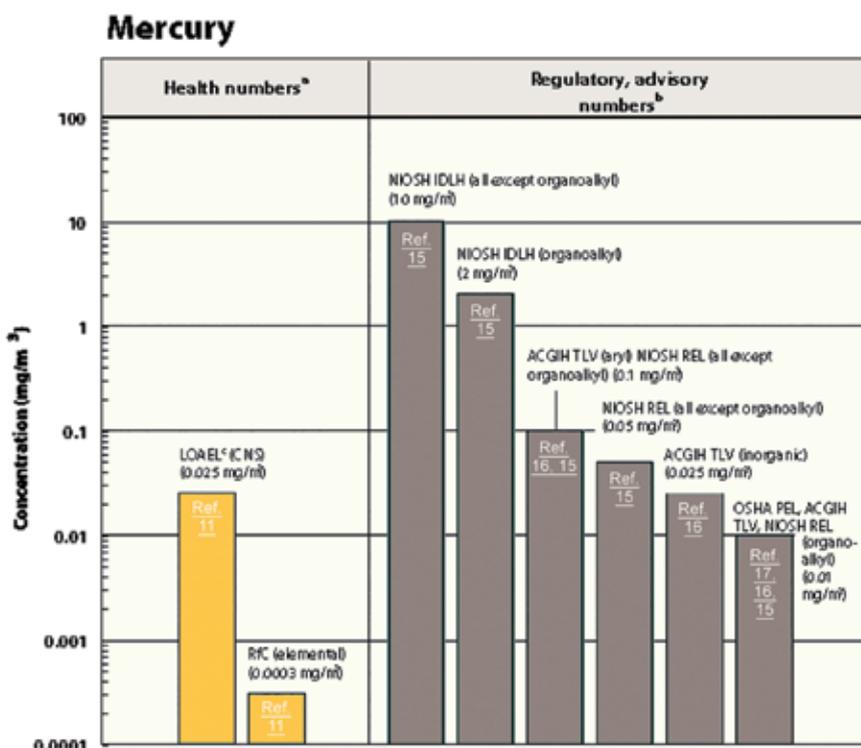
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entire area where droplets are visible. A special mercury vacuum is needed to vacuum up the dust and free mercury. If the spill was onto carpet or a porous material, those should be removed and disposed of (as hazardous waste) after vacuuming. Impervious surfaces should be dusted and vacuumed at least three times. Once you are reasonably sure all mercury has been collected and removed, have a qualified industrial hygienist conduct a clearance assessment, which should include air sampling for vapors. Once clearance testing passes, the area is ready for re-occupancy.



- **ACGIH TLV**-American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect.
- **NIOSH IDLH**-National Institute of Occupational Safety and Health's immediately dangerous to life or health value; the maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health effects.
- **NIOSH REL**-National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
- **OSHA PEL**-Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

▲ This graphic was taken from reference 1, EPA Hazard Summary.

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*Vince McLeod is the founder and senior member of the Safety Guys, and an industrial hygienist certified by the American Board of Industrial Hygiene. He currently serves as the senior industrial hygienist in the University of Florida's Environmental Health & Safety Division. He has 27 years of occupational health and safety experience at the University of Florida, and he specializes in conducting exposure assessments and health hazard evaluations for the university's 3,000-plus research laboratories.*

## SAFETY TIP

### DEVELOP SPECIFIC WORK PRACTICES FOR INDIVIDUAL EXPERIMENTS

By James. A. Kaufman

This simple idea preceded by 15 years the requirements of the OSHA Lab Standard for "Standard Operating Procedures," "Control Measures," and "Special Provisions for Working with Particularly Hazardous Substances." Today it's not just a good idea, it's the law!

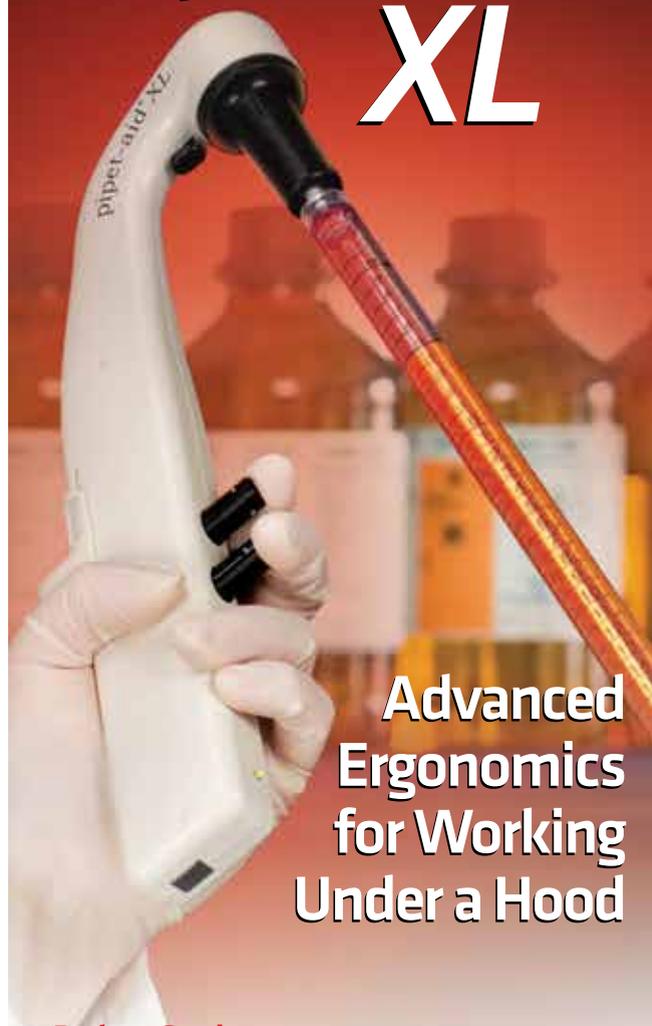
While the Lab Standard does not require specific work practices for individual experiments, it does stipulate that employers generate a list of recognized good practices that lab workers are expected to follow, i.e., wash hands before leaving the lab, never work alone, leave lab clothing in the lab, don't eat, drink or smoke in the lab, etc.

Control measures include elimination, substitution, engineering, administrative, and personal protective equipment (PPE) as methods for managing risks. Employers are responsible for ensuring that their lab employees understand these controls and can easily determine when to implement them. For example: when should chemical splash goggles be worn? Chemical splash goggles should be worn (1) whenever a chemical/biological known to be hazardous to the eye is being handled, (2) whenever a chemical/biological with unknown eye hazard is being handled, and (3) when handling any liquid hotter than 60 degrees Celsius.

Particularly hazardous substances include "select carcinogens, reproductive toxins, and highly toxic substances." The Lab Standard says that the employer must decide (1) whether these must be used in a "designated area," (2) when to work in a fume hood or other enclosure, (3) if procedures need to be developed for "decontamination," and (4) how to achieve the "safe removal of contaminated waste."

Source: Kaufman, James A., *Laboratory Safety Guidelines - Expanded Edition*, The Laboratory Safety Institute, [www.labsafetyinstitute.org](http://www.labsafetyinstitute.org).

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# HAZARDOUS *Spill* PROTECTION

**THIS ENVIRONMENTAL LAB'S PROJECT FOCUS REQUIRES KEEN SAFETY AWARENESS** by Mike D'Amicantonio

Ursus Remediation Testing & Technologies is an environmental services lab specializing in heavy metal and organic treatability studies, customized testing, and remediation services for engineers, scientists, and regulators to determine the most effective alternatives for achieving the remediation goals of a specific project. Services include sampling design, testing protocols, bench-level treatability testing, field dosage optimization, and in-field remediation implementation.

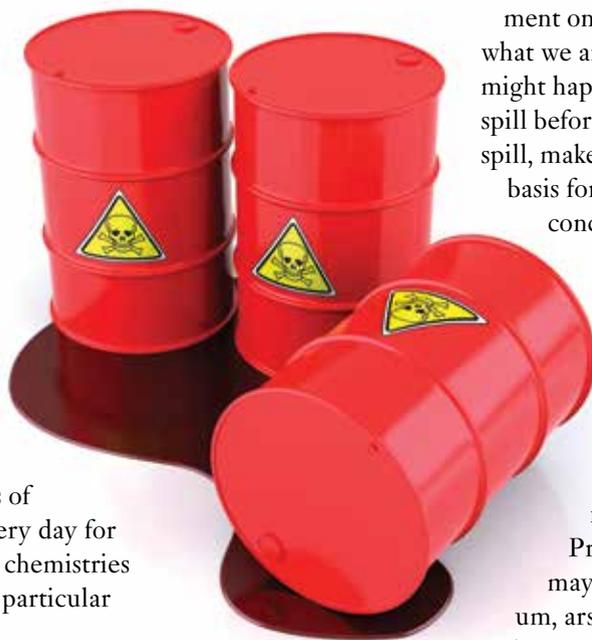
The lab conducts nearly 150 unique projects each year in applying inorganic and organic treatment strategies to sites with soil, groundwater, and industrial waste contamination. The objective is to render any contaminants of concern nonhazardous. The project focus of the business prepares this lab every day for a possible hazardous spill of the chemistries that may be tested and used in a particular remediation project assignment.

According to Andy Wenzel, principal owner of the lab, "Safety is a daily priority. It begins with constant awareness of the need, and the potential for hazards in the products we are working with each day; proper identification and storage of product inven-

tories; regulatory compliance; reminders in caution and safety signage; [maintenance of] wash stations; training of all personnel in pre-causal and responsive actions; readily available spill response tools; protective wearables; and diligence by everyone.

"By the nature of our business, which is project-based, we have the added protocol of making sure everything is in place and ready to implement on a specific project. Knowing what we are working with, knowing what might happen and how to respond to a spill before something accidentally does spill, makes us better prepared on a daily basis for anything that may happen," concludes Wenzel.

"Safety is a daily priority."



## Many different chemistries utilized in daily lab work

The company's lab projects utilize a number of different proprietary and nonproprietary chemistries. Proprietary reagent chemistries may be used to treat lead, cadmium, arsenic, chromium, selenium, antimony, and other metal-bearing wastes in soils and groundwater. The chemical properties of hydrating pozzolanic chemistries may be applied to lower the solubility of toxic contaminants in sludge and sediments, including PCBs and oil.



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Phosphate chemistries reduce leaching levels of heavy metals in industrial waste streams, forming metal-phosphate compounds that are stable under a wide range of pH levels. Redox chemistries include reduced forms of sulfur and metal salts and organic oxidizers, converting redox-sensitive metals such as hexavalent chromium, arsenic, and selenium to stable forms for safe disposal.

“Various combinations of treatment chemistries may be studied and applied, depending on the specific project objectives.”

Organic treatment chemistries are utilized to mineralize organic contaminants and treat comingled metal and organic wastes. Transitional metal catalysts are used to degrade chlorinated and non-chlorinated contaminants such as petroleum-based fuels and pesticides. Activated sulfate radicals, such as persulfate, are strong oxidizers capable of mineralizing a wide range of organic contaminants when activated by a catalyst. Catalysts include organic acids and chelated minerals.

Permanganate is used in mineralizing chlorinated hydrocarbons, and does not require a catalyst for activation. These organic chemistries are typically applied by either *in-situ* (chemical injection) or *ex-situ* (physical mixing) methods into soils, groundwater, and industrial waste streams to remediate hazardous contaminants.

Various combinations of these treatment chemistries may be studied and applied, depending on the specific project objectives, contaminant levels, mix of contaminants, site location, etc. No one project is the same as another.

### Multiple testing methodologies used to meet project objectives

A number of different testing methods may be employed to meet the remediation objectives of a project, including oxidant demand testing for initial screening of oxidant treatment chemistries to determine the amount of chemical needed to remediate the test material. Batch testing is a means to evaluate the effectiveness of the treatment chemistry when mixed with a test sample.

Column testing involves either pumping or gravity-feeding a treatment chemical through a column of soil. This procedure is useful in engineering chemical oxidant-reactive barrier walls. Attenuation testing uses chemical oxidation to change the geochemistry of the soil or groundwater being treated. Kinetic testing is the rate of contaminant destruction when reacting with the treatment chemistry, and is most applicable in designing the overall remediation strategy for a project.

### Project readiness means safety readiness for this lab

“We’re a small lab, and fortunately, a busy lab,” says Wenzel. “We work with a number of different chemistries and testing methodologies to help clean up our environment, one project at a time. We’re proud of our work, our expertise, our lab safety record, and our results.”

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“We work with a number of different chemistries and testing methodologies to help clean up our environment.”

Ursus Remediation Testing & Technologies is located in Mount Horeb, WI. Andy Wenzel has nearly 25 years of experience in environmental testing and remediation. He holds an MS in environmental sciences from the University of Wisconsin, Green Bay, and a BS in biology and a BA in computer science.

*Mike D'Amicantonio is a product development associate with Premier Magnesia, LLC. The company headquarters is in West Conshohocken, PA. The company is one of the world's principal manufacturers of high-purity calcined magnesium oxide and magnesium hydroxide products, including the trademarked product Amphomag® Universal Spill Sorbent and Neutralizer with pH Indicator.*

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**Michael Rummel**

# ASK THE EXPERT

## HOW TO DEVELOP VALIDATED HPLC METHODS by Rachel Muenz

**Michael Rummel** has held the position of chief operating officer at InSource Diagnostics, an independent laboratory that focuses on medication monitoring and compliance testing, for several years. Since graduating from the University of Wisconsin-Madison in 2005, Michael has pursued a career working in the analytical and clinical sciences. He has expertise in analytical chemistry assay development specifically with liquid chromatography/mass spectrometry, assay optimization, and sample preparation optimization and development. In his current position at InSource Diagnostics, he has become intimately involved in clinical workflows, regulatory requirements, and enforcement of strict quality control/quality assurance for LC/MS clinical assays. He has future aspirations of leveraging his knowledge to help develop a next generation of clinical diagnostics assays that involve less invasive sampling techniques and greater accessibility for patients.

**Q:** What specifically do you use HPLC for in your laboratory?

**A:** We specialize in illicit drug testing and medication monitoring, so we use HPLC in tandem with mass spectrometry, specifically triple quad tandem mass spectrometry (LC/MS/MS). It's used to confirm immunoassay screen results as well as perform direct quantitation of medications on human specimens.

**Q:** What are the most important things an HPLC method must have for the work you do?

**A:** HPLC is used to separate out target analytes away from other drugs and interferences that may be encountered in human matrices. One can imagine that from urine, to blood, to oral fluid—there are many different compounds, both endogenous and exogenous—that must be separated from our target analytes. Even more critical, HPLC is utilized to separate analytes from other target analytes with the exact same chemical mass. These are referred to as isobaric compounds which a mass spectrometer alone cannot distinguish between. HPLC adds another

dimension in order to resolve isobaric compounds in order to achieve accurate identification and quantitation. A prime example of a critical isobaric separation is discerning methamphetamine and phentermine. Street methamphetamine is an illicit substance, (there is a prescription medication for methamphetamine but it's rarely prescribed) and phentermine is a drug prescribed for weight management. There are obviously rather large implications in accurately identifying methamphetamine versus phentermine. Both compounds have the same exact mass and would look the same to a mass spectrometer so it is critical these two drugs are resolved using HPLC in order to distinguish one from the other.

**Q:** How do you develop validated HPLC methods?

**A:** It's a very laborious process. CLIA [Clinical Laboratory Improvement Amendments] is our governing body as InSource Diagnostics is a high complexity clinical laboratory. An LC/MS-based assay is considered a laboratory-developed test so there are many aspects of assay validation that are performed in order to ensure that it is stress-tested adequately. As part of the complete validation, accuracy, precision, linearity, carryover,

interferences, sensitivity, dilution integrity, analyte stability, and correlation studies against validated methods are evaluated. Additionally, because it is a mass spectrometry method, matrix contributed ion suppression/enhancement must be assessed as well. The length of a typical validation can take anywhere from two to four months, sometimes longer depending on the complexity of the assay. Since clinicians are making medical decisions that direct patient care based on our test results, utmost accuracy is imperative. There's no room for error. We have to ensure high quality and that begins at the validation process. Taking the time up front during validation definitely translates to a more rugged and robust assay upon going live with patient samples.

**Q:** You mentioned time is a key challenge in developing such methods, what are some of the other major hurdles you face? How do you overcome those challenges?

**A:** One of the biggest challenges with clinical samples is that they vary significantly based on disease state, collection device, geographic origin, patient diet, genetics, etc.

When developing a robust analytical method, you must ensure you are able to get the right answer regardless of the sample you are given. When we develop a new assay, we spend a significant amount of time evaluating different samples looking for matrix interferences or other endogenous or exogenous compounds that will present a challenge when the assay goes live. We then check our results against reputable reference laboratories to ensure that we are getting the right answer. At the end of the day, the more time and effort a lab spends during this phase of method development, the more robust the assay will be when it goes into production.

“Taking the time up front during validation definitely translates to a more rugged and robust assay.”

**Q:** What have been some recent changes or trends in validated method development for HPLC over the last few years?

**A:** Within the clinical industry LC/MS is becoming more rapidly adopted. It can be an incredibly powerful tool to have in the clinical laboratory, so more hospitals and independent laboratories, even some physician laboratories, are adopting LC/MS. This has especially been evident over the last five to ten years. With LC/MS becoming more prevalent in clinical laboratories, there is more opportunity to collaborate and share information. As a result, there is impetus for standardization of LC/MS/MS laboratory tests. For example, the CDC (U.S. Centers for Disease Control and Prevention) orchestrates a program for hormone and vitamin D standardization. The idea is increased consistency of results whether it's a laboratory such as InSource Diagnostics in California, or a laboratory in New York or Pennsylvania. I believe the trend for standardization and harmonization will continue.

**Q:** Where does validated HPLC method development appear to be moving for the future?

**A:** On the same note of increased standardization and harmonization, CLSI, the Clinical and Laboratory Standards Institute, released a guidance document to address the specific needs of an LC/MS/MS-based clinical assay validation. The publication was a collaborative effort from many different scientists and lab professionals throughout the country.

**Q:** What advice do you have for lab managers or professionals who are new to validated HPLC method development?

**A:** Do not underestimate the complexity of HPLC method development. It's important to have qualified personnel with the proper training and experience to perform HPLC or LC/MS/MS validations. It's not something you can just apply knowledge from a textbook and accomplish. It takes extensive training and experience and the person tasked with validation should have, at a minimum, four years of LC/MS experience.

*Rachel Muenz, associate editor for Lab Manager, can be reached at [rachelm@labmanager.com](mailto:rachelm@labmanager.com) or by phone at 888-781-0328 x233.*

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# INSIGHTS ON METABOLOMICS

**OVERCOMING CHEMICAL DIVERSITY,  
CONCENTRATION RANGES**

by Angelo DePalma, PhD

▼ A Metabolon scientist is cleaning the source on a platform instrument in preparation for the daily metabolomics run.



Within the past few years, genomics, proteomics, and metabolomics have created new disciplines within biology while inspiring the creation of techniques and methods that take life science analytics to new levels of sensitivity, specificity and understanding.

Metabolon (Research Triangle Park, NC) specializes in high-throughput metabolomics screening for clinical and research studies. Its core capabilities are based on platforms consisting of three Thermo Fisher QExactive™ hybrid quadrupole-orbitrap mass spectrometers with Waters UHPLC front ends. One LC-MS system is dedicated to negative electrospray, one to positive electrospray, and one to highly polar compounds. For fully quantitative targeted assays, Metabolon employs Agilent UHPLC systems connected to triple-quad MS from SCIEX.

Metabolon has experience with more than 350 analytical matrices, from human and animal biofluids to plant extracts and nonliving materials. The diversity of the company's more than 650 global clients confirms metabolomics' reach in research and clinical investigation. Half are academic and government organizations and the next-largest clientele groups consist of pharmaceuticals and biotechnology, but also included are organizations with interests in food, agriculture, consumer products, and even archeology. The company's platforms and informatics have also led to the development of diagnostics for obesity-related diseases and partnerships in genomics-based health initiatives with groups like Dr. Craig Venter's Human Longevity, Inc.

Data interpretation is huge for a lab that operates in the molecular space of 4,000 known compounds and an additional 8,000 identifiable unknowns in a typical biological matrix. Rather than rely on third-party software to help correlate metabolite profiles with biological states, Metabolon developed its own in-house program consisting of two million lines of code. The software performs an initial screen, but scientists confirm those results and ascribe them to the particular biological pathway under investigation.

Each analytical platform runs approximately 180 samples per day, which the company is looking to expand by acquiring more

instrumentation. This reflects one of the company's top priorities—throughput.

"It's imperative for us to maximize capacity and throughput while maintaining data quality," says Luke Miller PhD, VP of laboratory operations. And for each sample, this means calling out the largest number of identifiable compounds and pinpointing the greatest number of confirmed metabolites. Human plasma, for example, contains as many as 1,300 known metabolites.

## EXPECT THE UNEXPECTED

Sensitivity issues are usually related to low-abundance analytes, particularly in the presence of very high-concentration molecules—concentration dynamic ranges may be as high as 1,014. Miller notes that "unexpected situations" arising from matrix effects can also diminish sensitivity by suppressing chromatographic regions or causing outright column failure. "Lab managers must be prepared to detect diminished sensitivity and try to fix it."

Metabolon employs standard sample preparation methods designed for workflow efficiency. But when applied to novel matrices, these techniques may allow certain column-degrading compounds to slip through. Citrate in plasma, for example, negatively affects sensitivity, and in a high enough concentration will kill an HPLC column.

Columns are not the only sources of sensitivity problems. Compounds so abundant they fall above the linear dynamic range of the mass detector can overwhelm signals around them, but unlike HPLC-related failures, these events are transient.

Metabolon relies on long, automated, overnight LC-MS runs. When a column fails due to contamination or some other issue, subsequent data cannot be trusted until the problem is resolved. Thanks to modern communications, project leaders are alerted, sometimes in the middle of the night. Problems that can be solved remotely are handled that way. For the remainder, staff are expected to go on-site.

Hold time is an interesting topic with metabolites. We know that some sample types do not age well; for example, when bacteria multiply or digest analyte molecules from an environmental sample. While less prevalent in metabolomics, these

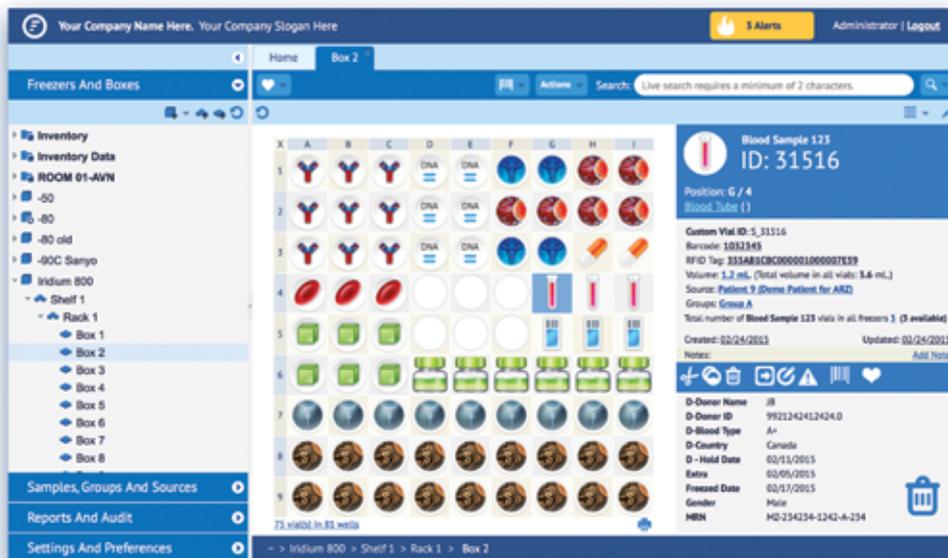
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effects nevertheless occur. Metabolon therefore asks clients to flash-freeze samples upon collection and transport them frozen. Samples are inventoried and stored at  $-80^{\circ}\text{C}$  on collection and maintained as cool as possible during sample prep. “We know that certain metabolites, particularly lipids, change upon storage, even at minus eighty,” Miller says. “We preach that as long as we have sufficient sample numbers to get a statistically valid read-out, and as long as each sample is treated identically and consistently, we can overcome slight changes that occur naturally.”

With 20-hour chromatography runs and instruments often operating seven days a week, Miller’s biggest worry is the unexpected. LC column failures lengthen or invalidate individual runs, but instrument failure and laboratory contamination have the potential to shut down operations. Metabolon uses risk-mitigation steps like providing clean, well-defined voltage to instruments; maintaining a constant temperature in the lab; and running a quality control check every sixth LC injection.

## HOLISTIC SYSTEMS VIEW

Yingying Huang, PhD, senior marketing manager for metabolomics and lipidomics at Thermo Fisher Scientific (San Jose, CA), identifies four persistent metabolomic workflow issues:

- Separations: How to cover the entire chemical space for small molecules.
- Signal detection: Noise elimination once separation is achieved.
- Compound identification: A significant bottleneck, particularly when peaks change from sample to sample.
- Data integration: Combining metabolomic data with other ‘omics to create a holistic view of systems biology.

“The separation challenge is not knowing how many molecules you need to solve the problem. You don’t know what you don’t know,” Huang says.

One thing we do know is that separating very polar molecules—for example, phosphate sugar isomers—is tough on conventional  $\text{C}_{18}$  and HILIC HPLC columns. The existence and position of phosphates convey deep knowledge of the history of a sugar molecule and from which biological pathway it emerged.

Labs turn to ion chromatography (IC) for such molecules, but until recently could not access MS detection due to incompatibilities between the potassium hydroxide-containing elution buffer and the spectrometer. Thermo Fisher Scientific has recently developed an ion suppression technique that removes the interfering species and allows mass detection for IC, thus opening the door to confirmatory analysis of thousands of highly polar metabolites. A Thermo Fisher application note demonstrates separation of 11 monophosphate sugar isomers

and nine diphosphates, quantitative over five orders of magnitude concentrations down to the femtogram level.

“With this new capability we can more closely study the TCA and glycolysis cycles,” Huang says.

In many instances multiple pathways produce identical sugar phosphates. Discriminating pathways that generate the same signal requires single- or double-isotope labeling of nutrient precursors and following the labels through critical transformations. Before widespread adoption of MS, labs relied on radioactive isotopes. Today MS easily discriminates between stable isotopes of carbon, for example, and the labeled species are relatively inexpensive.

## IMPROVING SIGNAL-TO-NOISE ISSUES

Signal-to-noise issues arise in metabolomics because the molecular targets are of low molecular weight and therefore singly charged. Proteomics targets, by comparison, are multiply charged. The more charge a molecule carries, the lower the mass/charge ratio and the higher the sensitivity and resolution.

Abundant sources of noise include high-concentration molecules, solvents, materials leaching off columns and impurities at the ionization source or in the autosampler, all of which are likely to be singly charged as well but present at significantly higher concentrations than many analytes.

Compound identification relates directly to chromatographic resolution, but this circles back to the question of noise. “Going to higher resolution will separate three molecules that previously eluted as one peak, but once you have that data you still must decide if peaks come from your sample or some other source,” Huang explains. “That’s where sophisticated data processing comes in.”

One relatively straightforward precaution involves strategic use of internal standards and injection of blanks, whose traces are subtracted from sample runs.

Quantifying the three ‘omics enables construction of gene activity, which reflects the up-and-down regulation of critical pathways. But integrating data from metabolomics, proteomics, genomics, and lipidomics and deconvoluting biological systems based on those interactions have been difficult. Huang says that while researchers are investing a lot of effort in integration, “we’re not there yet.” The key will be employing a systems or pathway approach, where genes represent an organism’s potential, proteins their machinery and metabolites the end product or phenotype.

## ARCHIVING CONSISTENT DATA

The laboratory of Professor Timothy Garrett at the University of Florida’s department of pathology uses triple quad and occasionally orbitrap MS for targeted metabolomics and a Thermo Fisher Q-Exactive orbitrap for global metabolomics.

Both systems have UHPLC front ends.

Garrett's most serious challenges are compound verification and throughput, both related in their own way to large numbers: the former to the large number of metabolites in typical samples, the latter to the lab's sample capacity. Like Metabolon's Luke Miller, Garrett recognizes that instrument robustness is critical for keeping things moving smoothly. "Instrument performance issues can turn a 20-hour run into a 40-hour run," he says.

In Garrett's opinion, instrument capabilities have for the most part kept up with the severe demands of metabolomics research. "Our triple quads are the most robust systems in our lab, requiring very little maintenance or calibration. The high-resolution [orbitrap] spectrometers are more finicky because they require more frequent calibration." And because they're high-performing, orbitraps generate large quantities of data that give rise to what Garrett calls "communication failures"—mysterious mid-run crashes that arise when instrument and computer stop sharing bits and bytes.

Garrett runs all samples in positive and negative ion modes to obtain the most information from each LC injection. This brings the number of metabolites of interest for his typical workflows to the 4,000 to 5,000 range. "Not all are endogenous metabolites, and not all are real metabolites," Garrett admits. "It's not like electrospray ionization on GC-MS, where you get most of what you want by running everything in positive mode."

For metabolomics work, when applicable, GC-MS is simpler and more highly reproducible than LC. Compound mass libraries are exhaustive and reliable to the point where a library search is nearly always confirmative. GC is limited, however, by molecular weight and the ability to form derivatives that don't stick to the column. But LC-MS, Garrett says, provides much greater metabolomic coverage.

LC is not without shortcomings, particularly when analyzing isomers with similar fragmentation patterns. Matched internal standards are an established workaround, but large isomers like prostaglandins can be "all over the place," according to Garrett. "But you can quantify them as long as the fragments are in the database."

Users of instrument columns over the past several years recognize how far LC-MS has progressed in terms of ruggedness and capabilities. Those improvements have not been unmitigated, however, because the more unique the combinations of LC system, column and detection platforms, the more difficult making sense out of retention times and masses becomes. MS platforms are innately inconsistent because of widely varying collision energies and patterns, and the LC system is a separate variable. Each combination or system in effect becomes its own standard.

It is this lack of inter-instrument uniformity that leads Garrett to wish that "lots of people would collect consistent spectra on the same instrument."

"Many instrument companies are putting in that effort, but it will take a very long time to [ensure] that every spectrum they publish is consistent. In the meantime, buying one of each company's mass spectrometers to be able to match with their fragment libraries would be quite expensive."

Metabolomics has been a rich area of research, but its ultimate goal is to create a systematized foundation for personalized medicine. "We need to be ready for anything: rare diseases, novel matrices, or some issue in the lab that affects the day's run," says Miller. "Eventually we hope to reach the point where we can do with metabolomics what we hoped to achieve with genomics and proteomics."

*Angelo DePalma is a freelance writer living in Newton, NJ. You can reach him at [angelo@adepalma.com](mailto:angelo@adepalma.com).*

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# UHPLC FOR BIOPHARMA WORKFLOWS

## BIOLOGICAL CAPABILITY, SPEED, AND RESOLUTION EXPAND THIS TECHNOLOGY'S CAPABILITIES

by Mike May, PhD

In biopharmaceutical research and manufacturing, many processes involve sophisticated separations. One of the most advanced separation technologies is ultrahigh-performance liquid chromatography (UHPLC). “There are two reasons to use UHPLC,” says Ken Cook, sales support expert, bioseparations and bio market Europe for Thermo Fisher Scientific (Waltham, MA). “The first is speed, and the second is resolution.”

As an example, Martin Vollmer, marketing manager, analytical and preparative LC, at Agilent Technologies (Santa Clara, CA), says, “Peptide mapping and glycan profiling of therapeutic monoclonal antibodies in the past sometimes required methods of 30 or even 45 minutes’ duration.” With UHPLC, he says, it takes only five to ten minutes.

In addition, Cook mentions variant analysis. “That’s often done with salt gradients that can take weeks to months to develop and usually an hour to run,” he says. “With UHPLC, you can develop a new method in about 15 minutes and run the analysis in two minutes.” He adds, “The reproducibility is also better with UHPLC.”

### Biological benefits

UHPLC also provides improved features that biopharma needs. As a recent advance, Vollmer mentions “bioinert LC systems, which prevent the unspecific interaction of analytes and instrument.” He adds, “True bioinertness is given by metal-free sample flow paths.”

In many cases, biopharma samples include very complex mixtures. For that, Vollmer says, two-dimensional LC is the “superior technology to separate all compounds, since it achieves peak capacities, unlike any other separation technology.” He adds, “The technology has become very user friendly with the launch of ready-to-go solutions like the Agilent 1290 Infinity II 2D-LC Solution.”

Several experts mentioned the value of UHPLC in glycan profiling. For example, Jennifer Fournier, product marketing manager at Waters Corporation (Milford, MA), says that glycan analysis is used in biopharma “from the very beginning of discovery, when you are looking to characterize new therapeutics, through manufacturing and quality control.” Despite that wide range of use, Fournier points out that preparing the sample for analysis creates the biggest bottleneck and introduces the

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“There are two reasons to use UHPLC. The first is speed, and the second is resolution.”

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most variability into the outcome. To overcome those challenges, Fournier says, “We revamped the method and streamlined and simplified it.” This resulted in Waters’ GlycoWorks *RapiFluor*-MS N-Glycan Kit.

Without this kit, says Fournier, even newer glycan derivatization protocols took three to five hours to complete. Waters’ new kit, though, runs the process in just 30 minutes. Beyond its being faster and simpler, Fournier also points out that the new derivitization label facilitates superior sensitivity. “There’s also the value that you get by seeing more because of the increased sensitivity,” she says. This enhanced ionization efficiency allows customers, for the first time, to use the Waters ACQUITY QDa Detector to assign a mass to every fluorescent peak generated, boosting confidence in each analysis.

### Collections of columns

In addition to UHPLC platforms, the columns matter just as much. The introduction of superficially porous particle columns, for example, provided fast and efficient separations at lower pressure compared to totally porous particle columns of similar

efficiency. “Those columns are available for any application now—be it peptide mapping, glycan analysis, charge variant analysis, or sizing and aggregation essays,” Vollmer says.

Other experts agree that the column really counts in the results. Cook says, “UHPLC itself is only the system that pumps and detects, and it’s useless without the column technology inside.” He adds, “Getting the right column is dramatically important.” He doesn’t believe that the UHPLC platform and columns must come from the same vendor, but he says that if you can work with a platform vendor that offers “a good collection of columns, you can go to [that vendor] for advice.” Some of Cook’s advice would be to use up-to-date column technology, which he says advances month by month.

In 2014, Anne-Charlotte Dubbelman, a postdoctoral researcher at the Leiden Academic Centre for Drug Research in the Netherlands, and colleagues—some from Janssen R&D in Belgium—published an article in the *Journal of Chromatography* in which they evaluated commercial UHPLC platforms, especially for drug metabolite profiling. They tested 17 drugs and a range of metabolites on UHPLC platforms using sub-2-micron particle columns. They also examined systems using core-shell columns and columns with porous particles. From these studies, they selected a “combination of solid-core particle column and mobile phase composition” based on “its selectivity, peak capacity, wide applicability and peak shape.” In conclusion, they wrote “[A] widely applicable, selective and fast chromatographic method was developed that can be applied to perform drug metabolite profiling in the timeframe of a quantitative analysis.”

## Simplifying the transition

In moving to UHPLC, most biopharma researchers need an easy way to speed up their methods but also maintain the capability to run validated legacy methods on their new equipment without seeing any difference from before. As

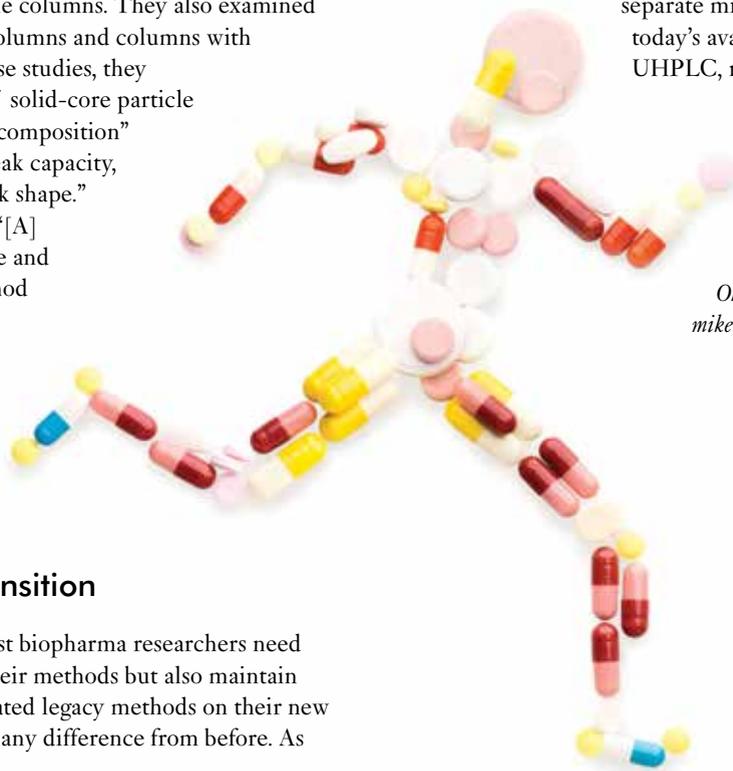
Vollmer says, “The capability to transfer validated methods from older LC or from multiple instrumentation to a new platform is of utmost importance and can save a lot of effort, time, and money.” Some tools simplify that transition. As Vollmer notes, “Tools like the Agilent ISET—intelligent system emulation technology—can mimic the behavior of almost any older-generation instrument and ensure a seamless transfer of validated legacy methods.”

Particular pieces of a platform can also make life easier. As an example, Cook says that finger-tight fittings reduce dead-volume problems. This dramatically improves a UHPLC’s performance.

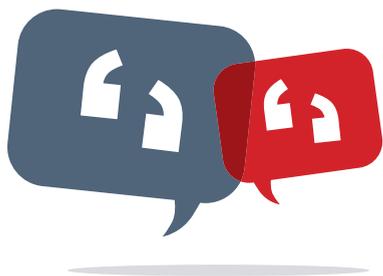
The key to the best use of UHPLC technology depends on where it will be used and for what specific application. Also, some applications fall into ready-made kits or protocols. On the other hand, UHPLC makes it faster and easier to develop new methods when needed. Consequently, the speed, precision, and reproducibility of UHPLC can be used by biopharma researchers or manufacturers focused on very specific applications or by someone who wants to use this

technology to explore new ways to separate mixtures for analysis. With today’s availability of columns for UHPLC, researchers can explore a wide range of approaches, even when working with the same platform.

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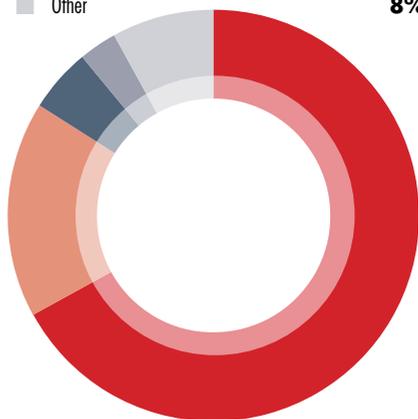
Benchtop - pH only	58%
Benchtop - multi parameter	49%
Portable - pH only	30%
Portable - multi parameter	14%
In-line - pH only	5%
In-line - multi parameterr	2%

## Methods used to measure pH as reported by survey respondents:

Glass-electrode method	71%
Hydrogen-electrode method	11%
Indicator methods	8%
Metal-electrode methods	7%
Quinhydrone-electrode method	0.4%
Antimony-electrode method	0.4%
Other	2%

Nearly 58% of respondents are engaged in purchasing a new pH meter. The reasons for this purchase are:

Replacement of aging system	67%
Addition to existing systems, increase capacity	17%
Setting up a new lab	5%
First time purchase	3%
Other	8%



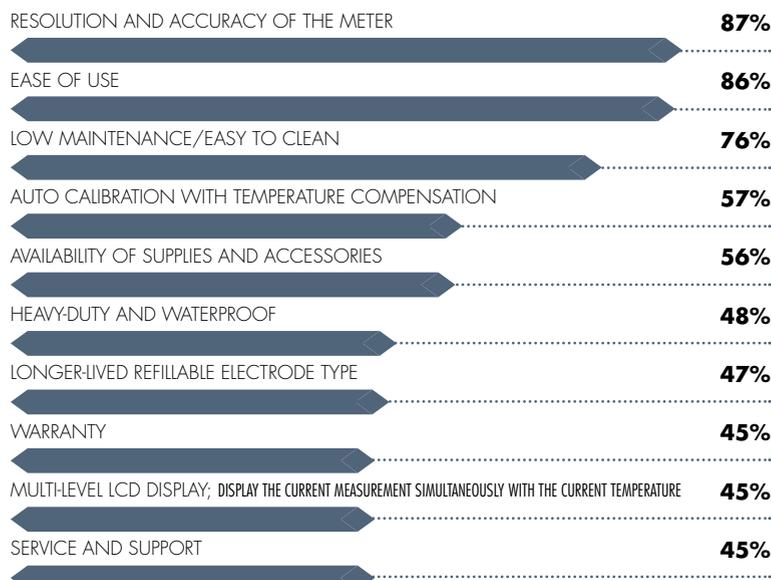
## TOP 6 QUESTIONS

### You Should Ask When Buying a pH Meter

1. What type of connector does the meter use?
  - Is it a BNC or DIN?
  - Is it proprietary or can other manufacturers' probes be used with it?
2. What is the replacement cost for a pH electrode?
3. What accessories are included with the meter?
  - What is the complete cost of all accessories needed to operate the meter?
4. What type of after sales support is offered?
  - If something goes wrong with the meter, can it be fixed locally?
  - What is the general turnaround time for repair?
5. What makes the company different from other companies that manufacture similar products?
6. What additional types of features are offered? (GLP data, PC connectivity (USB vs RS 232), calibration timeout, number of calibration points, ISE concentration readout, incremental methods for ISE and mv readout of concentration during calibration process).

## TOP 10 FEATURES/FACTORS

### Respondents Look for When Purchasing a pH Meter



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# Lab Manager

# LOOKING FOR THE RIGHT pH METER? WE CAN HELP

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The screenshot displays the 'pH Meters' section of the Lab Manager website. At the top, the browser address bar shows 'www.labmanager.com/productfinder/pH-Meters'. Below the navigation bar, a heading reads 'pH Meters' with a sub-header '108 Products / 0 Selected'. A large text block explains the tool's purpose: 'There are many different features of a laboratory pH meter to take into account before making your purchase, including accuracy, calibration type and number of calibration points, response time, operation, durability, reliability and value. The Lab Manager pH Meter Product Finder enables you to quickly and easily compare the latest pH meter models and request information and pricing from leading manufacturers. So, if you are in the market to purchase a new handheld or benchtop pH meter simply answer the questions below to narrow the search to find the best pH meter for your lab.' Below this, a question asks 'Do you require a benchtop or portable pH meter?' with two radio button options: 'Portable' and 'Benchtop'. The 'Portable' option is selected. The main content area is a grid of 18 product cards, each featuring an image of a pH meter and its name, such as 'Sartorius PB 11', 'Sartorius Professional pH Meter PP 15', 'Beckman Coulter 840 Series', 'Eutech Instruments EC400', 'Eutech Instruments EC300', 'Eutech Instruments EC450', 'Eutech Instruments PI110', 'Eutech Instruments PI120', 'Eutech Instruments PI120-C', 'Eutech Instruments PI100', 'Eutech Instruments Oyster™ Series', 'Eutech Instruments AP110 and AP115', and 'Hach Company HI 9142'. Each card has a 'Request Information' button. At the bottom of the grid, there are navigation buttons for 'Back', 'Next', and 'Select All'. Below the grid, there are more product cards for 'Free-standing SteamScrubber', 'Undercounter SteamScrubber', 'Undercounter FlaskScrubber', and 'Undercounter SteamScrubber with Viewing Window and Light', each with a 'Request Information' button.

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Dieter C. Gruenert, PhD



Greg Gocal, PhD

# ASK THE EXPERT

## TOOLS FOR GENE EDITING by Tanuja Koppal, PhD

**Dieter C. Gruenert, PhD**, is a professor of otolaryngology—head and neck surgery at the University of California, San Francisco (UCSF) and pediatrics at the University of Vermont (UVM). He has a PhD in biophysics from the University of California at Berkeley and was a postdoctoral fellow in carcinogenesis at L'Institut Suisse de Recherche Expérimentale sur le Cancer in Lausanne. He was co-director of the Gene Therapy Core Center at UCSF, director of the Division of Human Molecular Genetics at UVM, and head of the Stem Cell Research Program at California Pacific Medical Center. His research focuses on development of gene editing and cell-based therapies for inherited diseases and cancer. He has developed novel diagnostic and oligonucleotide-based therapeutic strategies to ameliorate disease pathology.

**Greg Gocal, PhD**, is the senior vice president of Research and Development at Cibus. With an extensive background in molecular biology, he has been central in developing the RTDST<sup>™</sup> technology in plant and microbial systems. Currently he leads the technology group and is part of the senior executive team tasked with exploring the many commercial opportunities to deliver on RTDS' potential applications. Prior to joining Cibus, Dr. Gocal led the molecular biology group of the Plant and Industrial Products Division at ValiGen. He earned a BSc in biochemistry/botany and an MSc in plant physiology from the University of Calgary. He received his PhD in plant molecular biology from the Australian National University and worked at CSIRO Plant Industry in Canberra, Australia. He continued to study the molecular biology of floral initiation/development as a postdoctoral scientist at the Salk Institute for Biological Studies in La Jolla, California.

### Dieter C. Gruenert, PhD

**Q:** Can you offer some historical perspective on gene editing?

**A:** We started work in gene editing in the early 1990s, and presented some of that work at the Cold Spring Harbor Gene Therapy meeting in 1992. We developed a small fragment [of DNA] homologous replacement (SFHR) strategy to target the cystic fibrosis (CF) gene in airway epithelial cells and demonstrated that those cells underwent genetic correction.

**Q:** Why didn't the field take off at that time like it has today?

**A:** One of the main reasons is that there was a lot of emphasis on cDNA-based therapies at that time. Our contention was that if you were going to have cell-independent expression of the transgene (correcting) gene, then it's not going to be under the regulation of a specific cell that expresses the gene. Hence, we decided to take a different path and go within the cell to try a "genetic surgery" type of approach. In our work, which was finally published in 1996, we had enhanced the efficiency of gene targeting. However,

funding for this type of work was not as exuberant as it was for viral cDNA-based therapies, so it was difficult to make significant progress on this technology. Gene therapy, in general, had another big setback in 1999 with the death of its first patient, Jesse Gelsinger. It wasn't until the early 2000s, with the papers on the use of zinc finger nucleases (ZFNs), followed by the studies on transcription activator-like effector nucleases (TALENs), and the more recent clustered regularly interspaced short palindromic repeats (CRISPRs), that things moved forward.

**Q:** What tools did you use for gene editing, and can you highlight some of their differences and similarities?

**A:** The concept of using endonucleases to introduce double-strand breaks had been around for quite some time, but no one had done it with any specificity, except for the work with homing endonucleases (championed by Collectis in France), and then with greater specificity in the studies with ZFNs. When Sangamo Biosciences took over the licensing for ZFNs, it became prohibitively expensive for most research

labs to have ready access to this technology. Since ZFNs weren't really user-friendly in terms of their construction and screening, we held off on the application of this potential for enhancing gene editing with double-strand DNA breaks (DSBs) until the TALENs became available. TALENs were made publicly available and were much more user-friendly to generate. We still use TALENs because we feel that they have more flexibility and specificity than the CRISPRs. While CRISPRs are easy to generate, they have limitations. As is the case with all targeting endonucleases, a main concern is off-target effects, and we really don't know at what level that's going to be a problem. Another limitation is the potential for an immune response to the nuclease that is generated. Introduction of the ZFNs, TALENs, or CRISPR/Cas9 systems all involve the delivery of a plasmid that encodes for a foreign protein that is potentially immunogenic. The other component of the gene targeting system is the donor DNA. We prefer not to use plasmids for our donor DNA and use fragments of DNA, either single or double strands, that are essentially homologous to the target sequence we wish to modify (except for the base changes we wish to introduce, e.g., to

correct a mutant sequence) and hence, have a seamless modification. This way, we don't leave a footprint in the genomic DNA.

**Q:** What advice do you have for lab managers looking to evaluate and use gene editing tools?

**A:** Know what it is that you are working with and how it applies to your system. Make sure that whatever tool/platform you choose, it is not going to disrupt the pathways you are looking to evaluate. Design your experiments so that you look at things comprehensively, keeping in mind the "big picture." Do a comparison of all the tools that are available. If you don't care about off-target events, then CRISPR/Cas9 is likely fine, but if you do care about off-target effects, then go with CRISPR/Cas9 nickase or the TALENs, keeping in mind that it is easier to develop allele-specific TALENs than CRISPRs. ZFNs are always an option, but they are a little more cumbersome in terms of the processing and lead time when compared to the other targeting endonuclease platforms. Most labs with competent people can readily utilize the TALEN or CRISPR/Cas9 technologies. In addition, core facilities in most universities can produce them for you at a reasonable cost. Make yourself familiar with the literature, and be careful of the hype, whether it comes from the vendor companies or other scientists. The papers will tell you if the lab made its own reagents or bought them from a company, and you can then evaluate the data and see if it's real or if there are some problems.

**Greg Gocal, PhD**

**Q:** Can you offer some historical perspective on gene editing?

**A:** I first came across gene editing as a graduate student, when I saw a paper in *Science* in 1996, where the mutation resulting in sickle cell anemia was corrected using a chemically synthesized oligonucleotide. I wondered how this could be applied in plants, and saw the huge potential to develop new traits or

understand how genes work by changing the spelling of genes. This field has been the Holy Grail in everything from microbial research and agriculture to human therapeutics, with an aim to precisely change the spelling of genes.

**Q:** What were some of the early challenges faced, and have they been overcome?

**A:** Some of the biggest challenges lie in bringing together the technologies necessary for gene editing. From a cell culture standpoint, being able to make a spelling change in a single cell and then being able to get that into a whole organism is a challenge. Another challenge lies in the efficiency of the technology, which is getting a certain percentage of cells to incorporate the change that you are trying to effect. If you are not using selection, how you then find those changes and have the whole organism get the change that is intended, is a third challenge. These are three areas that have to come together, and with recent improvements in cell culture, gene editing, and next-generation sequencing, we can see the progress being made to detect such genetic changes.

**Q:** How are you using gene editing, and what tools are you using?

**A:** We have a huge number of applications for gene editing, and from the beginning it's been like being a kid in a candy store! At Cibus, our focus has been on developing new traits in crop plants. We are working on herbicide tolerance and weed control that are required traits for farmers, and at the same time building on that for obtaining modified oils and starch, better drought tolerance, and better use of fertilizers that get applied to plants. We have developed traits in herbicide tolerance in a non-transgenic way in canola, flax, and rice. Beyond that, we are working in building disease tolerance in crop plants, and with precision gene editing, we will be able to address some of those issues in crop plants like potato. We are also working with a variety of oils for nutraceuticals and industrial use.

At the core of our technology is what we call the gene repair oligonucleotide, which

is a chemically synthesized piece of DNA that is protected in a variety of ways with a spelling change or a small number of changes buried toward the center of that molecule. This chemically synthesized oligonucleotide enables precision gene editing and repair, by finding its target in the genome and affecting the change. We are continuously improving this technology that we have now used for more than a decade.

**Q:** For what applications do you see gene editing succeeding?

**A:** We are completely focused on plant systems and making targeted spelling changes for various applications. However, the lowest hanging fruit at this time with gene editing is to generate loss-of-function mutations in a variety of target genes. Our sister company Nucelis is focused on using gene editing on fermentation products from yeast for applications in cosmetics. There are of course many more applications for gene editing in the human therapy area as well.

**Q:** What advice would you give to lab managers and people using gene editing?

**A:** In terms of successfully applying gene editing, you have to look at what you want the outcome to be. Is it a single cell or a whole organism? Is it a specific spelling change or loss of function in the gene you are interested in? Then you need to look at tools that are available to effect those changes, either alone or in combination. You need the correct skills in place for cell culture, screening, genomics, or sequencing and must have the right collaborations in place. As with any other technology, people can use gene editing for positive or negative outcomes. I believe gene editing can have tremendous positive outcomes in agriculture and human therapeutics, and we just need to make good ethical choices.

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

# INSIGHTS ON NEUROIMAGING

**TODAY'S TECHNOLOGIES REVEAL HOW THE BRAIN DEVELOPS, MATURES, AND DEGENERATES** by Mike May, PhD

Accessing the brain to unravel its structure and function is one of the greatest scientific challenges. This delicate structure consists of many regions—all made from many, many parts and even more connections—that communicate through chemical and electrical mechanisms. For centuries, neuroanatomists preserved, dyed, and sliced brains for microscopic examination, and neurophysiologists used a wide range of approaches to measure the signals flying around inside. Most of the techniques allowed brain scientists to look at only tiny pieces of a very large puzzle. They needed to see more and see it more clearly.

Overall, using imaging techniques to analyze the structural and functional features of brains from various animals and humans captures the attention of scientists around the world and from many fields—stretching from anatomy and medicine to computation and social sciences. This explains the U.S. government's \$4.5 billion investment in a 12-year program, the BRAIN Initiative, to map the brain.

Solving the many mysteries of the brain, however, will probably take more time and money than one initiative can provide. In addition, a collection of technologies and techniques will also be required. Fortunately, a neuroscientist's imaging options keep expanding.

## IMPROVING THE TOOLS

For any sort of imaging modality, two general tools impact its application to neuroimaging, says Ajit Shankaranarayanan, global manager for magnetic resonance neuro applications at U.K.-based GE Healthcare. One is whatever makes data acquisition faster, some sort of accelerator. The other is how the raw image data is converted into meaningful information about the brain. As an example, Shankaranarayanan mentions "segmentation" tools that identify the white and gray matter in a brain image, or software that picks out certain structures or damage.

Tools that help neuroscientists focus on specific features can be useful in basic and applied research. Imagine, for example, a technique that segments the hippocampus from

a brain image. This part of the brain plays a fundamental role in memory, which interests basic researchers, and some diseases, like Alzheimer's, might be impacted by it.

Some of today's imaging tools can reveal very small changes, like lesions in a brain's white matter. As Shankaranarayanan says, "These lesions can appear in the white matter in diseases like multiple sclerosis."

## A COMPUTATION COMMUNITY

In 2008 at McGill University in Montreal, Canada, neuroscientist Alan Evans and his colleagues started building a brain-mapping resource called CBRAIN. The need for this supercomputer-driven tool arose as neuroscientists examined ever more complex mapping, such as analyzing the temporal and 3D spatial differences between diseased and healthy brains across a large sample size.

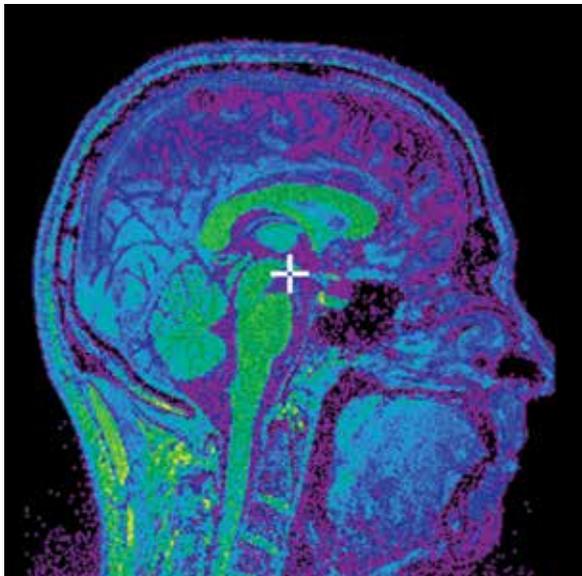
Evans says, "There are two big IT-related themes at play in leading-edge research today: big data analytics and international data sharing." CBRAIN provides a platform for advanced computational neuroscience on big data, and it allows for multisite consortia to collect, store, and share data internationally. Evans says, "The two environments together allow us to build big databases of imaging, genetic, and behavioral data that can be mined to answer many questions from many investigators worldwide."

Perhaps surprisingly, almost anyone can use CBRAIN. As Marc-Etienne Rousseau, system architect for CBRAIN, says, "The philosophy of CBRAIN is that things can be kept fairly simple for new users, but also can be quite powerful and flexible for advanced users." All you need is a computer and a recent version of Firefox or Chrome. That gives a user access to tools, computing sites and data storage via a web portal. People with high-end IT skills can use more advanced options.

CBRAIN can handle any kind of data. Rousseau says, "We built it for the general research 'Big Data' case where one needs to input data, do something to that data, then output and visualize the results." He adds, "Our

## Your Partner in Homogenization

current implementation of the platform is strongly focused on neuroscience, especially structural and functional MRI [magnetic resonance imaging], and processing thousands of scans for studies ranging from neurodegenerative diseases to normal brain development in children is our bread and butter.”



▲ *CBRAIN lets neuroscientists collaborate from around the world on large imaging data sets to analyze temporal and three-dimensional spatial differences between diseased and healthy brains. (Image courtesy of Marc-Etienne Rousseau.)*

The key to CBRAIN comes from the communities. As Evans says, “Basically, this is research on an industrial scale, as opposed to traditional research conducted in one investigator's lab, often addressing a single question over many years.” He sees value in both approaches but adds, “Big science is here to stay.”

One salient example of this is the so-called Big-Brain project. In collaboration with Katrin Amunts in Juelich, Germany, Evans' group built a 3D digital atlas of the human brain at 20-micron resolution. This one data set, occupying about 1 terabyte, was downloaded over 14,000 times in the first month after it was published (Amunts et al., Science 2013). Processing over 7,000 postmortem sections from a single brain, the collaborators built a 3D image that can be explored interactively (<https://www.youtube.com/watch?v=nJpFvQOYZLk>), with applications in teaching, neurosurgical planning, and basic research.

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## MEDICAL METHODS

For medicine, MRI and positron emission tomography (PET) are two of the most common imaging modes. With an MRI, magnetic and radio waves create images of the brain anatomy and basic physiology, such as blood flow. PET creates a 3D image from a radioactive tracer to measure more complex brain chemistry, such as neuroreceptor distribution.

Although much of the imaging from the past focused on structure—and much still does—it also helps image function. “An MR scanner provides the stability so that you can extract functions,” says Shankaranarayanan. For function, though, the signals tend to be very small. That requires a very sensitive technology that can, for example, extract data about blood perfusion in the brain. Shankaranarayanan says, “Perfusion is a function we can look at, and we can also look at oxygenation, indicating whether the brain is active or not.”

Beyond watching processes change, medical experts—more and more—want to quantify them. Shankaranarayanan says, “I see the field moving from looking at the images in a situation to also asking for quantitative numbers, because [they] can help with the diagnosis.”

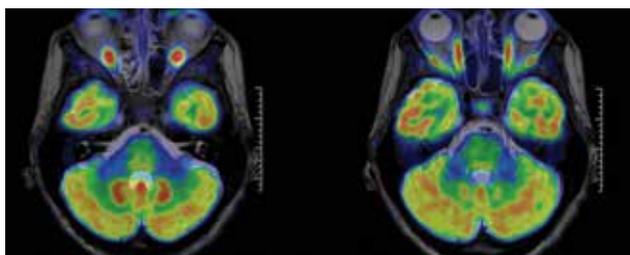
To make these technologies work faster, scientists at GE Healthcare even look to other fields. For example, to improve structural imaging, Shankaranarayanan says that a technology from communications called compressed sensing helps. “This involves taking a limited amount of data and producing an image using a mathematical algorithm. We combine that with structural imaging so you don’t lose information, but it can make acquisitions two to three times faster.”

To see how a brain is working, scientists often turn to functional MRI, or fMRI, which tracks the oxygen-

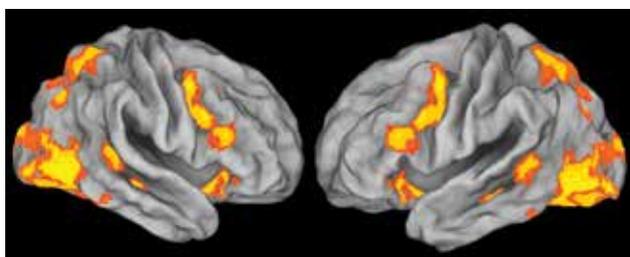
ation of the blood when someone is doing something. “Instead of activating the brain and trying to analyze a network,” says Shankaranarayanan, “we look at the fMRI when the brain is resting.” Then, using the latest technology like multiband, the scientists improve the temporal resolution of the imaging from two to three seconds down to 600 to 700 milliseconds. “Still, this approach preserves network information,” Shankaranarayanan explains. “Also, it’s more comfortable for the patient.”

“Also, it’s more comfortable for the patient.”

No single form of imaging is ever likely to answer all of the questions about the brain. Consequently, researchers often combine technologies. It gets easier to do this as vendors make platforms that include various imaging modalities. For example, GE Healthcare recently released its whole-body SIGNA PET/MR. Company background on this platform states “When these two powerful tools are combined, clinicians may be able to see early cellular changes that can be accurately mapped onto MR images.”



▲ GE Healthcare’s SIGNA PET/MR combines imaging modalities to reveal cellular changes mapped onto MR images. (Image courtesy of GE Healthcare.)



▲ This neuroimaging shows brain activity in healthy participants during an emotion-processing task. (Image courtesy of Rajesh Kana.)

## IMAGING AUTISM

By the numbers, autism appears on the rise. In 2012, Thomas Insel, director of the U.S. National Institute of Mental Health, wrote that autism—a broad range of developmental disorders—afflicts one in 88 children. In 2015, the U.S. Centers for Disease Control and Prevention put that statistic at one in 68 children. Maybe this condition is increasing, or it’s being detected more often. Either way, scientists would like to better understand this condition, and imaging helps.

Neuroscientist Rajesh Kana of the University of Alabama at Birmingham says, “Autism is a complex developmental disorder with no known single neural or genetic etiology.” He adds, “Hence, understanding the brain

organization and understanding the brain mechanisms are critical in learning about the neurobiology of this disorder.” With neuroimaging, an autistic brain can be examined for its organization and connections, as well as how it responds to external stimuli. “Since the brain can be investigated in live humans,” says Kana, “information gathered about the brain can also be associated with more precise and current behavioral information—rather than resorting to secondary resources, such as patient records or interviews of surviving relatives.” Moreover, a patient can be studied over time, which Kana says is “a vital dimension in the context of neurodevelopmental disorders.”

Exploring this disease, Kana uses several kinds of neuroimaging. Most of all, he uses fMRI to study the brain bases of behavioral and cognitive functions that tend to be affected in autism. “In fMRI,” he says, “we can create specific tasks that probe these functions and track the brain activity underlying such functions and how it is different in individuals with autism.”

He also maps the brains of autistic patients with structural MRI. Kana says, “This allows for the examination of the anatomy of the brain in terms of thickness of the cortex, volume, surface area, and the ratio of the folding in the brain.”

Kana collects other data with diffusion tensor imaging (DTI), which measures water diffusion in the brain, and Kana says that it “provides an indirect measure of the integrity of white-matter cables in the brain.” Consequently, DTI reveals connectivity in the brain. As Kana says, “The complexity of autism may entail distributed brain abnormalities, and DTI provides an important venue to investigate brain connectivity in autism.”

In addition, Kana’s team uses proton magnetic resonance spectroscopy (1H-MRS), which analyzes chemical concentrations in the brain. With this imaging technique, Kana can assess the concentrations of neurochemicals in various areas of the brain, and they reveal the health of the neurons.

“In sum,” says Kana, “these different neuroimaging techniques provide multiple sources and levels of information about the brain in autism.” In a recent study, for example, Kana and his colleagues used MRI, DTI and 1H-MRS to study the brain anatomy, connectivity, and chemical concentration through what Kana calls “a sophisticated machine-assisted pattern classification technique to understand which of these measures would best classify people with autism from neurotypical controls.”

The results show that a combination of connectivity in the white matter and information about brain anatomy classified the people as autistic or not with 91 percent accuracy. As Kana concludes, “This multimodal neuroimaging approach emphasizes that the brain abnormalities in autism may not be confined to a single area, [but] rather distributed across different areas at multiple levels and layers.”

In fact, many questions about healthy and diseased brains will require a range of imaging technologies. As neuroscientists acquire more sophisticated tools, they can address more complex questions. As a result, we will learn more about how our brains work and how to take care of them.

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## FOCUS ON CELL DISRUPTION

by Angelo DePalma, PhD

**R**enewed interest in cell biology has created the need for techniques that efficiently disrupt cells' outer membranes while sparing their contents. Chemical and mechanical methods are the two general approaches to cell lysis, with numerous methods within those categories. "The choice of method depends on what you're trying to get out of the cell," says Tim Hopkins, PhD, CEO of BioSpec Products (Bartlesville, OK).

Bio-Rad Laboratories (Hercules, CA) classifies cell disruption methods as gentle or harsh. The former include osmotic lysis (suspending cells in high-salt solutions), freeze-thawing, detergent, and enzymatic methods. Because these techniques are slow and relatively inefficient, they provide some protection against overprocessing when analyzing for sensitive molecules or organelles. Harsher techniques include sonication, French press, grinding, glass-bead homogenization (beadbeating), and blending-type mechanical homogenization.

Chemical lysis, which is sometimes combined with mechanical disruption, employs chaotropic agents, detergents, and enzymes. Most are available as kits. Chemical lysis is gentle but unpredictable, as disruption conditions and durations may vary significantly among samples. Mechanical systems involve an up-front investment, while kits represent a recurring expense.

Literature from Hielscher USA (Ringwood, NJ), which specializes in ultrasonic homogenization, suggests that chemical lysis can alter protein structure and introduce purification problems, while enzymatic disruption requires long incubation times and is not reproducible.

### Mechanical techniques

Manual cell disruption techniques have been used for decades. Although they are still preferred by some labs, they are low tech and mostly unautomated compared with more modern

mechanical methods. One method involves freezing cell suspensions and grinding the mass with a mortar and pestle. Freeze-grinding is slow, messy, and difficult to scale. Other methods squeeze cells between a pestle and the sample vessel wall, or through tiny holes under high pressure (French press). These methods do not generate significant heat but are slow and labor-intensive. All manual-mechanical techniques are unsuited to high-throughput operation.

Ultrasonic probes, rotor-stator homogenizers and beadbeaters are more modern—and popular—homogenization methods for cell work.

Ultrasonic probes operating at 20,000 cycles per second cause cavitation in aqueous solutions—microscopic areas of vacuum-like pressures and high temperatures that tear cells apart. Although temperatures may reach several thousand degrees Celsius, cavitation volumes are so small they do not heat the process significantly.

Assuming proper matching between sample and homogenizer, cell lysis by sonication takes between a few seconds and two minutes. Since sonication energy is user-defined on both handheld and benchtop sonicators, methods may be adjusted depending on the cell and end product. For example, DNA extraction requires "softer" disruption, while protein preparation from bacteria demands more rigorous sonication.

Hielscher suggests using short sonication burst cycles of up to 15 seconds on cooled samples to allow heat to dissipate without untoward effects on analytes.

Beadbeating, a technique perfected by Hopkins at BioSpec, shakes or vortexes cell samples sealed within microvials or microplate wells containing a large number of small spherical beads (0.1 to 6 mm in diameter) and usually, but not always, a lysis solution. The high-intensity wet-grinding process causes permeation of cell membranes or walls in less than three minutes. Beadbeating is well suited for high-throughput processing and also works well for small, intact tissue samples.

## Cool operation

Laboratories using mechanical disruption and targeting proteins or intracellular organelles must pay close attention to operating temperature. “Ideally, you should keep samples ice cold during processing,” Hopkins advises, “but realistically you’ll probably be fine if temperatures do not rise above culture or tissue source temperature.”

Despite best efforts to keep samples cold, endogenous enzymes can destroy proteins, particularly but not limited to the time between lysis and downstream processing when cell homeostasis no longer exists but enzymatic activity persists. Bio-Rad provides the following advice on avoiding enzymatic degradation:

- Lyse cells in strongly denaturing buffers (urea, thiourea, detergent).
- Operate above pH 9, where protease activity is minimized, using sodium carbonate or Tris as the buffering agent.
- Consider adding a chemical protease inhibitor to the lysis buffer. For best results, use a combination of inhibitors in a protease inhibitor cocktail.
- When studying protein phosphorylation, include phosphatase inhibitors such as okadaic acid, calyculin A and vanadate.
- After cell disruption, check the efficiency of cell disruption by light microscopy and centrifuge all extracts ( $20,000 \times g$  for 15 minutes at  $15^\circ\text{C}$ ) to remove insoluble materials.

## Tips for effective disruption

Another major mechanical disruption technique uses rotor-stator homogenizers. The handheld instruments work by repeatedly forcing samples through open slits or holes on the distal end of a static tube by a rotor turning inside the tube at 30,000 rpm. Rotor-stator homogenizers work rapidly and generate very little heat. On the negative side, it is not a

high-throughput method and may work poorly with certain monocellular organisms.

Sample disruption is a necessary early step in the isolation of RNA, DNA, proteins, and organelles from cells and tissue. Rotor-stator homogenizers are widely used for this purpose because they mechanically disrupt cells while sparing macromolecules from degradation.

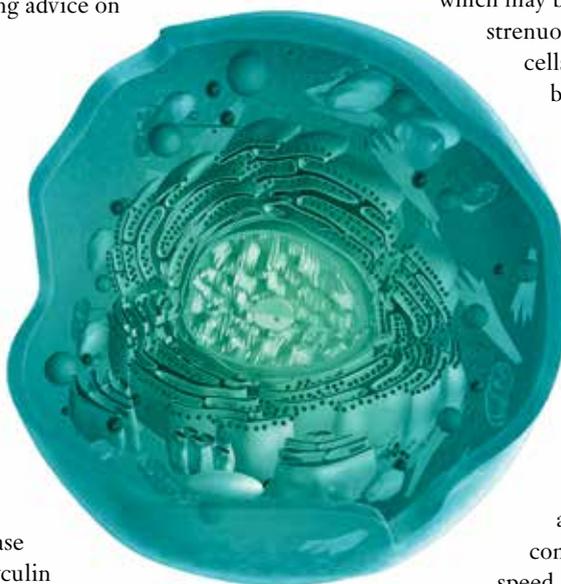
“Homogenization methods should always be tailored to the cell or tissue type,” says Holly Yacko Archibald, director of sales at PRO Scientific (Oxford, CT). Animal and plant tissues require more rigorous initial disruption methods, which may be followed by less mechanically strenuous cell disruption. Many cultured cells, Archibald adds, are easily lysed by simply vortexing their suspension in the presence of a suitable homogenization reagent.

Archibald advises purchasers of homogenizers for cell disruption to consider vessel and probe size, variable speed control, and cross-contamination avoidance.

Probe/vessel dimensions determine whether the probe will fit into the sample container and/or supply sufficient energy for complete homogenization. Variable speed control permits operators to ramp up from low to high power and back again to avoid creating pockets of sample inhomogeneity, and it is especially suited to organelle preparation.

Cross-contamination is more difficult to control with rotor-stator homogenizers than, say, with pipettors that universally use disposable tips. Cross-contamination results in the carryover of analytes from one sample to another; for example, the homogenate of treated versus untreated cells. Multiprobe homogenizers are one solution that provides multiplicity and automation but adds cost. The alternatives are single-use probes or the old-fashioned method of cleaning and sterilizing probes between runs.

*Angelo DePalma is a freelance writer living in Newton, NJ. You can reach him at [angelo@adepalma.com](mailto:angelo@adepalma.com).*



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Types of PCR systems used by survey respondents:

Standard PCR	80%
Multiplex PCR	30%
Real-time PCR / qPCR	71%
Digital PCR	2%
Other	1%

PCR applications as reported by survey respondents:

Gene expression	53%
DNA sequencing	40%
Cloning	36%
Pathogen detection	26%
Diagnostics	24%
SNP genotyping	19%
Site-directed mutagenesis	17%
Copy number analysis	16%
Viral quantitation	11%
Microarray/miRNA / RNAi validation	9%
Microsatellite analysis	5%
Other	8%

Nearly 54% of respondents are engaged in purchasing a new PCR system. The reasons for this purchase are:

Replacement of aging system	31%
Addition to existing systems, increase capacity	34%
Setting up a new lab	10%
New application requiring different instrument	16%
Other	9%



# ARE YOU IN THE MARKET FOR A... PCR SYSTEM?

Polymerase Chain Reaction (PCR) is a technology used to amplify a piece of DNA across several orders of magnitude. This technique employs thermal cycling, which consists of repeated heating and cooling of the reaction for DNA melting and enzymatic replication. PCR has found applications in a variety of fields including medical and biological research, cloning, functional genetic analysis, forensics, and disease diagnosis.

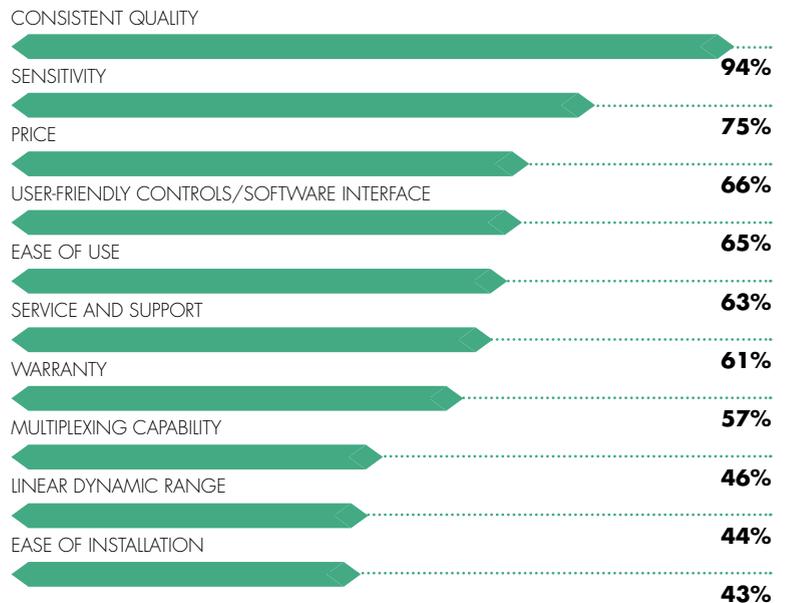
## TOP 5 QUESTIONS

### You Should Ask When Buying PCR Equipment

1. Consider the type of equipment you need, whether it be standard PCR, quantitative real-time PCR (qPCR), or digital PCR.
2. What sample formats do you require? While most users run their reactions in a 96-well format with 0.2 mL tubes, other formats are available.
3. Consider the ramp temperature and time. Ideally, you want a system with fast temperature ramp up/cool down time, and with low error.
4. How many users will be using the system? Systems which can run two independent PCRs at the same time might be desirable for labs with multiple users.
5. Consider your throughput requirements. For high throughput applications, systems that can accommodate larger plate formats, or that have integrated automation and robotics may be desirable.

## TOP 10 FEATURES/FACTORS

### Respondents Look for When Purchasing a PCR System



➔ For more information on laboratory equipment, including useful articles and a list of manufacturers, visit [www.labmanager.com/lab-products](http://www.labmanager.com/lab-products)

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## ADD-ONS TO CONSIDER

by Angelo DePalma, PhD

To most lab workers, even those who spend much of their days at or near fume hoods, these safety enclosures are part of the furniture or infrastructure. A hood is a hood is a hood—except when processes require special services or utilities. While many hoods are indeed production-level, off-the-shelf products, almost any productivity- or safety-enhancing feature may be added to standard models.

“About half of the fume hoods we ship are customized in one way or another,” says Chip Diefendorf, director of business development at Mott Manufacturing (Brantford, ON).

Physical dimensions are the number one modification specified by Mott’s customers. “They want them taller, wider, shallower, or deeper to accommodate whatever is going on inside,” Diefendorf adds. Some dimensional modifications are minor—for example, shaving an inch off a five-foot-wide hood so it will fit into an area 59 inches wide.

The next most common request involves the amount and type of see-through area used in the sash. Clear, laminated safety glass is by far the most frequently used material, and it is most often configured for the full height and width of the sash. But some customers request a smaller viewing area or colored glass. Purchasers who work with hydrofluoric acid, which etches glass, might request see-through polycarbonate.

Standard fume hoods feature a modest array of electric outlets, a small sink, a house vacuum, and house nitrogen. All may be upgraded—for example, to higher voltage, for accessing vacuum pumps below the hood floor or for introducing specialty gases from generators.

Less common modifications include location flexibility and accommodation for disabled workers.

Moveable hoods are part of the trend toward flexible lab configurations. These units tend to be smaller than fixed-location hoods and they require either flexible utility lines or multiple-location access to water, gas, exhaust, etc., which adds a great deal of cost to lab design.

Some lab directors specify that hoods comply with Americans with Disabilities Act workplace design specifications. Mott, for example, sells hoods with flexible

service connections, including exhaust, that allow raising and lowering the hood as needed.

### Flow, explosion proofing

Beth Mettlach, sales engineer at Labconco (Kansas City, MO), says customers frequently specify airflow monitors. One would think this feature would be standard, as the American National Standard for Laboratory Ventilation ANSI/AIHA Z9.5-2003 3.3.3 states that “All hoods shall be equipped with a flow indicator, flow alarm, or face velocity alarm indicator to alert users to improper exhaust airflow.” Yet the extremely popular variable-air-volume fume hoods already have monitors built in. “Having a built-in monitor would add unnecessary costs for those customers,” Mettlach says.

Many customers already own airflow monitors; even handheld thermal anemometers satisfy regulations and industry best practices.

Another popular customization is explosion proofing, which consists of removing all potential sources of sparks—for example, from electrical switches. Interestingly, fireproofing protects not the inside of the fume hood but the lab where it resides. The National Fire Protection Agency (NFPA), through its NFPA 45-2015 Fire Safety in Research Laboratories directive, states that due to the high influx of room air “... chemical fume hood interiors shall be considered as unclassified electrically ...” Unless, of course, an unusual hazard is identified.

“The room is electrically rated, not the fume hood,” Mettlach stresses. “It’s a common misconception among lab managers that if they’re working with flammable substances inside a hood, they need explosion proofing.”

NFPA goes to significant lengths to explain lab explosion hazards. In practical terms, storage or manipulation of large quantities of flammable liquids within the lab environment is sufficient. If your facility’s environmental safety team designates a lab as an explosion hazard and you’re installing a hood, it should be of the explosion-proof variety.

*Angelo DePalma is a freelance writer living in Newton, NJ. You can reach him at [angelo@adepalma.com](mailto:angelo@adepalma.com).*

FOR ADDITIONAL RESOURCES ON FUME HOODS, INCLUDING USEFUL ARTICLES AND A LIST OF MANUFACTURERS, VISIT [WWW.LABMANAGER.COM/FUME-HOODS](http://WWW.LABMANAGER.COM/FUME-HOODS)

# VISCOMETERS VS. RHEOMETERS

## A FLUID'S COMPLEXITY AND THE QUESTIONS TO BE ANSWERED DETERMINE THE RIGHT TECHNOLOGY

by Mike May, PhD

A fluid's viscosity—thickness, more or less—depends on many factors, and it impacts many applications. When you squeeze toothpaste onto your toothbrush and it comes out just right and stays where you put it, that's the right viscosity. As Robert McGregor, general manager, global marketing and high-end lab instrument sales at Brookfield Engineering Laboratories (Middleboro, MA), says, "Viscosity is more than one number. It's a curve." Moreover, the need to measure a material's fluid behavior varies based on what it is and how it will be used. That leads to a fundamental question: How do you know if you need a viscometer or a rheometer?

The search starts by knowing what you plan to do with the device. As McGregor says, "Be thoughtful to make sure that the instrument covers everything you're interested in." As a rule of thumb, says Ken Kreiman, product manager at Cole-Parmer (Vernon Hills, IL), if one number is enough, you can use a viscometer, but with more complex fluids you'll need a rheometer. Being more specific, Kreiman says, "There are two types of fluids." In Newtonian fluids—like water—the viscosity stays the same no matter how fast it is being sheared. McGregor says, "Water is the classical Newtonian material. It serves as the benchmark against which all other materials are classified for their relative viscosity value." He adds, "There are many Newtonian materials, especially in the petroleum and lubricant world." Conversely, the viscosity of a non-Newtonian fluid does depend on the shear rate. "The customer would choose a viscometer for a Newtonian fluid and a rheometer for a non-Newtonian fluid," Kreiman says.

McGregor also adds an easy decision tool: "For most customers who are new to the game, a viscometer it probably more than enough, and will give them every piece of information that they need in the immediate future." He adds, "If you want to measure properties like yield stress or creep, then you need to get in the rheometer arena."

### Being cost-conscious

Part of the reason to stay with a viscometer, if possible, comes from cost. McGregor says that a benchtop viscometer costs \$2,000-\$4,000, and his company's least expensive rheometer starts at \$4,500—going up to \$25,000. "The expensive equipment, though, does have advantages in flexibility, speed of testing, rapidity of getting samples to temperature, and high throughput," McGregor says. In quality-control applications, for example, McGregor says that a viscometer works fine for 10-20 samples per day, but that rheometers work better if that number is 50-100. Some applications require faster feedback. Imagine taking samples from a production line for testing. The QC people want the results as fast as possible to make sure that the line is operating correctly and producing the product with the required characteristics.

Depending on the needs, though, a viscometer can be quite versatile. "Most viscometers come with multiple speed range capability," McGregor says. "Therefore, they can measure a non-Newtonian material and show how its viscosity changes as a function of spindle rotational speed." He adds, "Viscometers possess capabilities that may not be harnessed by today's labs, because the test method has always been to record only one viscosity data point."

No matter which technology you select, the cost after purchase won't matter much. As Kreiman says, "Aside from calibration, there are very little maintenance costs for either a viscometer or a rheometer." Nonetheless, he says, "You can always add accessories to either unit in order to improve functionality."

In a rather complex area of instrumentation, though, it pays to get some advice ahead of a purchase. So talk to your colleagues or a vendor to get the tool you need for your tasks.

*Mike May is a freelance writer and editor living in Ohio. You may reach him at [mikemay1959@gmail.com](mailto:mikemay1959@gmail.com).*

FOR ADDITIONAL RESOURCES ON VISCOMETERS VS. RHEOMETERS, INCLUDING USEFUL ARTICLES AND A LIST OF MANUFACTURERS, VISIT [WWW.LABMANAGER.COM/VISCOMETERS](http://WWW.LABMANAGER.COM/VISCOMETERS)



**Types of laboratory evaporators used by survey respondents:**

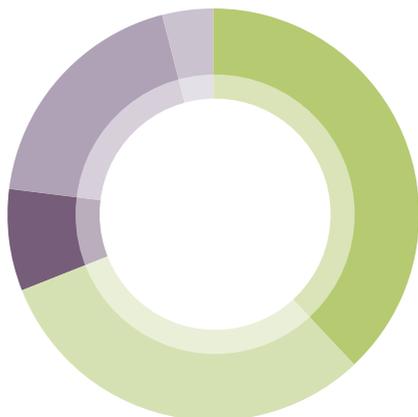
Rotary Evaporator	<b>65%</b>
Vortex Evaporator	<b>7%</b>
Nitrogen Blowdown Evaporator	<b>23%</b>
Vacuum System Evaporator	<b>42%</b>
Other	<b>2%</b>

**Primary purpose of evaporator as reported by survey respondents:**

Concentration of substances	<b>67%</b>
Sample preparation	<b>47%</b>
Extractions	<b>30%</b>
Distilling of low-boiling solvents	<b>23%</b>
Distilling of temperature-sensitive substances under vacuum	<b>16%</b>
Recycling of solvent waste	<b>12%</b>
Separation of material mixtures	<b>9%</b>
Distilling of oxygen-sensitive substances under inert gas	<b>2%</b>
Chemical synthesis under reflux	<b>2%</b>
Other	<b>2%</b>

Nearly 47% of respondents are engaged in purchasing a new evaporator. The reasons for this purchase are:

Replacement of aging system	<b>38%</b>
Addition to existing systems, increase capacity	<b>31%</b>
Setting up a new lab	<b>8%</b>
First time purchase	<b>19%</b>
Other	<b>4%</b>



# ARE YOU IN THE MARKET FOR AN... EVAPORATOR?

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

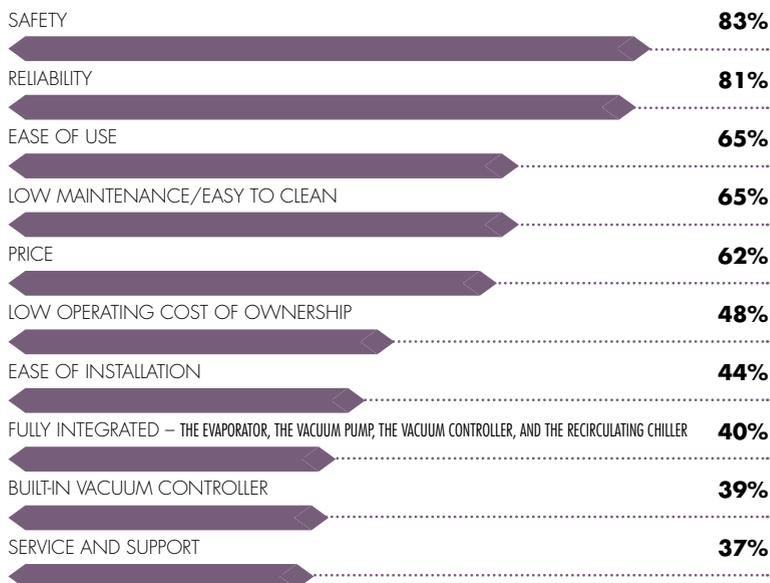
## TOP 5 QUESTIONS

### You Should Ask When Buying an Evaporator

1. What are your sample sizes? Microtiter plates and micro centrifuge tubes work best in a centrifugal vacuum concentrator. For large samples up to 450mls, a vortex evaporator is recommended.
2. What are your samples? Acids require an acid resistant system. Solvents damage plastic and rubber components; an appropriate system to prevent damage is recommended. A -50°C cold trap is ideal for aqueous based samples, a -85°C cold trap traps most solvents and a -105°C cold trap is recommended for alcohols.
3. Are your samples heat sensitive? Even at ambient set point, vacuum concentrators add heat through friction. A concentrator that has refrigeration built into it will give you the temperature control recommended to maintain the viability of heat liable samples.
4. Do you have limited space? A floor model with casters or small all-in-one benchtop model can be moved out of the way when not in use.
5. Do you prefer vacuum evaporation or nitrogen blow down? Some samples require evaporation under nitrogen (which is more gentle) for volatile solvents.

## TOP 10 FEATURES/FACTORS

### Respondents Look for When Purchasing an Evaporator



➔ For more information on evaporators, including useful articles and a list of manufacturers, visit [www.labmanager.com/evaporators](http://www.labmanager.com/evaporators)



# ARE YOU IN THE MARKET FOR A... LABORATORY MILL OR GRINDER?

In a laboratory, most materials required for sampling are, in practice, nonhomogeneous mixtures. The best method of obtaining a small representative sample of the nonuniform whole is to take a quantity of the material large enough to be compositionally representative and reduce it to a fine homogeneous powder. For this purpose, a laboratory mill or grinder is usually used.

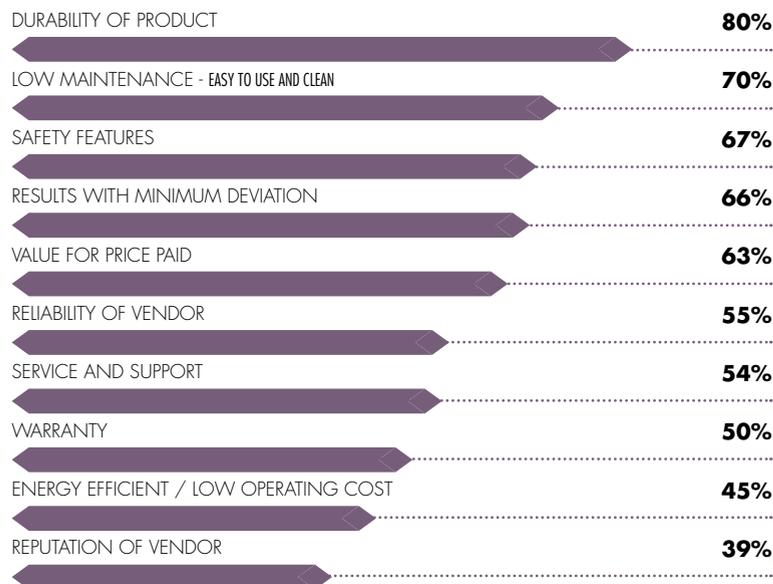
## TOP 5 QUESTIONS

You Should Ask When Buying a Mill or Grinder

1. Will the mill/grinder be used for wet or dry milling?
2. For dry milling, ask how finely the material needs to be ground and what are the properties of the material? Rotor beater, disc, and mortar mills, for example, are best for mid-range grinding (final fineness of ~0.01-0.1 mm).
3. For wet milling, ask what capacity of grinder you will need. Bead mills are usually best for small capacity applications while rotor-stator homogenizers should be considered for larger scale applications. For very large scale applications, industrial-scale mills are probably the best fit.
4. How important is preventing cross contamination? Bead mills are likely a good choice if you don't want any risk of contamination.
5. Based on the materials you will be milling, how long does the mill or grinder typically last? How much do replacement parts cost and how easy are they to get? What level of support/warranties does the company offer?

## TOP 10 FEATURES/FACTORS

Respondents Look for When Purchasing a Laboratory Mill or Grinder



Types of laboratory mills or grinders used by survey respondents:

Grinding Mill	41%
Rotor Mill	27%
Ball Mill	23%
Mortar Grinder	23%
Disc Mill	19%
Jaw Crusher	16%
CryoMill	15%
Mixer Mill	15%
Cutting Mill	12%
Knife Mill	11%

Primary purpose of lab mill or grinder as reported by survey respondents:

Research	43%
Processing	26%
Quality Control	19%
Clinical and Diagnostic	7%
Other	4%

Nearly 43% of respondents are engaged in purchasing a new laboratory mill or grinder. The reasons for this purchase are:

Replacement of aging system	42%
Addition to existing systems, increase capacity	32%
Setting up a new lab	4%
First time purchase	10%
Other	12%



➔ For more information on mills and grinders, including useful articles and a list of manufacturers, visit [www.labmanager.com/mills-and-grinders](http://www.labmanager.com/mills-and-grinders)

# A MOISTURE ANALYZER IN FOOD SAFETY AND QUALITY CONTROL LABS

**Problem:** U.S. food testing labs are closely monitoring discussions over proposed legislation regarding food safety. This year, lawmakers could approve more stringent safety standards. That means food laboratories will be looking for efficient and affordable equipment to help them adhere to regulations.

While water is an essential ingredient in many commercial food products, too little or too much can pose safety and quality issues. That's why food testing labs rely heavily on moisture analysis during the initial product research and development phase, and later on in quality testing laboratories. Maintaining the correct moisture levels is critical for safe food products, and also when determining product shelf life and expiration dates that help ensure food freshness, flavor, and stability.

**Solution:** The use of products such as Adam Equipment's PMB moisture analyzer is gaining popularity in food testing labs. Previously, labs had to rely on oven-testing to perform moisture analysis, which was time-consuming and inefficient. The PMB moisture analyzer does the job in a fraction of the time, providing reliable and consistent results.

This moisture analyzer accurately verifies food moisture content in less than five minutes and is easy to operate. The specimen goes into the heating chamber, which contains a 400-watt, energy-efficient halogen bulb. The bulb heats the sample in 1 °C selectable increments, evenly evaporating the moisture. Three heating options provide the flexibility to customize test methods and temperatures for different food products.

After evaporating the moisture, the PMB calculates the amount of moisture weight loss and responds with the moisture content. After testing several food samples, it's simple for users to adjust and control the amount of moisture in each batch. An automatic test-setting function enables easy recall for frequent testing of the same food products without additional programming. Users can log or print information, communicate with computers, or transmit test programs and results using the USB and RS-232 interfaces. There is no need for additional software to take readings, giving users the freedom to collect data in any location.

Food testing labs can run multiple PMB units simultaneously, to quickly assess the moisture content of multiple batches. This expedites the entire testing process for busy labs performing many tests on different foods.

An added benefit of a moisture analyzer like this is its ability to retain and store set-up information, saving the time and effort of having to re-enter the information in the next analysis. This feature is beneficial for frequently repeated food tests performed after adjustments are made in recipes or formulations.

*For more information, please visit [www.adamequipment.com](http://www.adamequipment.com)*



▲ Adam Equipment's PMB moisture analyzer provides a speedy, efficient way to verify moisture content in foods during the research and development phase and in quality control checks on food products.



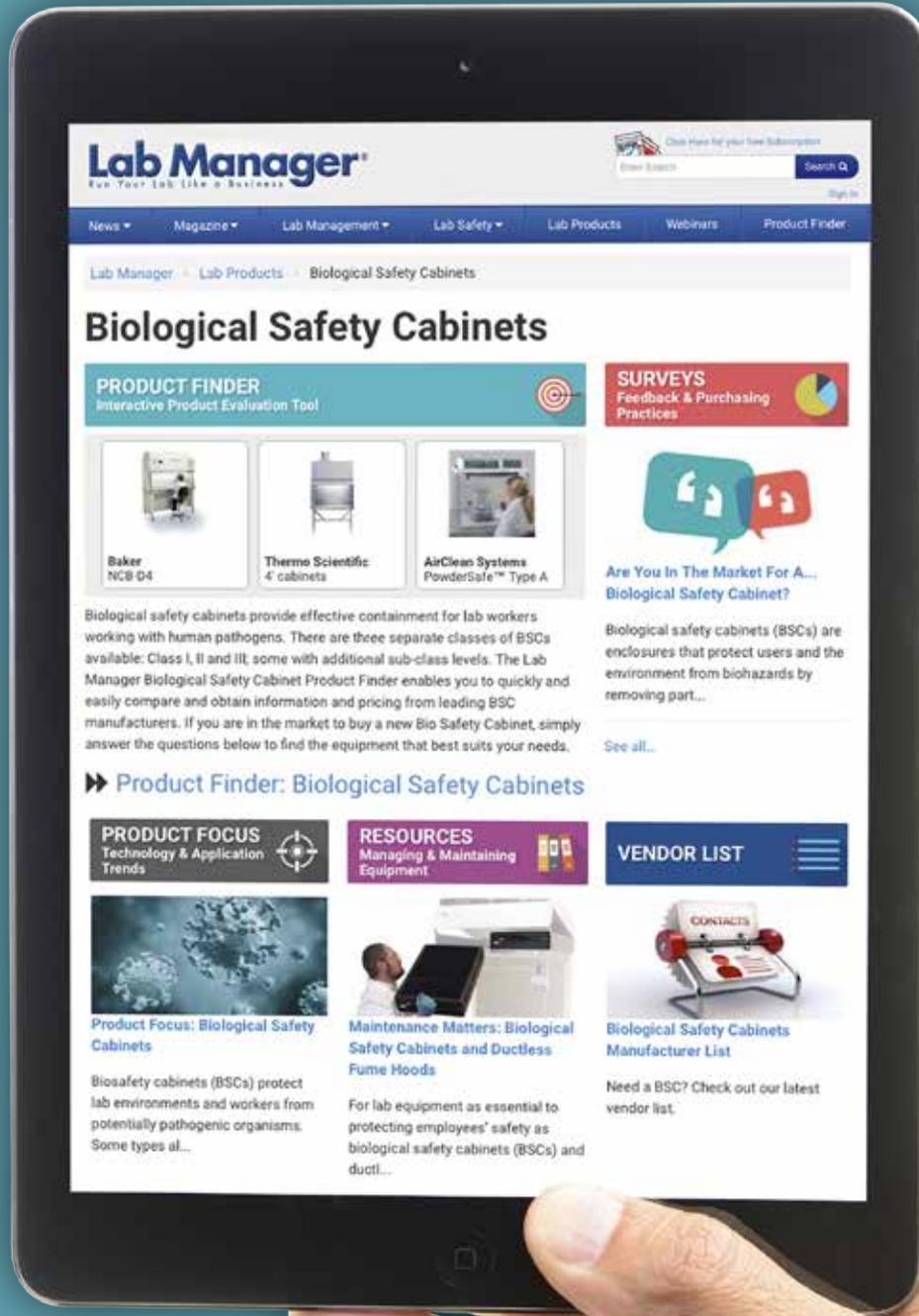
▲ Accurate expiration dates on food products are essential to help ensure quality and safety for consumers.

When it comes to purchasing laboratory equipment, we deliver.

# Lab Manager Product Pages

Delivering the information you need to make the best decisions possible.

Insights | Tools | Research | Applications | Resources

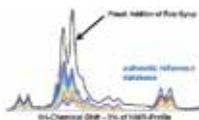


## ANALYTICAL

### Wine and Honey Screeners

#### FoodScreener

- Honey module delivers targeted and non-targeted analysis to simultaneously identify and quantify a multitude of honey characteristics using NMR
- Ease of use allows non-expert users to conduct analyses from measurement to final report in minutes, without chromatography
- Wine module allows easy and cost-efficient NMR-based wine analysis, now for the first time for key regions in France, Italy, and Spain



Bruker

[www.bruker.com](http://www.bruker.com)

### Process Analyzer

#### iONTRAC

- Combines the informing power of an ion trap mass spectrometer with a fast GC
- Can be customized to a wide variety of detection, analysis, and PAC/PAT applications directly on the plant floor
- Streams and ambient environments can be monitored in real-time and time-trend analysis or alarm conditions reported over industry standard Ethernet RJ-45



1<sup>st</sup> Detect

[www.1stdetect.com](http://www.1stdetect.com)

### GCxGC Mass Spectrometer

#### AccuTOF-GCx

- Designed for optimum throughput, operation, and uptime
- Offers improved resolution, accuracy, and sensitivity, while retaining the power and flexibility of the previous models
- Also provides 2D gas chromatography (GCxGC) using the Zoex thermal modulator and offers both powerful chromatographic separation and high-resolution mass spectra
- An optional combination EI/FI/FD ion source eliminates the need for source exchange for these experiments



JEOL

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### ICP-MS

#### PlasmaQuant® MS

- Features a free-running 27 MHz solid-state generator
- Offers neutral plasma for low kinetic energy spread of the analyte ions
- Provides robust plasma performance with 50% less argon consumption
- Gives users efficient decomposition and ionization of high solid matrices
- Includes variable plasma power, between 0.3 and 1.6 kW
- Handles organic matrices without changing the torch configuration



Analytik Jena

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## PRODUCT SPOTLIGHT

### CHROMATOGRAPHY, UNIFIED

First-of-its-kind system looks to increase speed and efficiency while reducing human error in analysis workflows



Officially launched at Pittcon 2015 in March, Shimadzu's fully automated supercritical fluidic chromatography-based Nexera Unified Chromatography system (Nexera UC) looks like it could be a game-changer in the chromatography world. The system can sequentially analyze up to 48 samples utilizing automatic extraction and chromatographic separation combined with high-sensitivity detection of targets by mass spectrometry. It is the world's first-ever unified and fully automated system that combines supercritical fluidic extraction (SFE) with supercritical fluid chromatography (SFC).

Removing human errors in the analysis workflow, while still achieving high speed and efficiency, was one of Shimadzu's key goals in creating the system, according to a recent company release.

"The Nexera UC system eliminates the need for complicated sample pre-treatment and enables highly reliable and stable analysis of delicate samples that are prone to oxidation or dissociation if exposed to air," the company said. "Notably, in the analysis of pesticides in food products, the state-of-the-art Nexera UC system takes only five minutes for a complete analysis sample pre-treatment when compared with at least 35 minutes for conventional systems."

In addition, the system has a much higher target analyte recovery rate and reduces the possibility of human error during analysis when compared to conventional manual systems. Designed to fulfil the measurement requirements of a wide range of applications, the Nexera UC achieves the highest levels of sensitivity by injecting the entire volume of eluent. Lastly, the system offers a wide range of separation modes, enabling the separation of a diverse wide range of compounds at once, which is not possible with single systems that are based on gas and liquid chromatography.

For more information, visit [www.ssi.shimadzu.com/products](http://www.ssi.shimadzu.com/products)

## BASIC LAB

### Workbench System

#### Gemini System

- This adaptable workbench features built-in functionality and unlimited flexibility
- Can be configured in a multitude of ways as stationary or freestanding, making it well-suited for renovations
- Adaptability provides long-term flexibility for labs with a high tenant turnaround
- Features a sleek, newer design; single and double sided benches are stylish and reconfigurable



Air Master Systems

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### Top-Loading & Analytical Balances

#### Symmetry®

- PT precision top-loading balances increase user's efficiency by providing a large weighing surface for placement of a variety of samples
- Weighing modes for PT model include parts counting, percent weighing, checkweighing, animal/dynamic weighing, and density determination
- PA analytical balances offer precise weighing of small samples; the three-door glass draft shield allows easy access to the weighing chamber



Cole-Parmer

[www.coleparmer.com](http://www.coleparmer.com)

## TOC Analyzer for Ultrapure & Process Waters

### Sievers\* M9

- Enhances productivity by producing TOC results in two minutes, twice as fast as its predecessor
- Offered in three versions: portable, online, or laboratory
- Now available worldwide and meets all relevant global regulatory requirements
- Engineered to improve output, the M9 enhancements promote simple operation and optimal data utilization
- Can now measure conductivity in grab sample or autosampler modes



GE Power & Water

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## Laboratory Balances

### MS-TS

- User guidance, built-in applications, and a large, glove-friendly touchscreen simplify daily weighing tasks and support the move towards lean laboratory and manufacturing practices
- Operable bare-handed or through cotton, rubber, or silicon gloves
- Provide accuracy, ease-of-use, and traceability
- A weighing-in guide helps users dose within the defined tolerances
- Standard checks and safety features provide added surety



METTLER TOLEDO

[www.mt.com](http://www.mt.com)

## Laboratory Balance

### Explorer Semi-Micro

- Provides full-range 0.01mg performance
- Features an ultra-fast stabilization time with audible stability alert
- Includes a large 5.7" touchscreen with graphical display
- Also features a highly accurate AutoCal™ internal calibration system
- Built-in ionizer included in auto-door models



OHAUS

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## Clear Storage Bins & Cabinets

### Treston®

- Made of crystal clear, transparent plastic, which is truly clear, not foggy or opaque
- Bins feature a corrugated bottom for easy picking, and can be equipped with length and width dividers and front and rear labels
- Many sizes are available, from as small as 2" x 7" x 1.5" to as large as 7" x 20" x 7" (WxDxH)



Sovella USA

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### ChemStar TPx™

- Provides advanced performance and safety features that suit demanding characterization needs
- Complements the Pulsar by providing a flexible, fully automated solution for the demanding applications of R&D labs while maintaining sufficient ease of use for routine applications
- Intuitive software interface allows the user to program and run a variety of temperature-programmed analyses and more



Quantachrome Instruments

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## CHEMICALS, KITS & REAGENTS

## Kit for Whole-Transcriptome Arrays

### GeneChip® WT Pico Kit

- Designed for gene expression array target preparation from as little as 100 pg of total RNA input
- Working with as few as 10 cells, the new kit offers a high degree of flexibility and precision
- Enables analyses of samples too small for other methods as well as the interrogation of small subpopulations of cells within larger samples

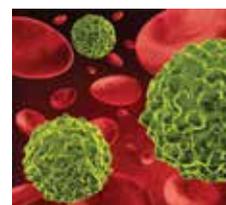


Affymetrix

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## Purified, Soluble Immunoreceptors

- Together with new indoleamine 2,3-dioxygenase (IDO) assay kits, these products can be used to screen for inhibitors of protein-protein interaction, as well as neutralizing antibodies that serve as positive controls for inhibition
- IDO is widely recognized as the next hot target behind the PD-1 and CTLA pathways for developing a new class of immunotherapeutic anticancer agents



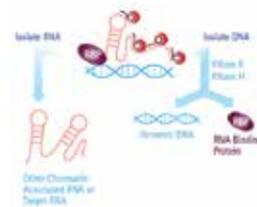
AMSBIO

[www.amsbio.com](http://www.amsbio.com)

## RNA Interactome Kits

### Magna ChIRP™

- Offer a simplified way to study the interactions of chromatin-associated RNAs by providing all the necessary components in one validated kit
- Use RNA as a target to reliably recover chromatin complexes
- Identify sites of genomic interaction for chromatin-associated RNA
- Allow researchers to more easily identify, recover, and analyze regions of chromatin that interact with chromatin-associated RNAs



EMD Millipore

[www.emdmillipore.com](http://www.emdmillipore.com)

## Transferrin ELISA Kit

- Allows for the quantitative determination of transferrin in human serum and plasma as well as canine serum
- Measures as little as 4.6 ng/ml of transferrin in serum and plasma, providing fully quantitative results that surpass semi-quantitative Western blot analysis
- Able to analyze up to 40 samples in duplicate in 2 hours



Enzo Life Sciences

[www.enzolifesciences.com](http://www.enzolifesciences.com)

## Cell Energy Phenotype Test Kit XFP

- Enables a unique real-time assay on live cells that determines their baseline metabolic phenotype and potential
- Designed specifically for use with the XFP extracellular flux analyzer
- The only method available [at the time of writing] that can provide a metabolic phenotype with which scientists can make direct, functional comparisons of both metabolic pathways between groups of live cells



Seahorse Bioscience

[www.seahorsebio.com](http://www.seahorsebio.com)

## INFORMATICS

## Liquid Handler Software Update ArtelWare v1.3

- New feature set extends the company's rounding out of the comprehensive capabilities of this software for its MVS® Multichannel Verification System
- Delivers advanced grouping and filtering tools, enabling the user to compare liquid handlers by make and model in addition to comparing pipetting performance of specific volumes and target solutions
- Includes interactive user feedback communication



Artel

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## Mass Spectrometry Software MassWorks™ for GC-MSD

- Now available as an option for GC-MSD systems through Agilent's worldwide channels from a recently entered partnership
- Can achieve up to 100x better mass accuracy to enable formula ID on this workhorse quadrupole system, through a patented MS calibration technology with the use of easily available PFTBA tune gas as standards
- Provides excellent spectral accuracy

Cerno Bioscience

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## Concurrent Molecular Proofing Capability CoMAP™

- Enables cancer researchers to gain rapid insight into the functional impact of DNA copy-number alterations
- Combines whole-genome copy-number data with gene expression profiles to easily and cost-effectively visualize and identify cancer driver events
- Now included in Affymetrix's Chromosome Analysis Suite (ChAS) 3.0 software
- Allows researchers to go from samples to insights in just three days



Affymetrix

[www.affymetrix.com](http://www.affymetrix.com)

## Rheometer Software Update RheocalT v1.2.19

- Now includes Test Wizards for rapid test creation, yield testing for the DV3T rheometer, improved layout and navigation, and additional import/export functions
- Test Wizard reduces the time and effort needed to set up popular tests such as: time to stop, time to torque, speed ramp/shear rate ramp, and temperature profiling
- Runs on Windows 8, 7, Vista, or XP



Brookfield

[www.brookfieldengineering.com](http://www.brookfieldengineering.com)

## Multi-Analyte Quantitation Software for GC/MS LabSolutions Insight

- Intuitive operation and multiple report viewing options improve the efficiency of multi-analyte data analysis
- Can be combined with Shimadzu's Smart Database Series for easy analysis of pesticides, forensic toxicological substances, metabolites, and environmental pollutants
- Features three chromatogram views (sample, compounds, and summary) so users can check differences in parameters, compound results, and summary of batch analysis all with the same software



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Cleaver Scientific

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- Includes several new grades of Collagenase, recombinant Nucleases DNase I and RNases A, T1 & T2 and Neutral Protease (Dispase®)
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Eppendorf

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Sartorius

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# Designing an Ultra-Low Freezer You Can Trust for Your Sample Storage

Understanding “How It’s Made Matters” was the tenet around which the Helmer Scientific Ultra-Low Freezer was designed and developed. Care was taken to focus on each aspect of the product to ensure that every component works together to create an optimized system that instills confidence in the user.

The benefits of the Helmer Ultra-low freezer go beyond what you can see and include design elements that provide a barrier against heat, an optimized refrigeration system, intelligent monitoring and diagnostic support, outstanding serviceability, and advanced manufacturing technologies that guarantee TrueBlue™ performance.

## Design Matters

A unique Heat Barrier System™ was designed to provide four (4) levels of containment, combining an ice-resistant sealing surface with non-conductive materials to keep heat out, providing superior temperature uniformity and reducing frost. Robust, high-quality materials were used in the design of the outer door, inner doors, and the frame and cabinet design. These combine to reduce the amount of heat transfer, provide a tighter closure to minimize changes in interior temperature during door openings, and provide a compressed sealing surface to prevent cold air leaks.

## Cooling Matters

The refrigeration system has been designed to optimize performance and protect the compressor. It provides maximum heat exchange delivering excellent uniformity and fast temperature response, increasing the overall efficiency and reducing the compressor run time. In addition, great attention to detail was paid to ensure the system works with the compressor to improve its reliability. The system can also adapt to changing environmental conditions and heat loading of product to further ensure reliable refrigeration performance.

## Intelligence Matters

Our ultra-low freezers are smart. The i.C3® Information Center provides critical information at hand, offering peace of mind and early detection of alarm states. Intelligent diagnostic information and temperature data is readily available on the home screen while samples are safely stored inside as a result of the many security features. Integrated access control is included on every ultra-low freezer to ensure sample protection and integrity.

## Serviceability Matters

Our outstanding serviceability was created by design. Field technicians were included on our design team to help organize the ultra-low freezer systems to create a freezer that is easily serviceable, reducing both downtime and repair costs.

## Manufacturing Matters

Advanced manufacturing techniques promote maximum reliability. Ultra-low freezers are assembled in our state-of-the-art, eco-conscious manufacturing facility by highly trained team members in a temperature and access controlled room that provides the controls needed to ensure consistent, reproducible results.

It’s all about sample protection and integrity. We get it.

**Confidence Matters.** That’s why “How It’s Made Matters”.



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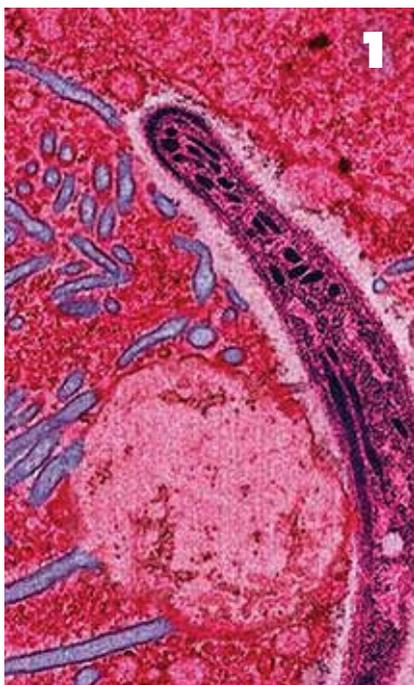
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# LAB MANAGER ONLINE

We look back at our web content since the May issue and look forward to what's in store for July.

### 1 Fighting Malaria More Affordably

Peter H. Seeberger and his colleague Andreas Seidel-Morgenstern from the Max-Planck Institutes in Potsdam and Magdeburg, Germany, recently won the Humanity in Science Award for their work in affordable anti-malarial drugs. They described their new process for making the drugs using air, light, and plant waste material in a recent presentation.

Read more at [LabManager.com/fighting-malaria](http://LabManager.com/fighting-malaria)

### 2 Trending on Social Media: Microplates for Cell-Based Assays

As of May 19, *Lab Manager's* top May issue article posted to Facebook was our Product Focus on microplates for cell-based assays. This article, which discusses how to overcome the challenges this type of assay presents, had received the most likes and shares on Facebook of any other article from our May issue.

Read more at [LabManager.com/CBA-microplates](http://LabManager.com/CBA-microplates)

### 3 Most Popular Webinar

Last month's top webinar on LabManager.com with 694 registrants was "Being an Effective Public Speaker by Avoiding 10 Common Mistakes," presented by Rick Parmely. This presentation identified ten public speaking traps and how to avoid them. Though it ran May 12th, you can still catch it on demand at the link below.

Read more at [LabManager.com/10solutions](http://LabManager.com/10solutions)

## NEXT ISSUE ➡

### The Latest in Laboratory Design

The image of the single researcher toiling away in a small, enclosed laboratory space is ancient history, as architects and designers have come to realize the benefits of more open, cross functional spaces. What else is new in laboratory design will be the subject of our July issue.



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