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CONTENTS

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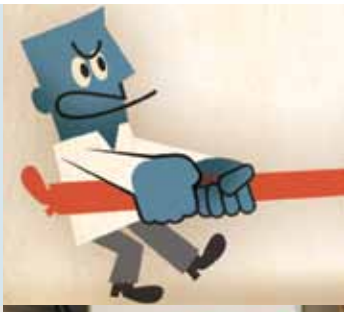

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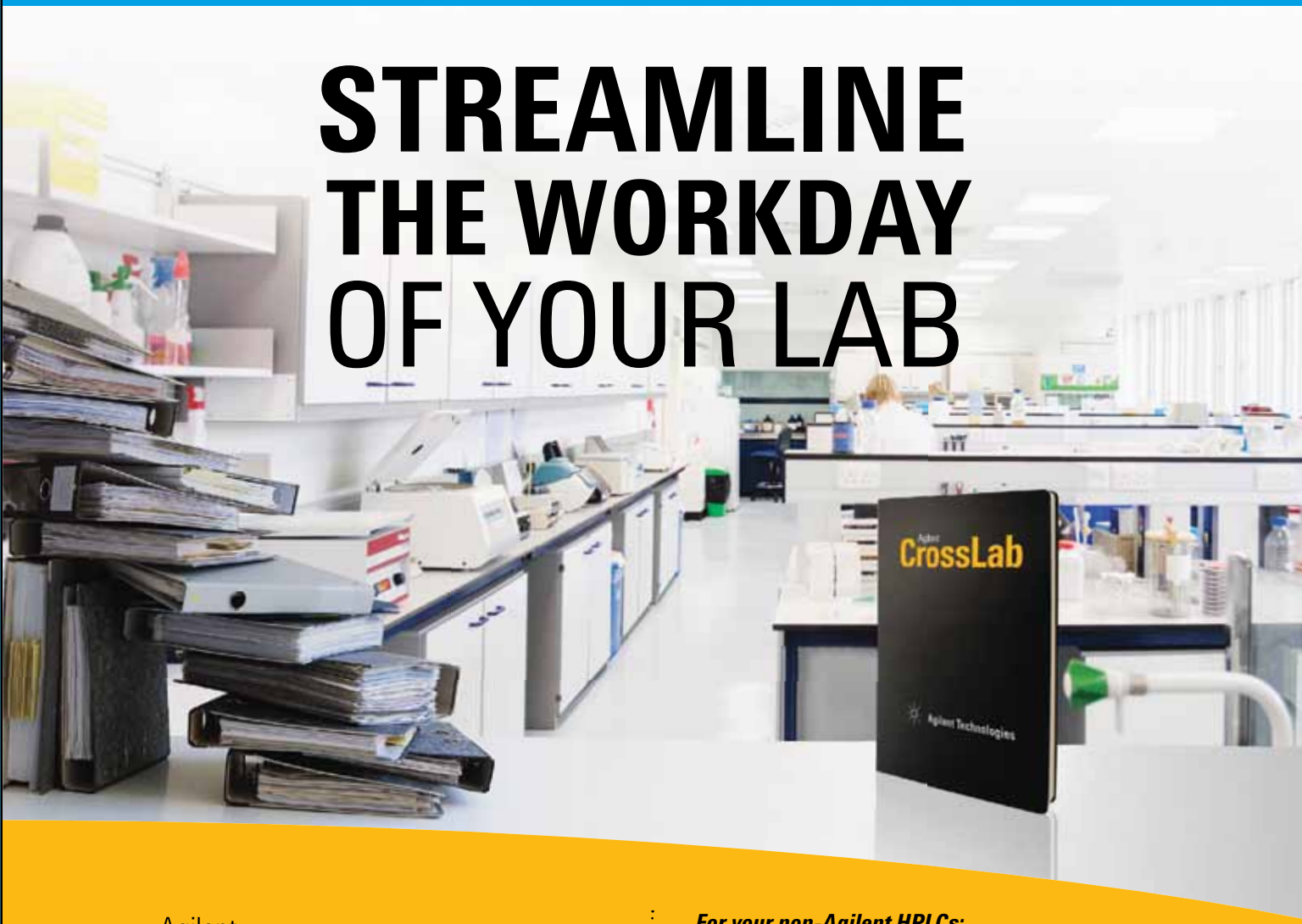

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Great Expectations

In this month's cover story, author John Borchardt describes the changes that have taken place since 2008 in priorities for hiring new laboratory employees. Most significant is that today's employers, rather than hiring newly graduated scientists and allowing them the time to master the required skills, "expect new hires to begin making meaningful contributions almost immediately." The reason is that the time and training required to get that new graduate up to speed are luxuries that most cannot afford. "In 1979 young workers received an average of two and a half weeks of training. By contrast, a study last year by the consulting firm Accenture found that only 21 percent of the employees surveyed had received any training at all in the past five years," says Borchardt. The same trend is reflected in this month's Salary & Job Satisfaction survey, in which 10 percent fewer respondents said their companies provided training.

For these reasons, "A seasoned candidate who brings a wide variety of skills and experience to the table is going to have an advantage over younger candidates," says Borchardt. A sentiment likewise echoed in our Salary Survey, in which one percent of this year's respondents were under 25, while 29 percent were older than 55, "indicating that the baby boomer bulge remains alive and well in today's lab."

But lab managers still need ways to identify and retain the best and brightest employees for their labs, be they newbies or veterans. For that, our cover story offers an array of strategies, key among them is to provide a workplace that cultivates and manages talent. As Mark Lanfear tells us in his Science Matters column (page 18), "Building an environment where your talent resources feel they are valued will not only build your credibility as an employer but will also serve to attract top talent when it becomes available."

Whether looking to hire or be hired, there is good and hopeful advice to be found in this month's Management article, "Career Counseling," in which the author identifies six key competencies everyone needs in order to roll successfully with career punches and changes, the first one being: Always have a Plan B. Turn to page 24 to find out what the other five are.

As for technology, this month's issue presents trends in HPLC columns, IT for gene sequencing, mass spec, UV-Vis spec, and vacuum pumps. But if yours is a cell culture lab, our INSIGHTS supplement this month explains all aspects of this burgeoning area. "Although cell culture is more than 100 years old, it has only been applied to the manufacture of biological drugs for about 25 years. Today mammalian cell culture is the workhorse production platform for most of biotech's protein therapeutics and increasingly for cell- and virus-based vaccines," says author Angelo DePalma. This removable supplement, which covers workflows and facilities, equipment, cell culture media, and contamination, will be a welcomed resource for anyone working in this field.

Separate from INSIGHTS, but cell culture-related, is our Technology & Operations article, "Preventing Cell Death" (page 38), which describes an ultrapure water system that lowers endotoxin levels below the limits necessary to propagate cell lines or cell cultures.

Whether running a cell culture lab, hiring new employees for any kind of lab, looking to advance your career, or purchasing equipment, we've got you covered.

Enjoy.

Pamela Ahlberg
Editor-in-Chief

Correction: On page 66 of the September issue, we misidentified BioTek Instruments headquarters as Princeton, New Jersey when the correct location is Winooski, Vermont.

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NEW AND MULTI-FACETED HIRING STRATEGIES LAB MANAGERS NEED IN THEIR ARSENAL

by John K. Borchardt

Since the end of the recession, the war for talent has raged anew in some laboratories. Laboratories in the petroleum, minerals, biotechnology, and other industries are actively recruiting experienced scientists, engineers, and technicians. However, simply screening large numbers of résumés will not enable your laboratory to win the talent war and hire the best candidates. This is because the war for talent is not the result of an overall skills shortage but rather a shortage of job candidates having the right combination of advanced skill sets laboratory managers require.

When advertising positions, guide candidates to your firm's website, where they are required to answer a series of questions pertinent to the job opening. Then look only at those candidates who were able to answer every question. By using well-chosen questions, you will winnow down the candidate pool to those individuals who have the combination of skills you need. You could also throw in some behavioral questions to help weed out candidates.

"Advertise openings on your firm's website and on specialized websites focused on science job openings.

Job openings posted on the major job boards are likely to prompt hundreds of responses, including many from individuals unqualified for the specific opening you are advertising. (Individuals post in the hopes that your laboratory also has other openings for which they are qualified.) Instead, advertise openings on your firm's website and on specialized websites focused on science job openings, such as the American Chemical Society's (ACS's) www.acs.org, www.thesciencejobs.com, www.sciencejobs.org, and others.

Clearly define the skills, experience, and personal characteristics you are looking for before beginning to screen résumés. Another challenge for human resources representatives and hiring managers is that job hunters attempt to game the system by including in their résumés keywords taken from job postings. This can add greatly to the number of false positives ("hits") that occur when searching résumé databanks for particular skill sets.

Find passive candidates. These are individuals who are not actively job hunting but would make good candidates. Use online professional networks such as LinkedIn to find them. Observing how they interact with others on discussion boards can give you insights into their professional behavior, work ethic, and how they interact with others.

Since the recession began, priorities for hiring new employees have changed. With the slow economic recovery, these new priorities remain the same. Just because the pace of hiring scientists and engineers remains lower than at prerecession levels does not mean that new employee hiring is any less critical. Talent recruitment and management remain important priorities for companies and organizations in both developed and emerging economies. However, while the priority has remained high, expectations for new employee accomplishments have risen. This is as true for laboratory hiring as it is for any another sector of economic activity.

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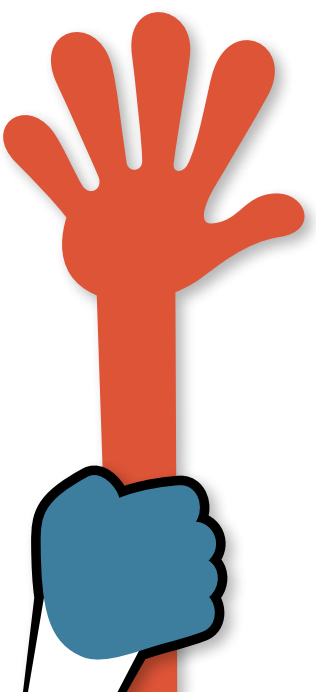
Employer expectations

"Today employers are no longer looking for a great brain and a world of potential," comments David G. Jensen, a recruiter specializing in the biotechnology industry. "They're looking for that one CV that lists the skills they need right now—not after six months of training." Jensen calls this "pinpoint hiring."[1]

My experience as an ACS career consultant has led me to conclude that the same is true for laboratories in other industries. Employers expect new hires to begin making meaningful contributions almost immediately. No longer are they allowed months to master responsibilities and "learn the ropes." These higher expectations have changed the patterns of hiring, particularly for scientists. For decades many laboratories, particularly those at large companies, preferred to hire newly graduated scientists rather than seasoned professionals. New graduates were presumed to have mastered the new technologies in their field and the latest in information technology. Operating under this assumption, employers were willing to grant new hires time to master the complexities of working in an industrial R&D environment.

This is no longer the case. In some countries, particularly the United States and Germany, companies prefer to hire older, even previously retired people to provide the talent they need. Familiar with industrial workplace culture, these people are better able to rapidly begin making contributions to meeting their new employers' goals. According to a June 2012 study by recruiting/outplacement firm Challenger, Gray & Christmas (CG&C), those people 55 years of age and older accounted for 69% of the total U.S. job growth since January 1, 2010: 2,998,000 jobs.[2] The reason? "A seasoned candidate who brings a wide variety of skills and experience to the table is going to have an advantage over younger candidates. For employers, one experienced candidate is worth two or three younger, greener candidates in terms of the ability to make immediate and meaningful contributions to output and the bottom line," says CG&C Chief Executive Officer John Challenger. Others have cited an institutional gap between the skills companies need and those being provided by the U.S. educational system.

> "Job hunters attempt to game the system by including in their résumés keywords taken from job postings."



Pinpoint hiring

Professor Peter Capelli of the University of Pennsylvania's Wharton School of Business has observed that managers want to hire "people who already have done the exact job they're applying for." Instead, Jensen has written, "For years there's been a big divide between the kind of people companies want to hire and the kind of people they see when they start running ads.[1] This makes life difficult for hiring managers, because personnel training budgets have been cut. "In 1979 young workers received an average of two and a half weeks of training. By contrast, a study last year by the consulting firm Accenture found that only 21% of the employees surveyed had received any training at all in the past five years."

Flexible work schedules and other arrangements can help lure these seasoned specialists to work in your laboratory. These include part-time employment, seasonal employment, opportunities to work out of a home office, and other options not traditionally found in laboratory work environments. A recent survey by Harris Interactive indicates that only 24% of Fortune 1000 companies provide such options. Doing so could give your laboratory a significant advantage in the talent war.

"Almost 38,000 ACS members are more than 60 years of age; they constitute 23% of the membership and are the fastest-growing demographic in the society," notes George Heinze, chair, ACS Senior Chemists Task Force.[3] "More than 18,000 of these members are still working full time. A large number of the others are engaged in part-time work such as consulting, contracting, and teaching." Many who lost their jobs during

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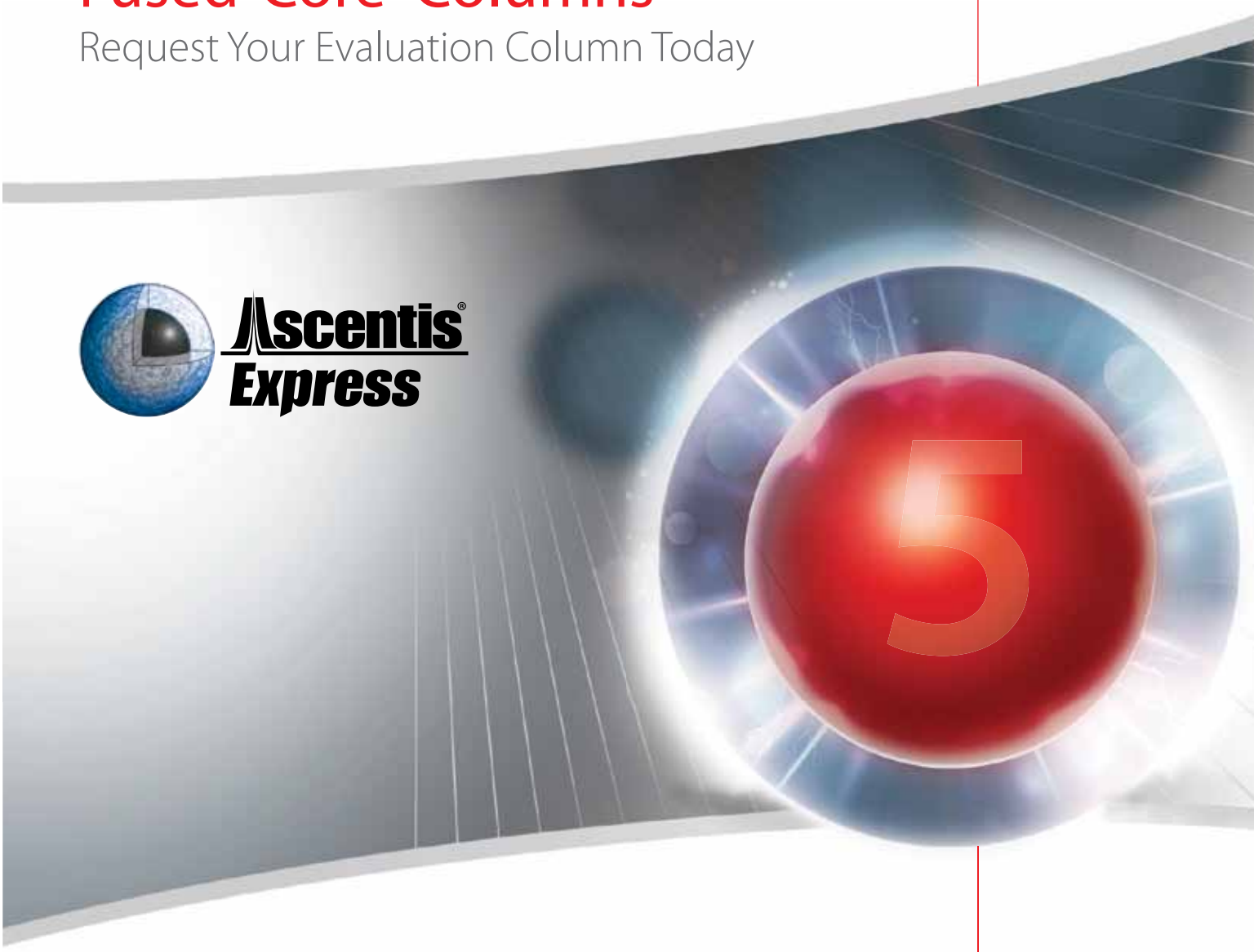

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the recession remain in the job market. These chemical professionals constitute a large and capable segment of the laboratory workforce that employers can tap. For a variety of reasons, older laboratory professionals have an increased interest in remaining in or rejoining the laboratory workforce.

Other ways to find seasoned employment candidates

Excellent seasoned job candidates often have the skill sets that laboratory managers need plus good judgment in using these skills. There are several ways to narrow down your search for seasoned employment candidates with particular skills. One is to use LinkedIn. Another is to use web-based services that perform candidate searches for you. YourEncore offers employers searches of its database of retired scientists and engineers. Individuals are usually hired on a project-by-project basis, with YourEncore acting as a staffing agency, which is the employer of record and handles salary and benefits administration. Other retiree employment websites include AlumniInTouch, SelectMinds, and RetiredBrains.

One can also take a more traditional route and use a recruiter to identify seasoned employment candidates.

"Older laboratory professionals have an increased interest in remaining in or rejoining the laboratory workforce."

Outsourcing instead of hiring

One strategy to tap the capabilities of seasoned scientists and engineers is not to hire them as employees at all. Instead, consider outsourcing work to seasoned scientists and engineers working as consultants. Seasoned employees are increasingly interested in starting their own businesses. In fact, according to the Kauffman Foundation, from 1996 to 2011 the number of baby boomers starting businesses increased by nearly 7%, the largest increase among all age groups.

"There is a wide range of individual, economic, and societal benefits for baby boomers starting new businesses," says William Zinke, 85, founder and president of the Center for Productive Longevity. The ACS has launched its ACS Entrepreneurship Initiative[4] to help its members launch their own businesses. Currently there are two programs. The Entrepreneurial Training Program is a partnership with the Ewing Marion Kauffman Foundation's FastTrac program. It offers three programs to meet the needs of members at different stages of their entrepreneurial plans. Whether you're just starting out or you're an established entrepreneur looking to optimize your venture's performance, members can apply to receive a $500 scholarship toward a 30-hour FastTrac course. Companies wishing to help seasoned employees start their own companies and become suppliers of services after their formal retirements could award them scholarships.

In June 2012 the new ACS Entrepreneurial Resources Center enabled approved applicants to support the development and launch of their entrepreneurial plans with free access to all ACS journals and Chemical Abstracts Service's SciFinder. Successful applicants can also use the professional services of ACS's legal, marketing, finance, human resources, information technology, and other outside support teams at low or no cost. However, to do so applicants must provide business plans indicating how their nascent businesses will create U.S. jobs for chemical professionals.

Another strategy is to reduce the need to recruit new employees by persuading seasoned employees approaching retirement age to delay full-time retirement by offering flexible work arrangements, such as less-than-full-time work schedules. Other possible inducements could include a sign-on bonus to work for a specified period past traditional retirement age and appealing duties such as mentoring younger employees. It is important to schedule discussions of these options two or more years in advance of a staff member's retirement. Given the large-scale staff reductions that have occurred at many laboratories during the recession, it is important to set these discussions in a positive context and make the incentives to delay retirement attractive.

A third strategy to reduce the need to hire additional employees is practicing open innovation[5] by licensing technology or acquiring development ideas from other companies. Open innovation is based on the idea that "competitive advantage now often comes from leveraging the discoveries of others," according to Henry Chesbrough, director of the Center for Open Innovation at the University of California, Berkeley.

Final comments

Old or young, job candidates respond to a workplace that promises to help them cultivate and use their talents. This means that laboratory managers need to develop different and more powerful talent management strategies.

Additional methods of finding qualified candidates are found in reference 6. Practicing several of the approaches discussed above is more effective than is focusing on only one. It seems likely that in the future laboratories will practice several hiring strategies rather than focus primarily on hiring bright young graduates and postdoctoral researchers.

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CONFLICT AND DISAGREEMENT ARE NOT ALWAYS BAD

IN FACT, THEY ARE ESSENTIAL TO HIGH-PERFORMING WORK TEAMS

by Merge Gupta-Sunderji, MBA, CSP

You likely have people in your lab who are responsible for different tasks, each of which is important. The real power however comes when you can get your people to work in synergy, to combine their individual skills and strengths to form a single cohesive unit that is greater than the sum of its individual parts. Challenges can arise though when your people don't always get along well with one another; which may lead you to think that as a leader, you should create harmony and agreement. Wrong! In reality, conflict is actually a good thing; your ultimate goal as a leader is to create an optimum balance between consensus and conflict—you want people to get along with one another, but you also want them to speak up when they need to, even if their message is unwanted or controversial.

In 1974, Dr. Jerry Harvey and three other family members embarked on a 53-mile road trip to Abilene, Texas in a 1958 Buick without any air-conditioning. Not only was the temperature over 100 degrees, but the entire drive was through a dust storm! It was only when they returned home at the end of the day that they discovered that nobody actually wanted to go to Abilene, Texas. It turned out that each person only agreed to go because they thought the other people really wanted to go. Dr. Harvey said later: "Here we were, four reasonably sensible people who, on our own volitions, had just taken a 106 mile trip across the godforsaken desert in furnace-like temperatures through a cloud-like dust storm to eat unpalatable food at a hole-in-the-wall cafeteria in Abilene, Texas, when none of us really wanted to go! In fact, to be more accurate, we had done just the opposite of what we really wanted to do." Today, this "Abilene Paradox" is used to describe any communication breakdown situation in which members of a team don't want to "rock the boat." In their desire to minimize conflict, each mistakenly believes that his or her own preferences are counter to the team and therefore does not raise any objections. The danger of the Abilene Paradox of course is that alternative ideas or viewpoints are not fully and critically evaluated.

Now you might think that the Abilene Paradox couldn't happen in your lab; after all, you are all experienced professionals who have been trained to be fair, unbiased, and open-minded. But this phenomenon isn't as unusual as you might think. If you are married or are in a committed relationship, have you ever ended up doing something you didn't want to do simply because you thought your spouse or significant other wanted to? Be honest! I think it is very likely that at least once or twice, you've taken a certain course of action, only to discover later that neither of you wanted to do that activity, but you both went along with it because you thought the other one wanted it. The Abilene Paradox can happen in your lab! And that means that it's your job to prevent it. If you want a high-performing team, you need to create an environment in your laboratory where healthy conflict is welcomed and encouraged.

*Leadership expert **Merge Gupta-Sunderji, MBA, CSP,** turns managers into leaders. Over 50,000 managers in eight countries have participated in her engaging and entertaining keynotes and workshops. With more than fourteen years of leadership at one of Canada's most respected oil and gas companies, Merge speaks from first-hand experience. She's an award-winning author of numerous articles, books and audio programs, and in November's webinar, she'll not only tell you about the other characteristics of high-performing teams, but will also give you specific and practical tools that you can use to build your own high-performing lab teams. Learn more about Merge and her leadership development practice at www.mergespeaks.com.*

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COMPETING FOR GOLD MEDAL TALENT: IT TAKES A STRATEGIC AND TACTICAL APPROACH

By Mark Lanfear

For two weeks the 2012 Summer Olympics held the attention of audiences across events in well-known—and not-so-well-known—sports. In more familiar competitions such as gymnastics and swimming, spectators largely understood the high stakes because of the year-round popularity of these events. But while the more obscure events might have been entertaining, how often do we really think about what it takes to win at track cycling?

Unfortunately in the world of business, whether it's in the sciences or any other large global industry, managers don't have the luxury of being able to sit back, analyze the workplace every four years, and understand just a portion of what's going on in the competition. This is especially true in the war for talent, where the best people will be harder and harder to come by, and competing for their loyalties is already turning into a complex feat requiring both brawn and brains.

The talent "Olympics," in fact, happens every day, and hiring managers must be able to uniquely compete in this battle on every front as technology, social media, and an increasingly diverse workforce pose extreme challenges for finding and retaining the right people. As in the Olympics, we are seeing the bar raised and "world records" being broken every day.

There are obviously some key areas in the talent war where all serious competitors need to excel. Start with where you are now. You probably have some world-class talent on your team now, but too often companies neglect opportunities for internal training and development. Recent studies have shown that those in highly technical fields, such as science, and even those at the tops of their games place a premium on being able to develop skills on the job. If current colleagues and consultants don't get these opportunities from their current employers, studies also show that they are certainly willing to go elsewhere. Building an environment where your talent resources feel they are valued will not only build your credibility as an employer but will also serve to attract top talent when it becomes available.

> "The best people will be harder and harder to come by."

Be the employer of choice, because there is nothing wrong with going to the market to find the needed world-class talent your team requires. Fine-tune your network of potential acquisitions who may be looking for their next opportunity to shine.

History has demonstrated that some of the current "best in class" talent with great experience exists in the passive market, and this can be a wise investment in your search if they truly possess the knowledge you need to take your organization to the next level. An investment here can fill the immediate gap you have in your team and get you the "gold." At the same time, don't be afraid to go after new talent, new ideas, and different experiences.

This means, don't be afraid to take risks when you're considering the younger, less experienced talent. Little bets here and there can pay off, and those who have the greatest potential and are hungry to prove themselves often don't have the most prestigious degrees to back them up. In fact, the next Steve Jobs—or any great employee—isn't necessarily waiting in the hallway of an Ivy League college or university. Make it a priority to look at schools that have newly developed programs in your areas of need, and take the chance that these new thinkers may be just what you require to help jump-start that next important project. They may be the anchor leg to the relay that puts your team on the medal podium.

While all these tactics in the war for talent have unique merits, how you go about using them may be just as important as using them at all. This is where the way you compete

for talent needs to stand apart from the crowd. Your organization's culture and goals are unique, and so must be the ways you attract and retain talent on a consistent basis. You'll need to eventually understand that no decision is ever too small for your attention when it comes to recognizing talent. Winning the talent war requires a cultural shift and team effort—not just a tactical job hunt, but a strategic and disciplined one as well. True strategic thinking, coupled with a customized action plan, is usually the missing component that could transform a good hiring plan into a culture of talent acquisition that leads to a high level of success for any corporation.

> "Too often companies neglect opportunities for internal training and development."

So know the competition—and know how to compete—but strive to be better than the competition. In 2012 we saw a number of the best individual Olympians and teams breaking their own world records, which shows us that after a lifetime of training, they're not really competing with outside forces or the person in the next lane, they're competing with themselves–to be the best now and for all time.

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THE SIXTH ANNUAL SALARY & EMPLOYEE SATISFACTION SURVEY

SALARIES STAY CONSTANT WITH SMALL GAINS IN BENEFITS REPORTED

by Pam Ahlberg

As in our previous Salary & Employee Satisfaction surveys, the results this year continue to reinforce the idea that laboratory professionals are for the most part happy in their careers and derive meaning and satisfaction from the work they do. However, there were a few surprises this year with regard to career growth opportunities. But before we get to those details, let's find out more about the participants in this year's survey.

Overview of participants

The majority of this year's survey respondents—73%—work in either industrial, clinical, or academic research facilities, with the balance employed by government, private, or contract labs. [Table 1] The largest groups of respondents are lab managers (47%) and researchers/technologists (35%), with a smaller number in academia and corporate and project management. [Table 2] Across all organizations, the primary fields of research are chemistry and biology, with the balance involved in environmental, clinical, and drug discovery work. [Table 3]

TABLE 1: Research Organization

Industrial Research Lab	28%
Clinical Research Lab /Hospital/Medical Lab	24%
Academic Research Lab	21%
Government Research Lab	10%
Private Research Institution	5%
Contract Lab	4%
Other	8%

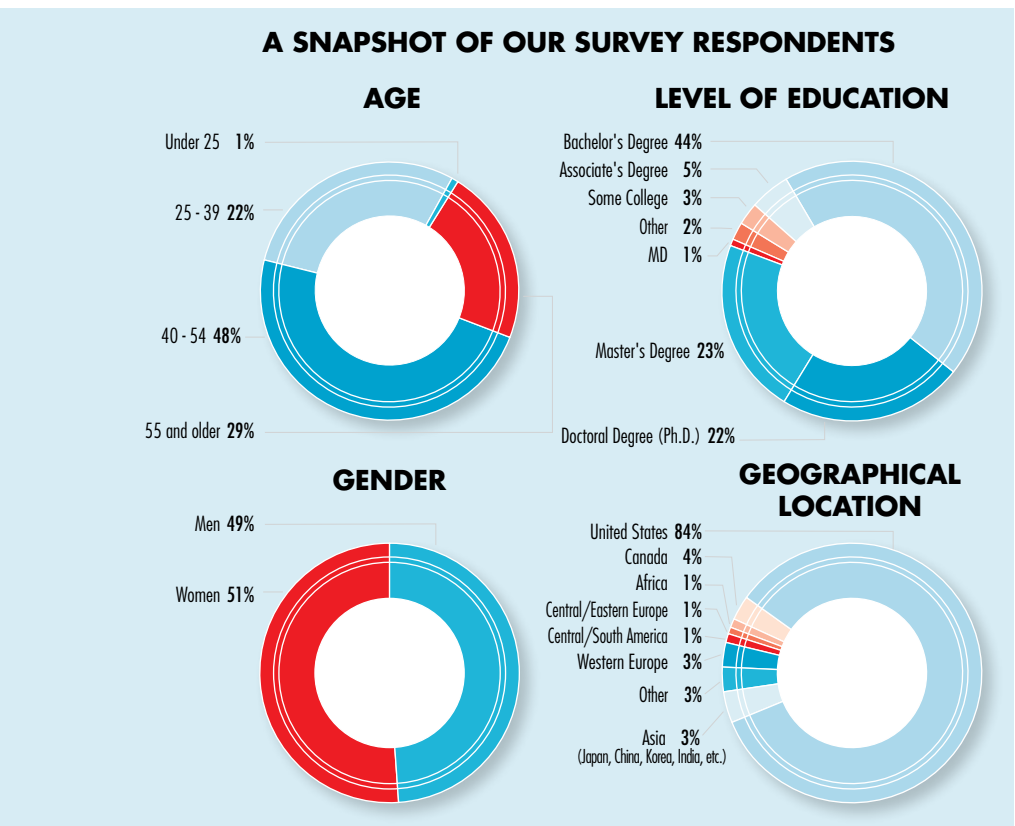

TABLE 2: Job Function

Lab Management	47%
Research Scientist	20%
Technologist/Research Assistant	15%
Corporate Management	5%
Professor/ Graduate/Postgraduate/Ph.D. Student	5%
Project Manager	3%
Other	5%

TABLE 3: Field of Research

Biology	40%
Chemistry	27%
Environmental	7%
Clinical	6%
Genomics/Proteomics	4%
Drug Discovery	3%
Other	13%

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What we have seen consistently since we began these surveys in 2007 is that longevity is the hallmark of the scientific research profession, with 48% of this year's respondents saying they have been working in the lab for more than 20 years. Compared with 42% in 2009 and 44% in 2010, there seems to be a steady increase in the over-20-year crowd and a similar decrease at the other end. This year only 1% of respondents told us they have worked in a lab for one to two years, compared with 5% in 2009. This indicates fewer new hires and aligns with the age distribution typically found within labs. [See pie chart on page 20.] One percent of this year's respondents are under 25, which is the same percentage reported in 2010. However, 29% are older than 55, compared with 25% in 2010, indicating that the baby boomer bulge remains alive and well in today's lab. In addition to longevity, loyalty to research institutions remains constant, with 22% of respondents telling us they have worked for their current employer for more than 20 years, a 6% increase over 2010.

TABLE 4: Annual salary, not including bonuses

	2012	2010
Less than $25,000	5%	11%
$25,000 - $34,999	5%	5%
$35,000 - $44,999	8%	7%
$45,000 - $54,999	14%	14%
$55,000 - $64,999	15%	12%
$65,000 - $74,999	12%	13%
$75,000 - $84,999	13%	8%
$85,000 - $94,999	7%	7%
$95,000 - $109,999	8%	11%
$110,000 - $124,999	5%	6%
$125,000 - $149,999	5%	3%
More than $150,000	3%	3%

Who's the boss?

This year we learned that 3% more respondents now had managerial responsibilities than did in 2010. And of those managers, 44% managed lab professionals only, while 35% managed both lab and non-lab employees. Exactly half of this year's respondents told us that the number of employees they managed was between one and four, while 38% said they managed between five and 24, and only 12% said they were responsible for staffs larger than 25.

Show me the money

Compared with 2010, there has been very little change in compensation. Those making less than $25,000 a year dropped from 11% in 2010 to this year's 5%, suggesting fewer new hires and more movement up the pay scale. Top to bottom, this year's results indicate compensation stability along with some modest increases. However, when it comes to bonus programs, 8% fewer respondents were participating—36% compared with 44% in 2010.

While 22% of this year's respondents said there had been significant changes to their benefits within the past year, that percentage was not any greater than what we've seen over the past two years. And when asked to explain, there were as many positive as negative comments regarding those changes. "Better health insurance," "Economy improved and bonus was higher," "Employee health insurance premiums have gone up and coverage has gone down," and "No merit or cost-of-living salary increases."

However, when asked specifically about their current employer-provided benefits, respondents identified modest improvements in the majority of offerings. Notable was a 10% increase in 401(k) matching programs. Other improvements included upticks in health, dental, vision, and long-term care insurance as well as in tuition reimbursement and contributions to pension or retirement accounts separate from 401(k)s.

Stability with less opportunity

One surprising and fairly dramatic response this year compared with 2010 was to the question of whether respondents would still be working at the same company with the same position within the next 12 months. Two years ago 41% said they agreed/strongly agreed; this year that number increased 33 points to 75%. This seems to indicate that two years ago lab professionals were less certain about their futures within their organizations—still feeling the aftershocks of the 2008 financial crisis perhaps. But this year's data suggests that while jobs might be more secure, the opportunity for growth or promotion has decreased. This same possibility is also indicated by answers to the question of whether respondents would be working at the same company *with a job promotion* within the next 12 months, to which 12% fewer agreed/strongly agreed and nearly 17% more *disagreed/strongly disagreed.* But despite what appears to be fewer growth opportunities within their organizations, nearly 12% fewer respondents said they would be leaving their current positions within the next 12 months than did in 2010. Different question, but the same answer when 25% more respondents this year *disagreed* with the statement "Within the next 12 months I will be working somewhere else in the same profession."

Training and career development

There was almost no change this year in respondents' answers to questions concerning job training and career development. In fact, when asked whether they felt their experience and skills were adequate for their current positions, 93% answered in the affirmative, the exact same percentage as in 2010.

TABLE 5: Within the next 12 months I will still be working at the same company with the same position.

	2012	2010
Strongly Agree	48.0%	12.2%
Agree	26.8%	29.2%
Neutral	10.9%	22.6%
Disagree	4.7%	17.6%
Strongly Disagree	5.9%	10.3%
Don't Know	3.8%	8.1%

TABLE 6: Within the next 12 months I will still be working at the same company with a job promotion.

	2012	2010
Strongly Agree	7.0%	7.9%
Agree	12.3%	23.8%
Neutral	22.4%	27.7%
Disagree	21.4%	20.5%
Strongly Disagree	27.4%	11.7%
Don't Know	9.6%	8.4%

TABLE 7: Within the next 12 months I will be working somewhere else in the same profession.

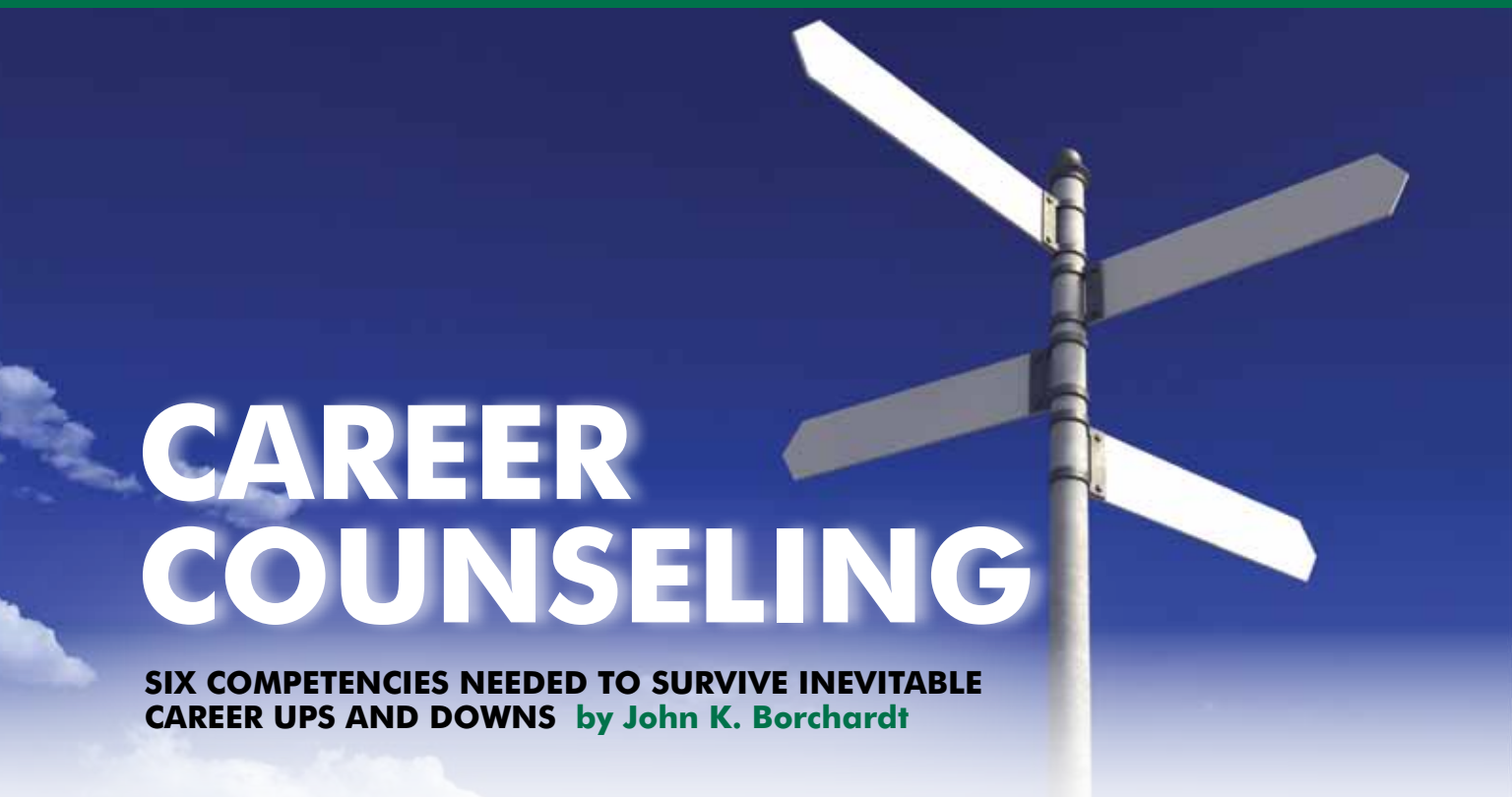
	2012	2010
Strongly Agree	4.6%	8.1%
Agree	9.4%	17.5%
Neutral	19.5%	30.7%
Disagree	24.7%	21.9%
Strongly Disagree	31.4%	9.6%
Don't Know	10.4%	12.2%

However, somewhat notable were responses to the statement, "This organization provides training or experiences to help me explore other opportunities within the company," to which 10% fewer said they agreed/strongly agreed than did in 2010. This reinforces the earlier suggestion that there are fewer career growth opportunities in today's research facilities.

Despite that, this year's survey paints a picture of general stability within the scientific research community, with no dramatic changes in compensation, benefits, or job satisfaction. That labs remain populated with more middle-aged and older employees remains a constant and something we will continue to pay attention to, begging the question of who will replace the baby boomers when they finally hit retirement age. Stay tuned.

If you participated in this year's Salary & Employee Satisfaction Survey, thank you. We look forward to returning to this important topic a year from now and will be counting on your participation.

FOR COMPLETE SURVEY RESULTS, go to:
www.labmanager.com/labmanager/downloads/Magazine/2012salarysurvey



CAREER COUNSELING

SIX COMPETENCIES NEEDED TO SURVIVE INEVITABLE CAREER UPS AND DOWNS

by John K. Borchardt

American Chemical Society (ACS) experts have concluded from ACS member surveys that members can expect to hold several jobs during the courses of their careers. These may be for a single employer but are more likely to be for several. The same is likely true of other industrial science and engineering careers. The era of the one-company, 40-year career is over. The employment world has changed dramatically in other ways as well. Hot technical specialties can "cool off" quickly.

To succeed in this constantly changing career environment, it is best to focus on six lifelong competencies that are transferable from one job to another and from one career to another. These are:

- Have a long-term perspective on your career. Maintain your skills even in areas in which you are no longer active.
- Satisfy your customers' ever-changing needs.
- Become and remain a creative, effective, and efficient problem solver. This requires developing critical-thinking skills.
- Develop a global perspective. This means developing cultural understanding and sensitivity. Mastering a second language can be a tremendous aid to career development.
- Become and remain motivated and persistent in the face of challenges.
- Live a healthy and balanced life. This is often essential to both career success and personal happiness.

Let's look at each of these competencies more closely.

Have a long-term perspective

Business and technology needs will change many times during the course of your career. Understanding these needs will enable you to remain flexible and successful. For example, during the mid-1980s the price of crude oil dropped sharply and remained low for more than a decade. In response, the oil industry cut R&D employment sharply. Some flexible scientists and engineers applied the technology they had learned to environmental remediation and continued to have successful careers, albeit in the environmental industry not the petroleum industry.

> "The era of the one-company, 40-year career is over."

Sometimes it can also pay to look back as well as forward. For example, a decade ago crude oil prices began rising again. The technologies I mastered during the 1980s became relevant again and extended to new areas such as producing oil and natural gas from low-permeability shale. I had never lost my interest in these technologies and today they constitute a major portion of my consulting business.

"Always have a Plan B," former ACS president Helen Free advised ACS members. A Plan B is a secondary course of action should unforeseen changes make your primary career plan outdated. Having a Plan B prepared provides peace of mind in uncertain times. Your Plan B provides focus and a sense of purpose should you be forced to change the direction of your career or you decide to do so voluntarily.

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For instance, I implemented a Plan B in 2004 when my employer closed its Houston laboratory and gave me an involuntary job transfer to a laboratory 1,000 miles away. I saw this possibility coming and had previously developed a plan to become a self-employed consultant and technical writer. Consequently, when my employer announced I would need to relocate to keep my job, I was prepared to implement my Plan B. I had already lined up consulting clients. My last day of employment was on a Friday and I began working on my first consulting project the next day.

Satisfy your customers' ever-changing needs

Your customers may be consumers or other companies that buy your firm's products or services. They may also be people working for your own firm who use the results of your work. Customers have constantly rising expectations for cost effectiveness, usually combined with lower prices.

This means making continuous small improvements in your firm's products and services as well as trying to find the next major innovation. As Ben Franklin noted, "Watch the little things; a small leak will sink a great ship." In Japan, this process is called kaizen and is the basis of the "economic miracle" that created the country's economic boom in 1980.

"Having a Plan B prepared provides peace of mind in uncertain times."

Achieving and maintaining customer satisfaction requires a process of innovation through team-oriented collaboration. This means you have to "focus on the thinking of your most forward-looking customers," according to consultant Bradford Goldense, president of Goldense Group, Inc. Business and career success often means going beyond this and understanding your customers' technology so well that you can visualize improvements that they do not. They often view their operational problems and limitations as "facts of life" they have to live with. If you can design a process or product that overcomes those problems or limitations, you can often win new business for your firm from both existing customers and companies that currently don't buy your products.

Become and remain a creative, effective, and efficient problem solver

This means developing "critical-thinking skills." This vague term involves questioning assumptions. For example, the assumption of customers that a problem is unsolvable and just something they have to live with. Critical thinking during problem solving also involves clarifying goals and evaluating evidence. This thinking is then used to develop an action plan. Critical thinking continues through assessing your conclusions when you think you have solved the problem.

Being willing to take calculated risks is essential in solving problems. Use your critical-thinking skills to reduce the risks you must take and then forge ahead. Goldense notes, "Innovation and risk are almost synonymous." President John F. Kennedy once said, "We should not let our fears hold us back from pursuing our hopes."

Every company occasionally encounters a major problem. When this occurs, don't find fault with others. Don't play the "blame game." Instead, find a remedy. The effort involved in finding and punishing a culprit is usually better employed in solving the problem and making sure it can't happen again.

Develop a global perspective

A global perspective is increasingly necessary for small and midsized businesses as well as large companies. This means you need to develop an understanding of the cultures and business practices of the organizations your firm does business with and sensitivity to their different perspectives.

Becoming fluent in languages other than your own is becoming increasingly important for career advancement. For example, a graduate school friend of mine, a native-born American and research chemist with Eastman Kodak, spoke Chinese. He was chosen by his employer to open up a lab in the People's Republic of China. Another graduate school friend spoke German very well. When his firm was acquired by a firm located in the German-speaking area of Switzerland, he was soon asked to employ his language skills as the American spokesperson in his employer's business and R&D meetings. He often went on business trips to Europe and had extended assignments at its global headquarters. His last position was executive vice president of research.

"Being willing to take calculated risks is essential in solving problems."

The United States is increasingly becoming a multicultural society. This means your employer is more likely to be marketing to consumers with different cultural backgrounds and to companies that employ women and minorities in influential positions. This requires you to have cultural sensitivity to people whose cultural perspectives are substantially different from yours.

Become and remain motivated and persistent

If necessity is the mother of invention, then persistence is its father. Being an effective problem solver often means being persistent. Benjamin Franklin, no mean inventor himself, said, "Energy and persistence conquer all things." Expressing the same idea somewhat differently in *Poor Richard's Almanac*, Franklin wrote, "Little strokes fell great oaks."

Perhaps the world's most prolific inventor, Thomas Edison's persistence in developing the incandescent light bulb is widely known. This was far from the only time he demonstrated persistence in his laboratory. He and his team performed 50,000 experiments to perfect the alkaline battery.

Actively manage your career

Your most important business is your own career. Take responsibility for it. This means reevaluating your career options as you progress in your career. Taking responsibility will help you identify exciting Plan B opportunities. A formal career plan that takes into account major life changes such as retirement from a full-time job is very helpful.

Seek out mentors and role models. They can help you navigate challenges and assess options at all stages of your career.

Don't be afraid to do something different. For example, after spending 13 years working on various aspects of oil field chemistry, my then employer killed most of its oil field chemistry R&D programs in response to low oil prices. Rather than remaining in oil field technology, I exercised a Plan B strategy and moved into paper recycling chemistry–a rapidly

developing area, as paper recycling was growing substantially in the 1990s. Moving into this area and successfully developing new products to deal with problems in removing ink from pulped wastepaper and solving other paper manufacturing problems was exciting and mentally stimulating.

"If necessity is the mother of invention, then persistence is its father."

However, I also continued keeping up with the literature in oil field chemistry. This was my Plan B. I actively moved back into this area when the field revived about a decade later. Currently, most of my consulting work is working with clients to solve oil production problems.

And now for something completely different

Doing something completely different may involve moving out of the laboratory completely. Some lab managers, particularly at junior levels, move into business management positions for their companies. Another example: foreign language proficiency can be the basis of a second career as a translator. The combination of scientific knowledge, industry experience, and mastery of a foreign language is a highly valuable skill set. Translation requires excellent writing skills in both languages. Translators usually specialize in one area: medicine, science, engineering, legal, etc. The choice of language is important. Those skilled in languages mastered by many American scientists such as German, French, or Spanish often are not able to charge as much

for their services as can those who are proficient in useful but less commonly mastered languages such as Japanese and Russian. Those proficient in the languages of countries with rapidly growing economies such as China (Mandarin) and Brazil (Portuguese) can expect a growing demand for their services.

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

"Your most important business is your own career."

Holding professional certification as a translator from an organization such as the American Translators Association is often important in being hired as a translator.

Live a healthy and balanced life

A healthy and balanced life is essential to having an enjoyable career. This means finding the appropriate balance between your career and your personal life. This balance often changes as you progress in your career. For example, an unmarried graduate student or young scientist may be quite happy with a life spent predominantly working in the laboratory and having few outside interests. However, this balance may change should our young scientist get married and have children. It may also change as the scientist becomes active in professional societies or an engrossing hobby. The key is to find a balance that works for you at any given time and to adjust that balance should your needs and interests change.

THE CHALLENGES OF HIGH PERFORMANCE COMPUTING

THE NEED FOR STORAGE AND MANAGEMENT IS MORE PRESSING THAN DATA GENERATION

by Bernard Tulsi

Research laboratories are expected to deliver high performance computing (HPC) systematically and reliably to keep pace with the unprecedented levels of computation, storage arrays, and networking switches researchers require to gather, evaluate, and move the voluminous data they have to grapple with. The unrelenting increase in the volume of data generated in modern laboratories poses tremendous challenges for managers and directors tasked with facilitating optimal performance while simultaneously minimizing power usage by computing systems, maximizing the efficiency of their cooling processes, and maintaining energy expenditures at the lowest levels practicable—at a time when prices are at historic highs.

"There is the real possibility that local utilities may be unable or unwilling to supply the power needs of HPC data operations."

Although such challenges appear daunting enough, they also have to be addressed in an environment overlaid with a solid interest in reducing carbon footprints and where there is much greater sensitivity about the potential impact of energy consumption on climate change. Furthermore, with some HPC systems consuming as much electricity as all the residential and commercial users in a typical small city, there is the real possibility that local utilities may be unable or unwilling to supply the power needs of HPC data operations. Recent reports suggest that planners of new or expanding HPC sites, some at multi-petascale and exascale levels, may have to consider myriad power options—even the deployment of small-scale nuclear power reactors are reportedly on the table—to address their energy needs.

Just a decade ago, such power issues would not have made it on a list of lab managers' top key concerns. Now, however, they are constantly listed among the top HPC challenges. Dell's HPC Global Director Tim Carroll notes that HPC has acquired heightened prominence with a corresponding increase in demand within the last decade, and acknowledges that his company, known mostly as a leading manufacturer of personal computers, is now heavily involved in HPC systems.

HPC has long been the purview of the national labs, which needed and were focused on large and powerful systems. This meant that as this sector evolved the highest end of the HPC spectrum received the most attention. Carroll notes that this did not necessarily translate into delivering more computational cycles into the hands of a greater number of researchers.

The current status in the HPC sector reflects both good news and bad news scenarios for lab managers. The good news is that because of the efforts of Intel Corporation and other processor manufacturers, the vast majority of the research community can fairly easily get enough computational power to solve their problems. "This is true for about 80 percent of the cases," says Carroll.

He points out, however, that because the computational problem has not necessarily been fully solved—it is just under control—now all the research clusters are generating data "at a torrential pace, and there is a storage explosion because the researchers don't want to get rid of any of the data."

Carroll says that some of the most compelling evidence of this issue could be seen among Dell's customers who are engaged in genomics, where a single researcher can generate one to two terabytes of data per day. Genomics researchers do not typically have a data generation problem; they have data storage and data movement problems—they have to manage immense data repositories that must be moved from one researcher to another and from one lab to another.

In a recent case, the 350-employee-strong Virginia Bioinformatics Institute at Virginia Tech addressed some of its I/O intensive and large genomic data challenges as well as its unique software and hardware requirements by deploying Dell's Power Edge C6100 servers with Intel's Xeon processors along with Intel's QuickPath Interconnect to enhance its system performance. While accelerating its research processes, the use of clusters from Dell and Intel enabled easy expansion, boosted the energy efficiency of the servers, and minimized the costs associated with power and cooling.

Similarly, The Translational Genomics Research Institute (TGen) opted to build a new HPC cluster to deal with the massive amounts of data generated by its clinical trials for neuroblastoma (one of the most common pediatric cancers). By deploying a cluster of Dell's PowerEdge blade servers and Intel's Xeon processors, TGen was able to achieve a twelvefold gain in its processing power for patient data, along with thrice the number of cores in the same floor space. The new scalable cluster initiative was capable of supporting 100 percent growth in data volume year after year and created the basis for 800 server cores to be managed by one IT administrator.

HPC is an important enabling technology for genomics/bioinformatics. In 2003, the aggregated cost to map the human genome was estimated at $3 billion, whereas today the bill for a similar undertaking could be as small as $1,000. As costs get lower, however, there is an exponential increase in the amount of data generated and in the demand for HPC capacity—data storage, immense memory capacity, and huge bandwidth connecting data repositories and computer clusters.

"Researchers engaged in weather modeling or related computer-intensive problems with lots of complex networking operations may face completely different sets of challenges," says Carroll. He adds that these are the elements that make the HPC field challenging, because there are a number of different infrastructure challenges under the umbrella of research HPC. "The bigger the laboratory and the greater the number of researchers to be supported, the greater will be the need for different types of solutions. The challenge for labs is to build the type of infrastructure that will meet the different needs of a number of researchers and in the face of tight budgets ensure that this is done in a way that focuses on supporting the researchers and not necessarily on solving infrastructure problems alone."

"In 2003, the aggregated cost to map the human genome was estimated at $3 billion, whereas today the bill for a similar undertaking could be as small as $1,000."

"One of our key capabilities is to quickly get together with lab management teams to assess the budget of the system—this is not just financial; it also includes power, space, cooling, and staffing," he says. "Once we understand those parameters it becomes easier to design and shape the right system, with the key requirement being whether it is usable for the researcher in addressing the problems at hand."

He says that once the equipment is agreed to and ordered, one key question is whether it is in place and running science in six weeks or six months. "And once it is there, does it just run so people don't have to think about it because it is stable and reliable and integrates well with the other aspects of the lab, or is it is like a finely tuned race car that is down half the time because of inappropriate architecture for the situation in which it must function?"

Carroll says that one important piece of advice he would give lab managers who are not experienced in procuring and managing these systems is never to tell researchers to request what they need and then take on the task of sourcing the systems without the involvement of the researchers who will be using them. "It will be much better and smoother if the people supporting these systems are a part of the process from the beginning and throughout."

Reflecting on how the sector has evolved, Carroll says there was a time when there were both HPC systems and commercial data centers. "Because the HPC needs for the supercomputers were so specialized and the power and cooling requirements were so different from traditional needs, they had to be separated.

"What has happened over time and has certainly accelerated over the last two or three years—with the growth of HPC and the shrinking of budgets to support these initiatives—is that traditional systems and HPC are moving to the same data centers. That is step one," says Carroll.

Eventually, he says, whether it is the next five or ten years, it will be possible to move workflows such that it can be decided at any given time what portion of the system is configured as HPC, what is serving up web capabilities, and which part is performing key functions. "This is the only way to get greater efficiency from the data centers, and it is not about money; it has to do with the fact that a lot of them are out of data storage space," says Carroll.

"Traditional systems and HPC are moving to the same data centers."

So the challenge is to be more efficient with the available space, according to Carroll. Current dynamics in this area are forcing an examination of how the same infrastructure could be used for multiple purposes and become more efficient. He says federal labs do not have budgets for additional buildings, which could take as long as ten years to construct and make operational anyway, while cash-strapped state labs do not seem to have much hope of accessing funding for new construction projects.

Any growth seems to be on the commercial side, especially in biology, genomics, and proteomics. "In fact, what we are seeing there is that rather than building conventional data centers there is a rapid adoption of containers or pods, which are totally self-contained from an environmental perspective, with complete capabilities installed on a concrete pad rather than in a building. It produces unbelievable efficiency from a power consumption perspective, using a far smaller footprint than would an entire building, without losing any functionality on the computer side."

Interestingly, according to Carroll, the sixty-second-largest supercomputer in the world was deployed by Dell last year at the University of Colorado. "It was in a container, not a data center; [there are] two metal containers sitting at the side of a building in Colorado."

"These pods will play an important role in raising efficiency. Most data centers are inefficient, with 15 percent to 20 percent of the power going into the building but not making it to the computers. A lot can be done to reduce carbon footprints just by making data centers more efficient.

"Our vision of HPC is that it should be analogous to GPS, a highly advanced technology that is being put to a number of everyday uses. Five years from now we should be able to make it easier for lab managers to deploy these systems for their researchers—we are not there yet, but the goal should always be to make it easier for more people to access this technology," says Carroll.

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

PUSHING DESIGN BOUNDARIES

FIVE TRENDS IN LABORATORY PLANNING & CONSTRUCTION THAT WILL IMPACT FUTURE RESEARCH FACILITIES

by Steve Copenhagen, LEED AP

The King Faisal Specialist Hospital and Research Center is an 894-bed multi-facility, multi-entity tertiary care hospital and one of the leading healthcare institutions in the Kingdom of Saudi Arabia. Image Credit: Cannon Design

The past 20 years have seen an explosion in laboratory construction as academic, pharmaceutical, biotech, and high-tech companies have increased the level of research and development in their respective fields. The design of these laboratories has evolved dramatically as architects and engineers have responded to the growing requirements of the research community. Here are five trends in laboratory planning and design that will impact every research facility.

Increased support equipment

The increase in laboratory support equipment has created a demand for increased space in labs. More analytical equipment—mass spectrometers, high-performance liquid chromatographs, X-ray refractometers—has become readily available and even commonplace in research. Bench space is at a premium as these pieces of equipment occupy a greater percentage of the lab area. Most labs were never planned for this quantity of equipment and, unfortunately, many newly constructed labs aren't either.

The growth of analytical instrumentation has added to the data storage and computational needs of labs as well. Personal computers and the network servers required to connect them create additional space demands at the benchtop and require dedicated server rooms. Building data cabling is constantly under pressure to provide the fastest and broadest network systems with high-speed connections all the way to the benchtop.

Advances in robotics will increase lab productivity and efficiency but will place further strain on available workspace. Already, robotic samplers and pipetting equipment are in fairly common use; new applications of robotic technology will cause lab planners to be yet more adept at spatial organization.

Support cores such as an imaging core, an omics core, or a characterization core are one design strategy that can begin to alleviate the space crunch. A support core is a centralized space containing equipment that may be shared by two or more research groups. Typical equipment in support cores are electron microscopes, mass spectrometers, or genetic sampling analyzers. Within a single lab, these types of instruments are not typically utilized at their full capacity—but when shared by multiple groups, they operate at a higher level of use. The support core also reduces space problems within individual labs and increases the utilization of these expensive instruments.

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Cores also can be established with a dedicated technician who provides technical and operational expertise of the instruments. This expertise is critical since instruments are constantly evolving both in software analytical tools and detection hardware. To increase the utilization of the instruments, the technician can provide instrument analysis as an in-house service and as a for-fee service to out-of-house users. Technicians also provide training on and maintenance of the instruments.

Space flexibility

Laboratories are not static. Over time, the research being conducted will change as will the research necessity. In most cases, gutting a lab and starting from scratch is not financially feasible. Flexibility in the original planning and design is a key strategy for accommodating change and growth.

At the most basic level, dimensional modularity allows labs to be reconfigured in the most cost-effective manner.

Flexibility also extends to mechanical systems. With the initial cost, lab mechanical systems can comprise up to 50 percent of the total construction cost, and later modifications to the mechanical system can be extremely expensive and disruptive. Flexibility in mechanical systems can be achieved by providing shafts, vertical space, and mechanical rooms that can be expanded in the future. The designer must right-size the building aspects that cannot be changed—floor-to-floor height, the structural grid, floor loads—in such a way that mechanical systems can be adapted to new requirements.

Building codes and safety guidelines

Building codes and guidelines, of course, provide for the safety of occupants. In the comparatively risky environment of the laboratory, more stringent codes are applied. And yet many of the provisions of laboratory building codes have been in place for decades and may not reflect modern safety advances. The lab designer should ask whether alternative safety methods might meet the intent of the codes; to do so will require close consultation with local authorities that have jurisdiction.

Energy/Sustainability

Energy efficiency and conservation, as in every building type, has become an important consideration in laboratory buildings. Laboratories are very dense energy consumers. To a greater degree than in most buildings, most of a laboratory's energy is consumed by mechanical and electrical systems.

To provide a safe working environment, laboratories have used the concept of high air-change rates to flush out any dangerous chemicals. This large volume of air is exhausted and not recirculated as is typical in non-laboratory environments. Designers work with the codes, safety officials, and owners to look for ways to reduce this cost without forfeiting the safety of the space.

With the development of sensors that sample the room air for chemicals, the room air-change rates can be reduced. When chemicals are detected, the building exhaust system is increased for the area where the chemical has been detected in order to flush the area.

Another sustainable idea is the separation of the ventilation air system from the heating/cooling requirements. Currently buildings use a combined approach, where the ventilation system provides air changes as well as heating/cooling. In laboratories where the required air-change rate is larger than needed just for safe ventilation, a lot of air is used to satisfy cooling loads. With the use of a separate device to supply water heating/cooling, such as a chilled beam, the air volume can be designed to satisfy the ventilation and makeup requirements and the chilled beam can be sized to provide the heating/cooling requirements.

> "The growth of analytical instrumentation has added to the data storage and computational needs of labs as well."

Innovative and translational research

Over the past decade, translational research has become the most significant trend in laboratory operation. Simply put, translational research is the rapid application of promising discoveries from the basic to applied research to products. In the case of clinical research, from the bench to patient treatment, innovative research is facilitated by the physical colocation of multidisciplinary teams, incubator partnerships, and industry.

A prime example of this concept is a project in Buffalo, NY, where Kaleida Health, the Jacobs Neurological

▲ *The Henry Bellmon Research Center is Oklahoma State University-Stillwater's only building dedicated exclusively to research. Designed with modern features, this state-of-the-art facility brings together researchers from different departments who collaborate on projects at the cutting edge of modern research. Image Credit: Cannon Design*

Institute, the Clinical Translational Research Center, and the Bioscience Incubator of the University at Buffalo came together in a single building to create the Global Heart and Vascular Institute. In this single building, innovative research and ideas can be seamlessly discussed, exchanged, refined, and tested. With the inclusion of the incubator facilities, ideas don't get lost in academia, they get pushed out into the marketplace.

Conclusion

Laboratories have evolved far beyond the dark, isolated spaces of the past. New types of research, new approaches to research and new interdisciplinary interactions have all combined to push the design of labs into new territory. Increased support equipment and instrumentation, space designed with flexibility, modern safety advances meeting building codes, increased demands for sustainability, and the innovative research model have all impacted and will continue to shape how researchers work in their laboratories. Planners, designers, and owners who successfully respond to these directives will create institutions of leadership with the next generation of research discoveries.

Steve Copenhagen, *LEED AP and principal with Cannon Design, has more than 35 years of experience and specializes in research and discovery projects. He can be reached at 415-243-4170 or scopenhagen@cannondesign.com.*

PREVENTING CELL DEATH

ULTRAPURE WATER SYSTEM LOWERS ENDOTOXIN CONTENT BELOW PRESCRIBED LIMITS

by Katrin Toeppner and Dr. Elmar Herbig

The cell wall components of gram-negative bacteria, such as *E. coli* and pseudomonads, are designated as endotoxins. They have a hydrophilic polysaccharide and a lipophilic lipid component and, unlike the bacteria from which they originate, are highly heat and pH-stable. Endotoxins belong to pyrogens, i.e., they can cause fever if they come in contact with mucous membranes or if they enter the bloodstream (with reference to Steck, 2006, [1]).

According to the prevalent pharmacopeias, the defined limit values for endotoxin content may not be exceeded during the manufacturing process of pharmaceuticals.

In mammalian cell cultures that are used to produce biopharmaceuticals, such as immunoglobulins, the presence of endotoxins can lead to cell death. For this reason, ultrapure media, i.e., ultrapure water, with levels proven to be below the limits must be used to manufacture biopharmaceuticals or to propagate cell lines or cell cultures.

The objective of this study is to demonstrate that the ultrapure water produced by the arium pro VF water purification system exhibits an endotoxin content that is far below the prescribed limits and that can be used for applications of the categories mentioned above.

Endotoxin testing

A method for detection of endotoxins is the so-called LAL (Limulus Amebocyte Lysate) test, which uses the clotting reaction of a lysate of amebocytes isolated from the horseshoe crab (Limulus polyphemus). This reaction involves a primitive evolutionary coagulation cascade in which proteases are sequentially activated, thus resulting in the formation of a clot.

The coagulation cascade (also called a Limulus Enzyme Cascade, see [2], [3]) can be triggered by endotoxins or alternatively by ß-glucans, which are short-chain polysaccharides found in the cell walls of yeasts and molds. The ß-glucan pathway may lead to false-positive results [1]. Based on coagulation, the liquid, colorless lysate reacts by coagulation to form a solid, milky gel, hence the term "gel-clot method." As the sensitivity of the lysate is extremely high, it is imperative to rule out a false-positive reaction caused by contamination with endotoxins or ß-glucan. For this reason, exceptionally high purity requirements must be placed on ultrapure water.

In addition to the gel-clot method, the endotoxin content can also be assayed using a quantitative chromogenic method. In this method, a synthetic chromogenic peptide, a chromogenic substrate, is added to the lysate. Whereas in the gel-clot method, a gel clot is formed by the clotting enzyme, the synthetic chromogenic substrate in the chromogenic method is split by the clotting enzyme, resulting in a color change to yellow. The intensity of the yellow coloration correlates directly with the endotoxin content of the sample (chromogenic test). Preparing the lysate for either the gel-clot or the chromogenic method must therefore be done using ultrapure water.

Figure 1. arium® pro VF ultrapure water system.

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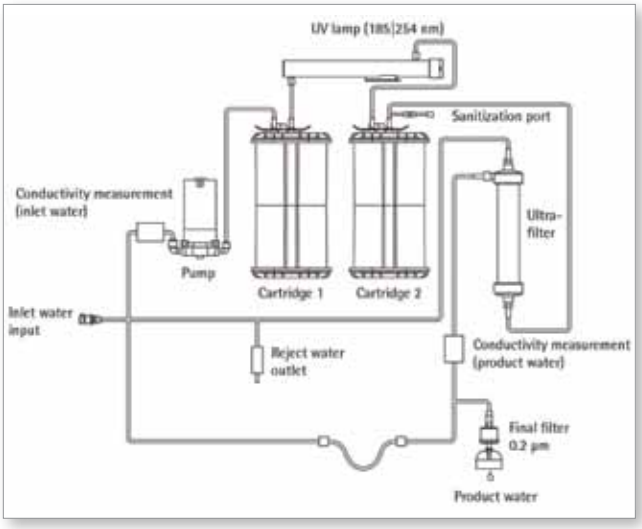
An ultrapure water system

The arium® pro VF system (Fig. 1) is designed to produce ultrapure water from pretreated drinking water and removes any contaminants still present in this potable water. Ultrapure water production requires continuous recirculation and a constant water flow rate, which is achieved using a pump system with controlled pressure. The conductivity of the water is measured at the feed water inlet and at the downstream port, or product water outlet.

The system used in the tests described in this paper operates with two different cartridges. These are filled with a special active carbon adsorber and mixed-bed ion exchange resins to deliver ultrapure water with a low TOC content. Moreover, the unit has an integrated UV lamp that has a bactericidal and oxidizing effect at wavelengths of 185 nm and 254 nm, respectively.

Furthermore, the system has a built-in ultrafilter module used as a crossflow filter. The ultrafilter membrane utilized in this filter retains colloids, microorganisms, endotoxins, RNA and DNA. A 0.2 µm final filter installed at the water outlet serves to remove particulates and bacteria during dispensing of the ultrapure water stream. The process that the unit employs to produce ultrapure water is shown in Figure 2.



▲ *Figure 2. Schematic flow diagram.*

Test methods

In the tests performed to assay the endotoxin content in ultrapure water obtained from the system, both the gel-clot method and the chromogenic method were conducted.

Gel-Clot method:

The lyophilized lysate (Charles River Endosafe R 15006) was dissolved in ultrapure water obtained from the system and frozen by portions in pyrogen-free test tubes. An endotoxin standard series consisting of LPS E. coli 055:B5 (Lonza N 185) was prepared in concentrations of 0.001 EU/ml to 25 EU/ml using ultrapure water from the arium pro VF system. The dissolved lysate was tested using the endotoxin standard prepared in order to verify that it had the sensitivity indicated (0.06 EU/ml). A sample of 100 µl was pipetted into 100 µl of the lysate and incubated in a water bath at 37°C. After one hour, each tube was individually removed from the water bath, turned by 180° and assessed for gel-clot formation.

Chromogenic method:

The chromogenic substrate (Charles River Endochrome K R1710K) was dissolved in ultrapure water produced by the water purification system. This chromogenic substrate and the endotoxin standard samples were pipetted into 96 endotoxin-free well plates in a ratio of 1:1. The absorption of each sample was measured continuously at one-minute intervals over one hour at 405 nm using a TECAN Safire plate reader at 37°C.

Results

In the range of 0.001 EU/ml to 0.05 EU/ml, the gel-clot method showed a negative result; i.e. no gel-clot formation (no endotoxins detected; see Table 1). A concentration of ≥ 0.1 EU/ml resulted in the formation of a gel clot. This result shows that within the detection sensitivity limits of the gel-clot method, no endotoxins were present in the ultrapure water filtered by this particular system.

The 60 absorption readings at 405 nm (Figure 3) in the chromogenic method yielded curves with different slopes depending on the specific endotoxin content of the standard samples. The times that were needed to reach a specific absorption were determined using a special computer program and used as the basis for extrapolating the samples with an unknown endotoxin content (for values, see Table 1 - chromogenic assay). As the standard samples with the lowest concentrations (0.005 and 0.001 EU/ml) and the arium water did not attain the extinction value of 1 required to calculate the endotoxin content, they were assessed as below the detection limit.

The values attained with arium pro VF ultrapure water were considerably lower than those plotted for the curve of 0.001 EU/ml.

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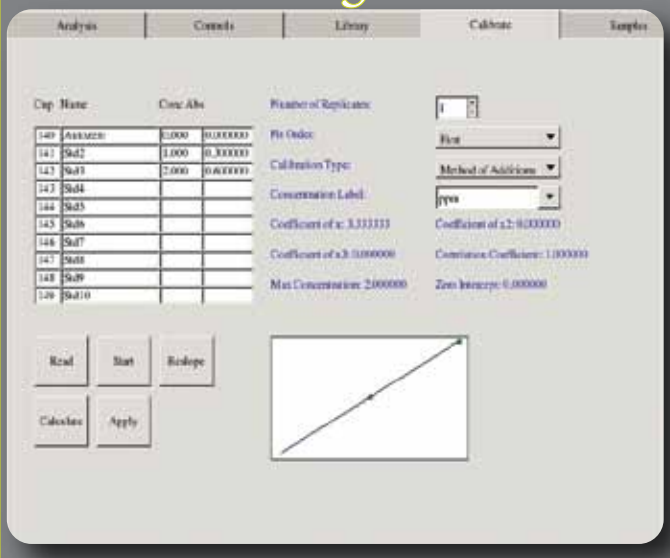

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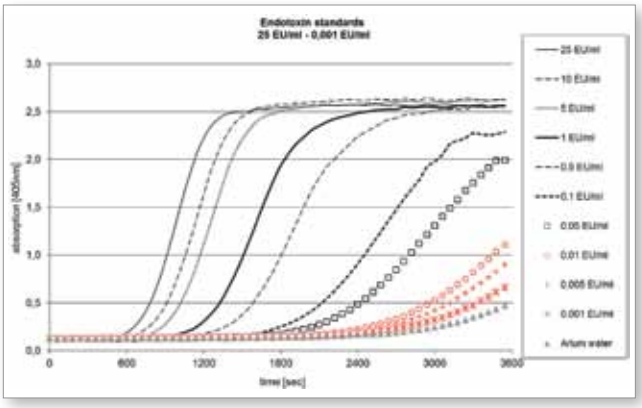
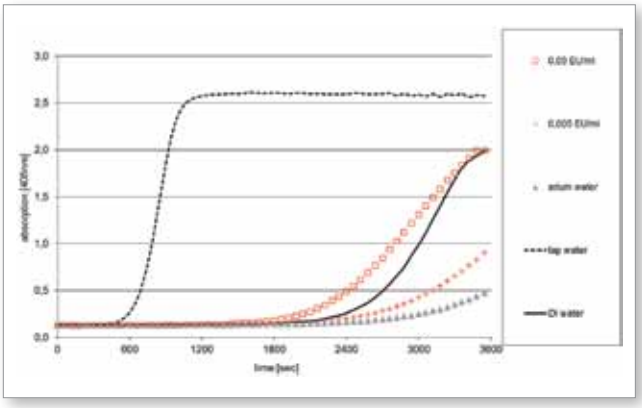
Sample	Endotoxin Standard Prepared [EU/ml]*	Gel Clot	Chromogenic Assay [EU/ml]*
arium® pro VF Ultrapure Water	0	No	0**
Endotoxin Standard	0.001	No	0**
Endotoxin Standard	0.005	No	0**
Endotoxin Standard	0.01	No	0.009
Endotoxin Standard	0.05	No	0.055
Endotoxin Standard	0.1	Yes	0.083
Endotoxin Standard	0.5	Yes	0.63
Endotoxin Standard	1.0	Yes	1.2
Endotoxin Standard	5.0	Yes	4.47
Endotoxin Standard	10	Yes	8.4
Endotoxin Standard	25	Yes	25

** EU/ml, endotoxin unit; 1 EU approximately corresponds to 100 picograms of endotoxin (as a rule of thumb)*
*** Below the quantifiable detection limit*

➤ *Table 1. Assay of the Endotoxin Content in arium pro VF Ultrapure Water and Endotoxin Standard Samples Using the Gel-Clot Method and the Chromogenic Method.*



➤ *Figure 3. Absorption readings for endotoxin standard samples over a 60-minute period using the chromogenic method.*



➤ *Figure 4. Endotoxin assay of water samples.*

Figure 4 shows the data collected on endotoxin concentrations in tap water, deionized water (DI water) and arium water in comparison with two selected endotoxin standards (0.05 EU/ml and 0.005 EU/ml).

The endotoxin content in water samples was calculated from the values measured using the endotoxin standards and is shown in Table 2.

Sample	Endotoxin Concentration [EU/ml]
arium® pro UV Ultrapure Water	< 0.001
DI water	0.02
Tap Water	25

➤ *Table 2. Table Showing the Endotoxin Content in Different Water Samples.*

In the DI water sample, endotoxins of 0.02 EU/ml were detected, which was below the currently valid limits for WFI (water for injection). In tap water, with 25 EU/ml an exceptionally high endotoxin load was found. This finding was not further analyzed. By contrast, an exceptionally low value of < 0.001 EU/ml was measured in ultrapure water obtained from the system, which is far below the usual limits encountered.

Discussion

The test results show that ultrapure water produced by the arium pro VF system can be readily used as an affordable alternative for preparing samples to be assayed in endotoxin tests as the detectable concentrations of endotoxin in the ultrapure water produced are exceptionally low (<0.001 EU/ml). The results obtained confirm earlier tests in which an endotoxin load of <0.001 EU/ml was found in arium ultrapure water [4].

The endotoxin concentration is far below the limits required by the United States Pharmacopeia, which therefore makes this water theoretically suitable for use in the manufacture/endotoxin monitoring of pharmaceutical products. Examples of such uses are product formulations, diafiltration solutions, chromatography buffers and water for extraction, rinsing and sanitization steps as well as for cell culture solutions.

Precisely within the scope of cell culture applications one has to pay attention to contaminations in the various steps of these processes. To maintain control over the effects of endotoxins on such cultures and on the sensitivity of cells, particularly with respect to such endotoxins, the media for cell growth must be demonstrably free of detectable endotoxins (see also [5]).

Acknowledgements

Our special thanks go to Dr. Stephanie Steck of Rentschler Biotechnologie GmbH, Laupheim, Germany, for reviewing the manuscript of this paper and for her constructive discussion on this subject.

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Adapted to the original German article from Dr. Herbig, June 7, 2012

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ARE YOU IN THE MARKET FOR A...
LAB WASHER?

Anyone who works in a lab quickly learns the value of labware washers. Today, washers are almost as common in laboratories as they are in kitchens. Any lab that uses glassware for analysis, science, or engineering is a potential user. Washers are found in schools, research institutions, pharmaceutical companies, and water and wastewater analytical labs, and are used in many industries such as public health, forensics, chemical R&D, petrochemicals, electronics, medical devices, optics and cosmetics. Washers are usually specified according to their capacity. Under-counter models sport about 4.5 cubic feet of wash chamber, medium-capacity models range from about 5 to 10 cubic feet, and larger capacities have above 10 cubic feet. Another way to categorize washers is by where they are located: in centralized cleaning rooms or at the point of use. Organizations with a central washer often hire a technician to pick up and deliver glassware.

Washer detergents formulated specifically for laboratory washers can meet specific needs. There are a wide variety of detergents–phosphate-free, chlorine-free, surfactant-free and non-ionic or ionic. These detergents leave no residue on the glassware so they are safe for sensitive applications such as tissue culture or instrumental analysis. Some laboratory washers automatically dispense liquid detergent and weak acid neutralizing rinse solutions. This eliminates the need to manually fill the detergent cup and rinse the dispenser before each use. Using a built-in pump, the washer automatically meters the precise amount of detergent and acidic rinse solution into the washer at the appropriate cycle.

The following brands of lab washer detergents are used by our respondents in their labs:

Alconox powder detergent	59%
Alcojet mechanical washer detergent	14%
Citranox liquid acid detergent	16%
Lipsol detergent, concentrate	7%
Liqui-Nox phosphate-free liquid detergent	30%
Sporicidin disinfecting solution and towelettes	6%
Other	9%

The top ten factors/features our readers look for in a lab washer:

	Important
Durability of product	96%
Consistent washing and disinfection results	93%
Low maintenance–easy to use and clean	93%
Service and support	93%
Price	93%
Warranty	90%
Reliability of vendor	89%
Safety features	79%
Energy efficient / low operating cost	73%
Reputation of vendor	71%

Most of our readers use their lab washer several times each day:

Several times daily	41%
Several times each week	32%
Once a day	10%
Once a week	10%
Two to three times a month	5%
Less than once a month	2%

Lab washer components respondents are currently using include the following:

Lower baskets	28%
Upper baskets	27%
Direct injection (for beakers, pipettes, flasks)	26%
Test tube baskets	12%
Slides and Petri dish baskets	4%
Don't know	2%
Other	1%

The amount of time spent per day on hand washing glassware in the labs of survey respondents without a lab washer:

Less than 1 hour	64%
1 - 2 hours	29%
2 - 3 hours	6%
Over 3 hours	1%

The applications survey respondents use their washers for include:

Cleaning moderate volumes of small items	40%
Cleaning large volumes of small items	26%
Cleaning large, difficult-to-clean items	19%
Glassware sterilization	11%
Sterilization of liquids in vented glass containers	4%

Types of lab washers our readers are using or planning to purchase:

	Using	Planning to Purchase
Small capacity washer	21%	4%
Medium capacity washer	27%	14%
High throughput washer	6%	4%
Large capacity washer	9%	3%
Don't know	6%	5%
Other	1%	0%

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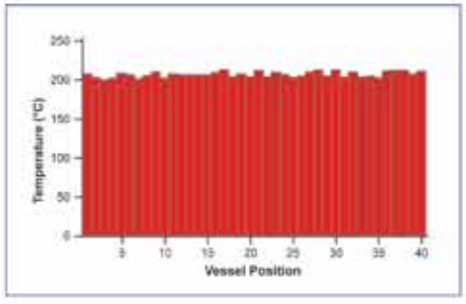

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ARE YOU IN THE MARKET FOR A...
GAS CHROMATOGRAPHY SYSTEM?

Two interesting and fairly recent trends in GC systems are "fast GC" and the use of hydrogen as the carrier gas. Hydrogen is much less expensive than helium. It also has superior optimal linear velocity and produces a very low effective plate height, meaning more theoretical plates are available for a given column length. Because of its lower density relative to helium, hydrogen works extremely well with very narrow-bore columns. Fast GC provides benefits of lower instrument and human resource costs, higher revenues for high-throughput testing or service labs, and more rapid method development. Perhaps best of all, these benefits accrue with no additional capital investment. Ultra-high-performance liquid chromatography, by comparison, requires purchasing an instrument capable of generating and withstanding high backpressures. Fast GC is achieved by shortening column length, ramping up temperatures faster, and raising the carrier gas flow rate. The negative effects on resolution are countered by narrowing the column's internal diameter, reducing the film thickness, and (a second trend) switching from helium to hydrogen carrier.

According to Agilent Technologies' website, troubleshooting your GC system starts with isolating the problem:

Is it injection, flow, column, detection, electronic or some combination?

The company adds users should know what can and can't cause the symptom and what to do about it:

- Broad solvent peak–injector problems, technique, sample problems
- Split peaks–injector problems, mixed solvent
- No peaks –wasn't introduced, wasn't detected
- Bonus peaks–In Sample or Back Flash
- Response changes–activity, inlet discrimination, detector problem
- Peak tailing–flow path or activity
- Peak fronting–overload or solubility mismatch
- Shifting retention–leaks, column aging, contamination or damage
- Loss of resolution–peak broadening, separation decreasing
- Baseline disturbances–column bleed, contamination, temperature
- Noisy or spiking baseline–electrical or contaminated detector
- Negative or flat-topped peaks–detector problems
- Quantitation problems–activity, inlet or detector problems

Troubleshooting tips courtesy of Agilent Technologies

Type(s) of detector(s) our readers use with their GC instrument:

Flame ionization (FID)	**34%**
Thermal conductivity (TCD)	**12%**
Electron capture (ECD)	**14%**
Nitrogen-phosphorus	**2%**
Flame photometric (FPD)	**5%**
Photo-ionization (PID)	**3%**
Mass spectrometer	**26%**
Other	**3%**

Types of GC columns our readers use in their labs include the following

One single porosity column	**40%**
One mixed bed/linear/multipore column	**29%**
Two or more mixed bed/linear/multipore columns	**12%**
Two or more single porosity columns	**17%**
Mixed bed/linear/multipore column with oligomer column	**2%**

The types of gases survey respondents use include:

Helium	**22%**
Acetylene	**1%**
Air, industrial	**10%**
Argon	**7%**
Carbon dioxide	**4%**
Cryogenic	**2%**
Hydrogen	**20%**
Nitrogen	**19%**
Nitrous oxide	**1%**
Oxygen	**4%**
Propane	**1%**
Zero air gas (<1 ppm hydrocarbons)	**9%**
Other	**1%**

Our readers' top ten most important features/factors they look for in a GC system include:	Important
Quality of data	**93%**
Resolution	**93%**
Precise and accurate flow rates	**91%**
Sensitivity	**91%**
Accuracy	**89%**
Ease of maintenance	**86%**
Service and support	**84%**
Ruggedness and reliability	**81%**
Availability of supplies and accessories	**78%**
Price	**78%**

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ARE YOU IN THE MARKET FOR A... THERMAL ANALYZER?

Thermal analysis is the broad category of at least 20 techniques that measure some fundamental property of matter as a result of adding heat. For example, dilatometry measures volume changes upon heating, thermomechanical analysis quantifies the change in dimension of a sample as a function of temperature, and thermo-optical analysis detects changes in optical properties on heating or cooling. This discussion applies mostly to two techniques, differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA), although many of the ideas presented here apply to other types of thermal analysis. DSC and the related micro-DSC measure the amount of heat required to change the temperature of a sample. DSC is most often used with materials that undergo phase changes. Homogeneous or nonhomogeneous materials that melt or freeze, or that undergo transformation from one solid form to another, are excellent candidates for DSC. Notable examples include the glass transition temperature of polymers and the interconversion of crystalline polymorphs in the pharmaceutical industry. Approximately 60 percent of thermal analyses involve DSC. TGA is often used to quantify residual solvent or moisture content of a sample (for example, in foods and pharmaceuticals). A related technique, evolved gas analysis, analyzes gas decomposition products.

Simultaneous Thermal Analysis (STA) combines the benefits of thermal analysis and differential scanning calorimetry (measurement of the energy flow to or from the sample, quantifying the changes as exothermic or endothermic) into a single experiment. Seven percent of the respondents are currently performing STA in their research and another 40 percent are planning to use STA within the next 12 months.

Survey respondents' top ten factors/features they look for in a thermal analyzer:

	Important
Reliability	80%
Ease of use	67%
Service and support	58%
Low maintenance/easy to clean	54%
Price	54%
Safety	51%
Warranty	49%
Low operating cost/ cost of ownership	48%
Ease of installation	39%
Versatility	39%

The types of analyses our readers are performing or planning to perform in their labs:

	Currently performing	Planning to perform
Dielectric Thermal Analysis	3%	5%
Differential Thermal Analysis	9%	6%
Differential Scanning Calorimetry	18%	5%
Dilatometry	1%	1%
Dynamic Mechanical Analysis	3%	3%
Evolved Gas Analysis	5%	2%
Thermogravimetric Analysis	13%	7%
Thermomechanical Analysis	5%	1%
Thermo-optical Analysis	4%	1%
Other	6%	2%

Our readers work with the following materials which require them to perform thermal analysis:

Organics such as lubricants, pharmaceuticals, paints, adhesives, etc.	29%
Polymers	26%
Minerals, inorganic chemicals, and other inorganics	19%
Metals / alloys	10%
Other	10%
Ceramic / glass / building materials	5%

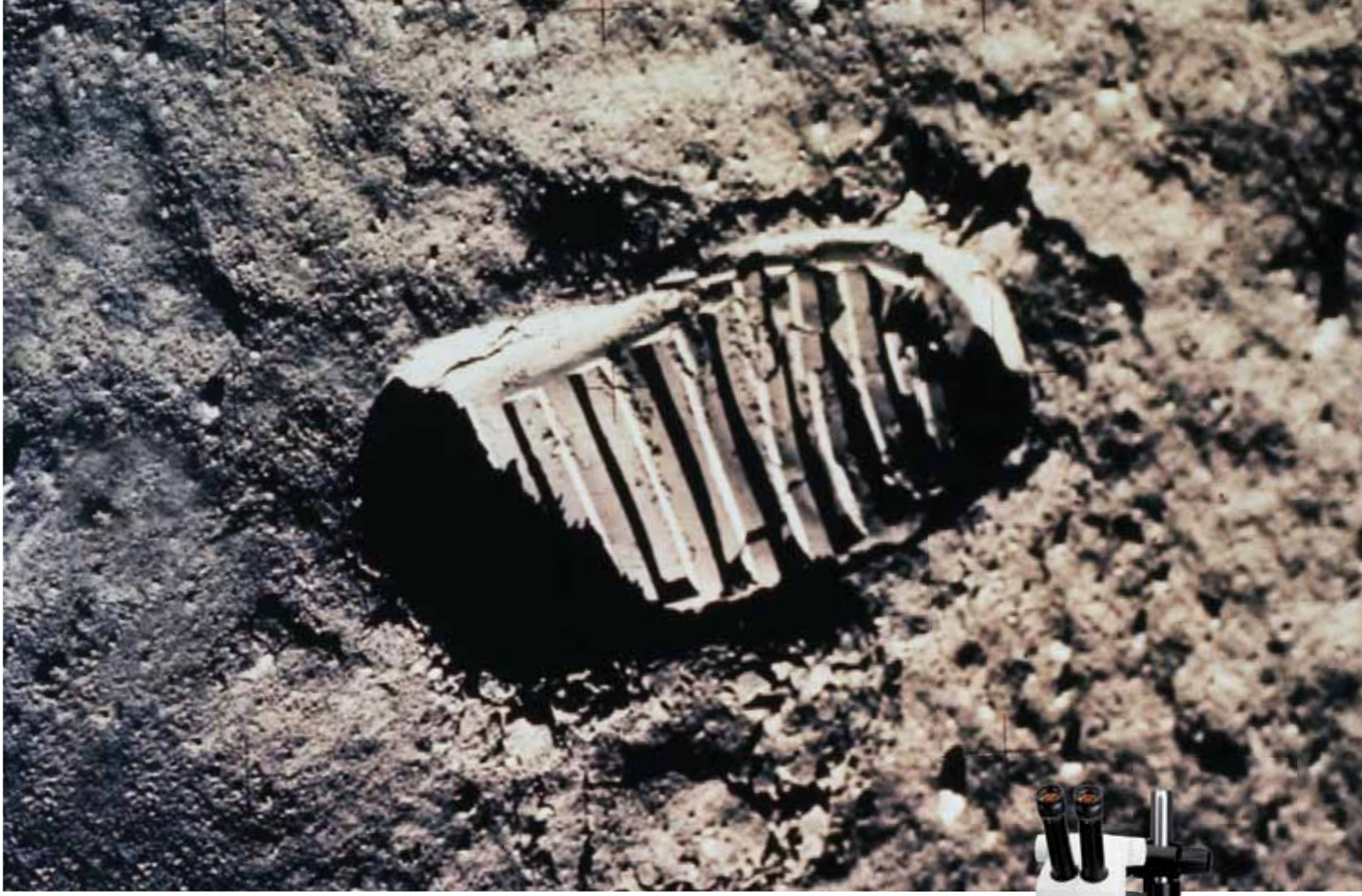
The physical states of the materials our readers analyze:

Powder	28%
Liquid	20%
Pellet	13%
Thin film	12%
Fiber	10%
Paste	8%
Gel	6%
Foam	4%

The type of information our readers require from their thermal analyses:

Quantitative	24%
Qualitative	9%
A mixture of both	67%

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



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HPLC COLUMNS

EVOLVING TECHNOLOGIES PROVIDE WIDE RANGE OF CHOICES

by Angelo DePalma, Ph.D.

Liquid chromatographers have a wealth of choices when it comes to columns and systems: HILIC, chiral, mixed mode, supercritical fluid (SCF), normal phase, ion exchange. But the pharmaceutical industry's influence on LC products is such that reverse-phase (predominantly C18 and C8) remains the most popular chromatography mode "by a large margin," says Denis Boudriau, product specialist at SiliCycle (Quebec, Canada).

HPLC's conservative side notwithstanding, one is hard-pressed to find a more innovative, self-reflective instrument market. New technologies replace old, and vice versa.

For example, SCF is considered a niche industrial application, yet Waters (Milford, MA) recently released UPC^2, an SCF system in an analytical LC-like format. Doug McCabe, senior marketing manager at Waters, described early versions of analytic SCF as "ad hoc." "SCF was never taken seriously. This system was built from the ground up."

Like other SCF systems, UPC^2 is capable of chiral separations, but Waters is targeting it for non-chiral applications and positioning the UPC^2 as a crossover system bridging the capabilities of LC and GC.

Choices old and new

"The wide spectrum of columns available on the market makes selecting this most important component of an LC system extremely difficult," Boudriau tells *Lab Manager Magazine*. Column purchasers should consider column cost, availability, expected lifetime, particle size of media, selectivity, resolution, efficiency, and reproducibility. Also consider the vendor's reputation, their level of support, and the availability of printed or downloadable product specifications and application notes.

Laboratories are hanging on to their 5 µm columns even though 2µm-to-4µm packings have surpassed them in performance—and despite the new sub-2µm class of UHPLC stationary phases: "Most chromatographers are reluctant to revalidate their older methods, even though they would save time and enjoy higher throughput," Boudriau states. "The time and cost involved in revalidation represents a deterrent stronger than the potential gain in adopting smaller particles."

The UHPLC replacement?

HPLC columns, systems, and methods appear to be reaching a kind of dynamic equilibrium. "UHPLC is here to stay," says Gaurang Parmar, HPLC product manager at Sigma-Aldrich/Supelco (Bellefonte, PA). "But many users are finding that it is best to use UHPLC at moderate pressures, where column choices are greater."

According to Stephen Luke, product manager at Thermo Fisher Scientific (Waltham, MA), HPLC users cited factors related to speed (e.g., throughput, reduced run times) as a top priority 62 percent of the time. Resolution (23%) and sensitivity (7%) were a distant second and third. Particle-size technology and bonded-phase chemistries have contributed the most toward meeting these objectives.

> **"HPLC's conservative side notwithstanding, one is hard-pressed to find a more innovative, self-reflective instrument market."**

Although column particles have trended downward, progress has not always been linear, as monolithic and fused-core (a.k.a. "core shell") technologies demonstrate. Fused-core technology in particular has been undergoing constant improvement in functionality and manufacturing.

Conventional particles are homogeneous in composition throughout; a fused core consists of a porous shell surrounding a rigid silica interior. This design enhances mass transfer because analytes diffuse into and out of just the shell rather than the entire particle.

Vendors claim performance for fused-core columns that in some ways compares to sub-2µm technology, but with much lower backpressures.

In June, Thermo Fisher Scientific introduced a new line of Accucore columns based on the company's Core Enhanced Technology™. By enlarging the pore sizes from 80 to 150 angstroms, Thermo Fisher has optimized the new C18 columns for proteins and peptides, whose development is expanding in the pharmaceutical industry.

Accucore particles have a 2.6µm diameter and a very narrow particle size distribution—very nearly monodisperse. Accucore also incorporates advanced bonding and a consistent, automated manufacturing process.

Because backpressures are manageable, the columns can be made quite long—150mm or 500mm. "They look like GC columns," Luke says. "Working with fully porous material in such long columns would generate intolerable backpressures. The benefits of the new technology are more highly resolved peaks, higher efficiency, and longer column life."

Technological convergence

Fused-core technology exposes interesting dynamics within the related worlds of HPLC columns and systems. While sub-2µm technology has been adopted at cutting-edge research and development labs, the uptake of UHPLC has not been as robust for routine work as some predicted.

"We learned, eight years after introducing the first sub-2µm system, that there's a place for both UPLC® [Waters' trademark] and older systems," McCabe admits. "HPLC is a very different marketplace, more conservative than consumer electronics. We hoped everyone would adopt the new technology, but that's not happening."

Cost, system complexity, higher maintenance, and a desire to retain legacy methods were the three most popular explanations for UHPLC's slow adoption. Today, low-to-medium-pressure fused-core columns provide an added disincentive to switch. Boudriau mentions UHPLC's high cost as an impetus behind the popularity of fused-core technology, calling the latter a "great alternative."

Yet, as Luke explains, adopting that technology optimally involves a good deal more than simply swapping out a column. Yes, it will work in most systems because of the low back-pressures. "But there's no point in having a very sharp peak that runs rapidly if you have huge dispersion volumes in the instrument. If you want to use these columns, there's a bit of optimization involved."

Parmar calls the desire to adopt cutting-edge technologies while simultaneously maintaining and optimizing existing instruments "convergence." This is a trend he says will continue despite the "huge amount of UHPLC technology adoption in the U.S. and Europe." Part of this trend involves playing the particle size "game" with different stationary phase types. For example Supelco had a 2.7µm particle to address needs for higher resolution and more rapid chromatography on non-UHPLC systems. In June it launched a line of 5µm fused-core particles, under the Ascentis® Express label, to lessen the backpressure burden even more (compared with UHPLC) while maintaining high performance on legacy systems.

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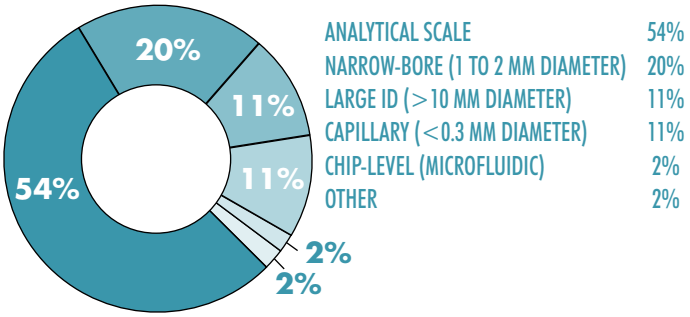

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MASS SPECTROMETERS

DIVERGENT TECHNIQUES FILL KEY APPLICATIONS

by Angelo DePalma, Ph.D.

Mass spectrometry (MS) has not quite become a routine acquisition for every lab that might benefit from it. Nor are MS instruments yet capable of serving routine users and experimenters equally well. But the characteristics and performance of instrumentation serving high- and low-end applications overlap more now than ever.

High-end MS instrument development is driven by performance, specifically sensitivity, mass accuracy, resolution, and dynamic range. Power users thereby achieve routine results more rapidly or find answers that are unachievable with low-end instruments.

Performance also drives mid- and low-end instrumentation, but these users don't necessarily require top-of-the-line spectrometers to get the job done. With performance a second-tier desirable, mid- to low-end users differentiate among vendors in terms of service, interface, and workflow suitability.

"How those users go about obtaining an answer becomes increasingly important," says Steve Smith, Ph.D., senior director, MS product management at Waters (Milford, MA). "And it's not just about 'ease of use,' an overused term that is losing its original meaning."

Customer-centered design

User-instrument interactions represent the core of a Waters program, "user-centered design," that puts hypothetical customers in front of instruments in simulated real-world situations *before* the operating software is written. As a company guide asks and answers questions, Waters films subjects and experts as they interact with the instruments and one another. "This has been standard practice for years in consumer electronics," Dr. Smith notes.

> **"High-end MS instrument development is driven by performance, specifically sensitivity, mass accuracy, resolution, and dynamic range."**

Waters' Xevo™ MS instrument line was the first to benefit from user-centered design. Xevo simultaneously mass-quantifies the target analyte and the matrix, which is critical where the sample milieu affects the target's properties such as suppression or enhancement of ionization or it introduces interference effects.

Dr. Smith likens this approach to applying a zoom lens for the target and a wide-angle lens for the matrix. This concept arose from users who expressed a need for simultaneous quantitative analysis of analyte and background. "This information was there all along. We didn't have to improve the resolution or sensitivity, just design the instrument more intelligently," Dr. Smith tells *Lab Manager Magazine.*

Tandem analysis driving MS

Industry-wide, the shift from conventional liquid chromatography (LC) to ultra-high-performance LC (UHPLC) has provided a huge boost to MS as a detection mode. UHPLC is the generic term that describes high-performance LC run on a stationary sub-two-micron particle phase. Waters, which first commercialized the technology during the early 2000s, owns the UPLC® (ultra-performance liquid chromatography) brand.

UHPLC provides improved sensitivity, speed, and resolution at the chromatography end, thereby reducing matrix effects during mass detection, but it places speed demands on the MS instrument, which is why some analysts are switching from quadrupole to time-of-flight (TOF) MS. TOF has the benefit of acquiring spectral data at full sensitivity much more rapidly than a quadrupole instrument can. "That's why we're seeing

TOF in more routine analyses, for 'qual-quant' applications where the exact mass number provides identification and the remaining data provides qualitative information," Dr. Smith says.

Combining MS and fast LC has fueled adoption of MS by enabling laboratories to process complex samples within normal throughput requirements with no compromise in data quality.

Until relatively recently, the high-performance characteristics of modern MS were available only in very high-priced MS systems, mostly at large companies and core research facilities. For much of its history MS was an expert-based instrument driven by high-end applications.

Reaching its potential

While much has changed, and for the better, MS technology has not reached its full potential for serving all modern laboratories that might benefit, says Blas A. Cerda, Ph.D., senior business director for mass spectrometry at PerkinElmer (Waltham, MA). "MS still lags in terms of financial or cost issues and ease-of-use requirements for a broad range of laboratories."

> **"MS technology has not reached its full potential for serving all modern laboratories."**

Nevertheless, two recent developments have made MS more broadly attractive. LC single-quadrupole MS systems, particularly integrated with UHPLC and supported by intuitive data processing software, have emerged and provide significantly increased sensitivity and ion source flexibility (e.g., ESI and APCI) with dual probes. The second development is LC-TOF MS systems that offer mass accuracy to 1ppm, five orders of linear dynamic range, increased sensitivity, innovative direct sample analysis front ends, and flexible ion sources with dual probes. "The current generation of single-quadrupole and TOF instruments addresses a wide range of applications and thus allows the laboratory to leverage the investment and operational costs of adopting MS, which results in a cost-effective business model," comments Dr. Cerda.

A view from the field

Heribert Dollt, Ph.D., who heads a bioanalytics lab at Hoffmann-La Roche (Basel, Switzerland), uses LC-MS as well as uncoupled (flow injection or nanospray) MS. Because his group makes decisions on new projects based on MS results, control and analytic software need to be robust, reliable, and user friendly. "Unfortunately, we all too often discover quite rudimentary bugs, suggesting that the software was compiled without much input from MS experts." Dr. Dollt notes "strange things" occurring in the areas of automatic data handling and interpretation, high-throughput analysis, and data deconvolution. He cautions that apparent user-friendliness can mask underlying deficiencies. "Scientists often blindly rely on software-generated results, with a dubious data 'interpretation' as the consequence." Another area of concern is the addition of peripherals such as autosamplers, LC, and fraction collectors, which may lead to "time-consuming surprises."

Vendors can improve the situation by employing open software architecture and providing facile interfacing to peripheral instruments as well as a more accessible interface for data handling, reporting, and data exchange to a laboratory information management system. The downside: "These tools quite often demand a higher degree of IT expertise, are not very user friendly, or are limited to only report writing." A more universal tool such as macro recording, which was available on old Macintosh computer systems, "offers flexibility in adding functionality down to the level of instrument tuning," Dr. Dollt says.

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VACUUM PUMPS

SIZE, CAPABILITY, GREEN FACTORS, AND MORE COME INTO PLAY

by Mike May, Ph.D.

Scientists started using true vacuum pumps more than 350 years ago, and investigators used suction pumps for more than 400 years before that. Consequently, removing gas to create a vacuum is not new in science. Nonetheless, the way of removing that gas keeps changing. "There's a movement away from house-vacuum systems and toward smaller lab systems or dedicated individual pumps, partly for energy efficiency," says Roland Anderson, laboratory products manager at KNF Neuberger (Trenton, NJ). "This change provides vacuum where it's really needed." Other experts agree. For example, Peter Coffey, vice president, marketing and sales, Vacuubrand (Essex, CT), says, "We have noticed that a lot of new science buildings do not include central vacuum systems."

Part of that transition arises from the complexity of central systems. "A central vacuum relies on a couple of very large pumps, usually in the basement, that provide vacuum to lab benches through a network of pipes that run throughout the entire building," Coffey explains. In some cases, though, simpler solutions create their own problems.

Waste with water

One of the simplest ways to create a vacuum involves water. A Venturi vacuum pump, or aspirator, uses running water to create a vacuum. In fact, a *Lab Manager* survey published in July 2012, reported that 36 percent of the respondents still use aspirators in their labs. Coffey adds, "I recently heard of a major research facility that is being built without a central vacuum supply and for which the scientists plan to use aspirators."

"There's a movement away from house-vacuum systems and toward smaller lab systems or dedicated individual pumps, partly for energy efficiency."

Although aspirators seem like a simple fix in some cases, these devices can make poor choices. As Coffey points out, aspirators "waste and pollute massive amounts of water. For example, a single water-jet aspirator used 10 hours a week in a lab will waste 45,000 gallons of water a year, and contaminate it with solvent vapors as it does so." He adds, "Water-jet aspirators are much cheaper than buying a vacuum pump, but the operating cost and environmental impacts more than offset the purchase cost savings—in some areas in a year or two."

Selecting a system

Lab designers still select large systems in some cases. "Though they are inefficient and not cost-effective, house vacuums are still very popular when developing new research buildings with dedicated lab space," Anderson says. "When renovating labs, scientists are considering smaller, local multi-user vacuum systems or individual pumps for common laboratory applications."

Coffey says that central vacuums get bypassed for several reasons. "The vacuum from a central system is one-size-fits-all, even though chemists, biologists, and physicists all need vacuum of a very different character," Coffey says. "In the modern multidisciplinary science building, the different disciplines need different vacuum." That's not all. Coffey adds, "The different requirements of the different scientific disciplines often end up leading to conflicts, with the uses made by one discipline compromising the vacuum characteristics needed by other scientists."

A central system can even create environmental problems in some cases. "The vacuum system sucks vapors into the walls, so there is risk of cross-contamination between labs and condensation of toxic vapors in the piping," Coffey says. As Anderson mentioned above, central

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systems also use more energy. In some installations, the pumps for a central system run all the time, even when no one is in the building.

In addition, individual pumps provide more flexibility over time. "With a fixed installation," Coffey says, "the vacuum utility cannot adapt as the science, space needs, or budgets dictate." Individual pumps even keep labs up and running longer. "If there's a problem with such a system, only one pump needs to be changed," Anderson says.

Some vendors also offer systems that bridge central and individual vacuum pumps. Jacquie Richardson, Ph.D., director of organic chemistry teaching labs at the University of Colorado at Boulder, describes using such a system: "Each student bench has a connection. The one downside is that if one student leaves their vacuum spigot open, it messes things up for the other students at their bench." She adds, "That's easy enough to remedy with [teaching assistant] oversight, though." Overall,

"When renovating labs, scientists are considering smaller, local multi-user vacuum systems or individual pumps for common laboratory applications"

she says that she's very pleased with such a system.

Transitions in technology

Beyond moving from aspirators to pumps, the technology inside the latter even changes. For example, rotary vane pumps use oil and others use a diaphragm, which is oil-free. Anderson calls the oil-free approach greener, adding that it "provides enough vacuum for many labs."

With rotary vane pumps, Anderson says, working with wet vapors "gets moisture in the oil and it starts to break down, like the oil in your car." Then the oil needs to be changed and the old oil must be disposed of, and it can be contaminated by the vapors.

Although Anderson points out that rotary vane pumps supply higher flow and deeper vacuum than diaphragm pumps, he says that the latter provides enough suction for most applications. Nonetheless, he adds that researchers still need rotary vane pumps for some

"Some vendors also offer systems that bridge central and individual vacuum pumps."

applications such as lyophilization.

When it comes to evolving vacuum-pump technology, other features also matter. As Coffey says, "Users often are looking for a quieter pump than they have, because vacuum pumps are often one of the noisiest pieces of equipment in the lab." Many users agree. For instance, Faleh Salaymeh, staff scientist II at Relypsa (Santa Clara, CA), wants a vacuum pump that is accurate, durable, reliable, and quiet. He says, "I like the silence or quietness of [our pump's] operation, considering it is running all day in a laboratory with personnel around." His system also includes a remote control pad that he calls "a welcome addition."

In the end, picking the right vacuum pump changes life in the lab and beyond.

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UV-VIS SPECTROPHOTOMETRY

THE NEW LOOK OF A MATURE PLATFORM

by Angelo DePalma, Ph.D.

Ultraviolet-visible (UV-Vis) spectrophotometry is arguably the most common as well as one of the oldest forms of absorption-based analysis. UV and visible regions of the electromagnetic spectrum are contiguous: UV wavelengths range from 10 to 4000 angstroms; they are visible from 4000 to 7000 angstroms.

According to data from Strategic Directions International (Los Angeles, CA), the market for scanning UV-Vis spectrophotometers is approximately $400 million per year, with an annual growth rate of six percent.

"Overall miniaturization, speed, ease of use, reliability, and mobility will be the ongoing drivers for growth in UV-Vis spectroscopy over the next decade," says Thomas Sahiri, president of Implen (Westlake Village, CA). He predicts that ongoing innovation will make these instruments relatively inexpensive, easy to use, and fast for diagnostics, day-to-day routine lab applications, and on-site testing. "New optical components are enabling important new features such as easier cleaning, consumable-free operation, and automatic virtual dilution, which significantly increases the instrument's dynamic range."

Additional factors fueling innovation in UV-Vis instrumentation are shrinking lab space, increasing demand for small-volume UV (driven mainly by life science markets, specifically nucleic acid and protein analysis), and the pressure to shorten analysis times.

Sahiri notes that photodiode array spectrophotometers are becoming less expensive, smaller, and more feature-rich. "The introduction of fiber optics in spectrophotometers has increased the system flexibility significantly, while manufacturers are constantly improving the performance of the small, fast systems without moving parts. USB stick-type mobile spectrophotometers will provide a new step to miniaturization that will open new application fields for diagnostics, off-site research, forensic analysis, and food testing."

Replacing more costly, time-consuming assays

"HPLC detectors are the most common application of UV-Vis technology," notes Merlin K.L. Bicking, Ph.D., president of ACCTA (St. Paul, MN), an analytical chemistry consulting and training company. "But conventional spectrophotometers still play an important role in many laboratories across a variety of industries."

UV-Vis has been an integral part of testing for content uniformity and dissolution in the pharmaceutical industry. Dissolution tests are conducted to determine if a pill or tablet will dissolve under physiologic conditions. The process involves taking samples from the dissolution test at specific time points and analyzing them for levels of active ingredients. The standard analysis by liquid chromatography involves preparing calibration standards, collecting and filtering samples, and then transferring all the solutions to autosampler vials for analysis. The typical HPLC cycle time is 5 to 10 minutes per sample, plus time for sample prep, mobile phase preparation, and solvent disposal.

> "The market for scanning UV-Vis spectrophotometers is approximately $400 million per year."

"If the formulation does not contain any unusual components and the active ingredient has a relatively unique absorbance spectrum, a UV-Vis is an attractive alternative," according to Dr. Bicking. Fully automated systems allow direct transfer of the dissolution media to the UV-Vis instrument. "Using a diode array spectrophotometer, results can be obtained within one or two minutes of collection. Furthermore, software is available to automatically calculate the desired dissolution parameters. Even without automation, these systems require considerably less time and effort than HPLC."

Other "replacement" applications exist throughout industry.

The requirement is that the target analyte shows reproducible UV-Vis absorption without interference from other species.

Although UV-Vis is a mature method, its speed and power continue to support cutting-edge research. At her lab at the University of Kansas, Melinda Toumi, Ph.D., uses UV-Vis spectroscopy to ensure quality and accuracy in several of her workflows. "We perform UV absorbance measurements at 280 nm for protein concentration as well as Bradford assays that use the visible region of the spectrum." Toumi also relies on UV-Vis to assure low endotoxin levels in purified DNA. "These early experimental steps are vital to obtaining meaningful results since many subsequent reagent quantities are calculated in relation to the protein concentration."

Streamlining plate-based assays

When Ronald Earp, Ph.D., president of BMG LABTECH (Cary, NC), was in graduate school, he used non-scanning UV to capture surface plasmon resonance data. In 2004, Earp spearheaded the use of non-scanning UV-Vis detection in microplate readers. "Full-spectrum capture existed for cuvette-type readers but not for microplate readers," he tells *Lab Manager Magazine*. The benefit of non-scanning spectrum acquisition is speed—the entire UV-Vis spectrum is captured in microseconds, including all assay-relevant wavelengths.

This is the basic idea behind Thermo Fisher Scientific's NanoDrop UV-Vis instrument, in which a sample droplet obviates the need for a cuvette.

Instead of using a monochromator or filters, the full-spectrum approach excites the sample with a full-spectrum xenon lamp emitting from around 200 nm to 1000 nm. An array of charge-coupled device detectors (similar to sensors in digital cameras) on the collection side are tuned to receive transmitted light 1 nm apart along the entire spectrum. No mirrors, gratings, scanners, or moving parts are involved.

Conventional microtiter plate assays involving three wavelengths require three separate measurements and operator involvement. The non-scanning approach provides absorption or transmission at all three wavelengths, with optical density ratios or full spectra as needed. The dynamic range for BMG's UV-Vis readers are approximately three optical density units, which according to Dr. Earp is sufficient for most biological assays. BMG's readers also have a cuvette port for situations that demand the more traditional format.

For example, nucleic quantitation or purity assays employ the ratio of absorbance at 260 nm to the absorbance at 280 nm, with an additional measurement at 340 nm for cellular debris. DNA is considered pure when the $A_{260/280}$ is 1.8 or higher. For pure RNA, the ratio must be two or higher. Similarly, the non-scanning approach can quantify the conversion of NADH to NAD+ at 340 nm while simultaneously quantifying protein at 280 nm.

"Traditionally, doing these types of microplate assays with UV required reading the plate many times," Dr. Earp comments. Alternatively, fluorescence assays are more sensitive than UV but require separate reporter reagents for each analyte or event, plus associated preparation.

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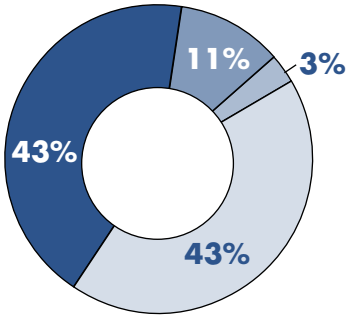
WHAT TYPES OF UV-VIS SPECTROPHOTOMETERS ARE OUR READERS USING IN THEIR RESEARCH?



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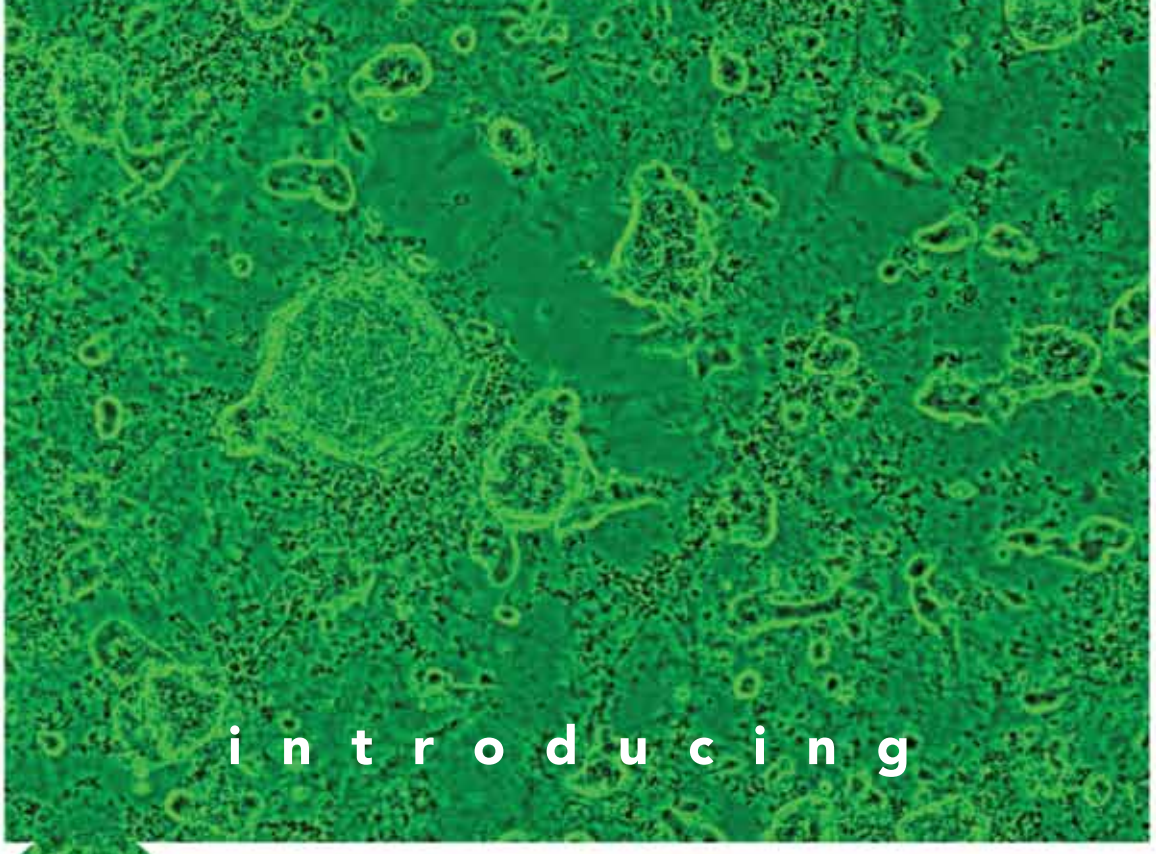

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GENE SEQUENCING

HANDLING THE EXPONENTIAL GROWTH IN RAW AND PROCESSED GENETIC DATA

by Angelo DePalma, Ph.D.

Gene sequencing is all about data—3.2 gigabytes for a single human genome, with several times that for making raw sequences relevant to real-world problems.

Mining the genome for medical intelligence multiplies the data "crunch" for gene sequencers and value-added services that annotate gene sequences for their relevance to protein and metabolite concentrations, and to both diseased and healthy states.

Massively parallel, high-throughput sequencing has raised the data-handling ante significantly. Traditionally, sequencing labs have expanded their data-handling capabilities by purchasing and networking more "boxes"—central processing units (CPUs) and storage. But the sheer volume of data has necessitated the need for an alphabet soup of advanced computing architectures such as compute unified device architecture (CUDA)-enabled graphics processor units (GPUs), general-purpose (GP) processor combinations, multicore CPUs, and GPU-CPU clusters.

Hybrid-core approaches

Another approach, generally referred to as hybrid-core or heterogeneous computing, employs different processing units (GPUs, CPUs, co-processors) and diverts computational tasks to the "correct" unit. "Heterogeneous computing involves different computing resources where they are most appropriate," explains George Vacek, Ph.D., life sciences director at Convey Computer (Richardson, TX), a computer manufacturer that serves the life science and other industries.

Convey's hybrid core consists of a standard Intel core integrated with a co-processor. An application's key instructions can then be off-loaded from the core to the co-processor, speeding up the overall application.

"Hybrid-core architecture is really good at pattern matching, graph analytics, and executing algorithms used in bioinformatics and next-generation sequencing," Vacek says.

"Next-generation or short-lead sequencing generates lots and lots of data. The rate at which sequencing is improving on a dollar basis is expanding exponentially, even for small or very modest facilities," Dr. Vacek explains. "The challenge, if you experience a three-order-of-magnitude increase in the amount of data you generate, is you can't have a thousand-fold increase in the size of your server or data center."

> **"Massively parallel, high-throughput sequencing has raised the data-handling ante significantly."**

Sequencing labs experiencing data woes run into physical limitations of space, budget, and management related to power, cooling, and cabling. Hybrid core computing replaces between five and 25 traditional servers with a single server maintained in Convey's facilities, without the expense and logistical issues.

Convey says it can replace ten servers for reference mapping of next-generation sequencing with one server. "Think of this as the same effective throughput with one-tenth the equipment, or finishing a job in one-tenth the time," Vacek says. "That's a huge cost savings for power, cooling, and cabling. And if you have ten times as many systems, even if they are fairly stable, the laws of statistics tell you there will be ten times as many server failures, not to mention replacement. So there are some real savings in operating costs."

"Once we could afford whole-genome sequencing, we found a significant bottleneck in the time required to process the data," said Laura Reinholdt, Ph.D., a research scientist at The Jackson Laboratory (JAX) located in Bar Harbor, ME. "That's when biologists here began to seek tools and infrastructures to more expediently manage and process the expanding volumes of NGS [next generation sequencing] data." To solve this problem,

JAX sought heterogeneous computing to complement its existing compute clusters.

In biology research, higher-performing informatics means more than simply completing the job faster. "It brings other positives to research; for example, you can try less-approximative methods you wouldn't have tried before, or larger data sets, or attack larger problems that were impractical or literally impossible," Vacek tells *Lab Manager Magazine*. "The real advantage is driving new areas of science and achieving higher-quality research."

"We've had assemblies we couldn't complete on our 256-node cluster simply because they were taking too long," said Dr. Guilherme Oliveira, president of the Brazilian Association for Bioinformatics and Computational Biology and a member of the Board of the International Society for Computational Biology. "We evaluated several platforms and are excited to be working with a hybrid-core system."

"Downstream" data management

The data crunch in sequencing is due to a significant degree to the precipitous drop in the cost of whole-genome mapping, which has been driven by personalized medicine. Personalized medicine seeks to differentiate, on the basis of genes or other biomarkers, subsets of diseases like cancer. Personalization is based on the observation that genetic differences may signal radically different prognoses, and suggest differing approaches to treatment for individuals with, for example, prostate cancer.

The connection between Moore's Law and the cost of sequencing a genome says a lot about the two disciplines and how they connect. Moore's Law states that the complexity of integrated circuits doubles every 18 months or so. Between the late 1990s and 2008, the cost of sequencing a genome similarly halved over approximately the same 18-month timeframe.

"In biology research, higher-performing informatics means more than simply completing the job faster."

The widespread adoption of second-generation sequencing in 2008 changed everything. The progression beyond traditional automated Sanger sequencing—the technology responsible for the Human Genome Project—to second-generation techniques had the immediate effect of accelerating the drop in cost per genome from a Moore's Law-type relationship to a halving every two to three months. The imminent adoption of third-generation sequencing could bring about the much-anticipated "thousand-dollar genome" within a few years, according to Hank Wu, director of translational informatics at Remedy Informatics (Sandy, UT). Remedy provides software for connecting genomics with scientific and clinical data to enable "translational" research connecting basic R&D to clinical practice. Among the company's offerings are software platforms for enabling the basic research on which personalized medicine depends. "Personalized medicine, which depends so heavily on genomics, is now pushing toward clinical relevance," Mr. Wu says. "Personal genomes may become as common as a routine doctor's visit."

Yet even as the price drop for sequencing is falling five times more rapidly than Moore's Law, the level of assigning relevance to genes, their downstream products, and health status remains vastly underserved. This downstream genomic bioinformatics, Remedy Informatics' specialty, is equally critical to making genomics an everyday tool with the potential of dramatically lowering health care costs.

"Gene sequencing is no longer the weakest link. Rather, it's our ability to aggregate and harmonize genomic data with the clinical world," Wu says.

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

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

Alexander Sherman

ASK THE EXPERT

CHOOSING THE RIGHT IT SYSTEM AND DATA INFRASTRUCTURE

by Tanuja Koppal, Ph.D.

Alexander Sherman, director of systems in the Department of Neurology and director of strategic development and systems at the Neurological Clinical Research Institute at Massachusetts General Hospital, discusses why the right choice and setup for data collecting, data handling, and data sharing infrastructure is important to help establish successful research collaborations. He emphasizes the need to think early and clearly about standards and nomenclature for collecting and labeling samples and subsequent data, to enable linking and analyzing them when they have been collected at different locations at various time points.

Q: Please tell me about your collaborative research network focusing on rare diseases.

A: My interests lie in rare diseases, and in order to find a cure for such diseases, the research community has to collaborate. Hence, I am interested in learning how technology, processes, and know-how can help move research forward. In order to get the pharmaceutical industry interested in such diseases, we need to create networks of academic institutions and hospitals to run clinical trials with appropriate patients, looking at the right outcome measures. The Amyotrophic Lateral Sclerosis (ALS) consortium started with several hospitals in New England and now it has become a global network with research sites in Europe and Canada. We have a scientific committee to help us agree on what to do, which new drugs and approaches to look into, and which companies to work with. Our focus is on clinical—not basic—research, so it is important for people in the lab to align themselves with the right team in the clinic that will eventually move their research forward.

Q: How important is it for the data infrastructure in clinical research to be set up in a way that fosters collaboration?

A: We have to think first about all the different types of data we can possibly collect from patients. It could be various types of clinical data, clinical images, or collections of biofluids and tissues. We have to think about these different types of heterogeneous data sets and see what needs to be done to link them all together. To this goal, we have introduced the concept of virtual biorepositories. As you know, specimens from patients with rare disorders are very valuable. Hence, in an academic setting, people compete for the same resources and the same glory, and they don't like to share. So we changed the paradigm and suggested to the ALS community that they don't have to share anything; they simply register their biospecimen with the network. The technology we developed allows researchers within the network to search for a particular biospecimen, track it to a specific individual or institution, and then approach them directly. This is a way for the research community to collaborate without any obligation to share. However, in order to analyze the collected data and biofluids, we have to agree upon and enforce certain standards for collecting, storing,

> "Specimens from patients with rare disorders are very valuable."

Alexander Sherman has 29 years of experience in research, research infrastructure development, software development, software architecture, expert systems design, clinical trials systems design, data management, and clinical research management. He has worked with Massachusetts General Hospital and the Neurological Clinical Research Institute for the past 10 years. He is responsible for the successful design, development, and deployment of software systems for numerous clinical trials and biomarker studies in neurological diseases and for the technological platform behind the NEALS ALS Consortium (www.alsconsortium.org), a research network of 105 academic institutions around the world. He also served as CEO of PharmaContent, Inc., a software development company that designs and develops software systems for clinical research. Sherman's other relevant experiences include a position as a board of directors member for Clinical Data Corporation, a biotechnology company, and as a director of strategic development at CogniMed LLC, a company that developed expert systems for disease management. He holds a master of science degree in nuclear engineering and he graduated from a doctorate program in nuclear engineering. He is a frequent speaker at academic and industry conferences, and has many publications on the topics of collaboration in clinical research, data, and biospecimen sharing, and technology utilization for these purposes.

and labeling biosamples to guarantee their quality. You have to think ahead on whether and which data can be shared and *a priori* agree on the common data elements (CDEs) to capture and the nomenclature of biosamples to be used. We also have to agree on what to put on a vial label, as it not only identifies your sample but also links it back to the data. Careful planning is a must.

"It's important to agree *a priori* on the data collection and nomenclature."

Q: Why are the CDEs & biospecimen nomenclature so important?

A: If every lab collects data in different ways, you will not be able to harmonize your data and perform meta analyses on the aggregated data. So it's important to agree *a priori* on the data collection and nomenclature. Currently, the National Institutes of Health (NIH) is attempting to develop disease-specific CDEs to provide a framework for collaboration. Some data elements are not disease-specific, but a majority of data elements, such as functional scales and questionnaires, are specific to certain diseases or disease areas and have to be measured and collected in a certain manner for the data to be shared later. This is not ideal, but it is a first step. While trying to gather data for the ALS network, we found that one of the untapped resources is data from research projects and clinical trials that exist at various pharma companies. With a nonprofit company, Prize4Life, and generous support from the ALS Therapy Alliance, we started a project to create a Pooled Resource Open Access ALS Clinical Trials (PRO-ACT) database that allows the merging of data from Phase II and Phase III trials from public and private sources. But we had some challenges as the data was collected over a period of 20 years, by multiple companies and institutions, with no standard for data collection in place. Some of the data sets arrived without data dictionaries. In some cases, we had to go into the disease histories and do some reverse engineering to figure out basic patient information. To harmonize this data, we have designed and developed a platform that allows us to build a common data structure (CDS), map individual data sets to the CDS, and then import the data according to the maps.

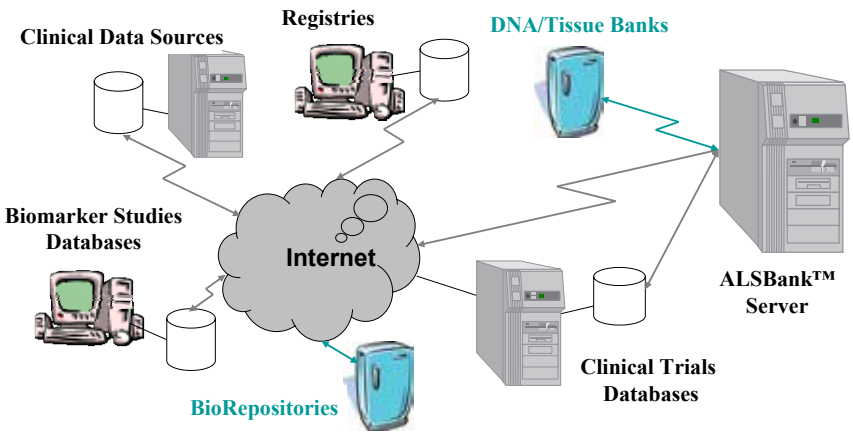
Q: Do the systems and tools used for collecting the data need to be standardized?

"You have to think about data quality before starting the collection effort."

A: It is sometimes important to know which analytical tool was used to make certain measurements as results may vary. It is less important to know what tool was utilized to collect and store the data, as long as one can identify and harmonize the data from the various databases. There have to be standard operating procedures (SOPs) in place on how to collect, enter, and clean the data. The data capture system has to be smart enough to interact at the point of entry to prevent inaccurate data from being entered. You have to think about data quality before starting the collection effort. Ideally, an independent data management team will plan ranges for data fields, create queries, and work with individual researchers. Just collecting data does not guarantee its quality.

Q: What about long-term data storage and protocols for disaster prevention and recovery?

A: It's important to back up all your data and know what to do with it. Should it be in the same location where the original data is kept? If it is, then you are protecting against theft or system damage but not from a natural disaster like an earthquake or a fire. Should the backup copy then be sent to a faraway location or a safe deposit box? With newer approaches like storing data in the cloud and in virtual storage sites, you don't have to worry about data synchronization. The concern, however, is around data security and access. Data backup is also important for auditing purposes and one should not forget to periodically restore the backups to ensure that they're being backed up correctly. You have to think about all possibilities and procedures. Finally, people who collect, capture, back up, and monitor data all need to be properly trained and their training records need to be maintained.



▲ *The image illustrates the concepts of Virtual BioRepository, in which databases and biospecimen storage units are decentralized, while accessible for searches to the research community.*
(Source: Sherman et al. Amyotroph Lateral Scler. 2011)

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BIOHAZARD CONTROL

GUIDELINES FOR AN EFFECTIVE EXPOSURE CONTROL PLAN

by Vince McLeod

Working in biological containment facilities or with infectious agents is serious business. The research performed usually entails indigenous or exotic agents with the potential for severe or lethal disease. Two examples of infectious pathogens that have received a lot of attention recently are yellow fever and West Nile virus. Obviously, if released they have the potential to cause extensive harm or damage to people, the environment, and the community. Needless to say, we do not want these agents to get out into the community nor do we want our employees who are working with these agents to be in harm's way. The foundation for safe operation of any biological containment facility is an effective exposure control plan. This article discusses the basic elements of a comprehensive exposure control plan, what each element should contain, and tips on successful implementation.

> "The foundation for safe operation of any biological containment facility is an effective exposure control plan."

The exposure control plan is basically a biosafety manual written to address the unique conditions of the current research, facility design, and personnel operations necessary to carry out the laboratory's mission. One excellent free reference is the CDC's *Biosafety in Microbiological and Biomedical Laboratories*,[1] which contains comprehensive information on biological risk assessment and summary statements for many common infectious agents.

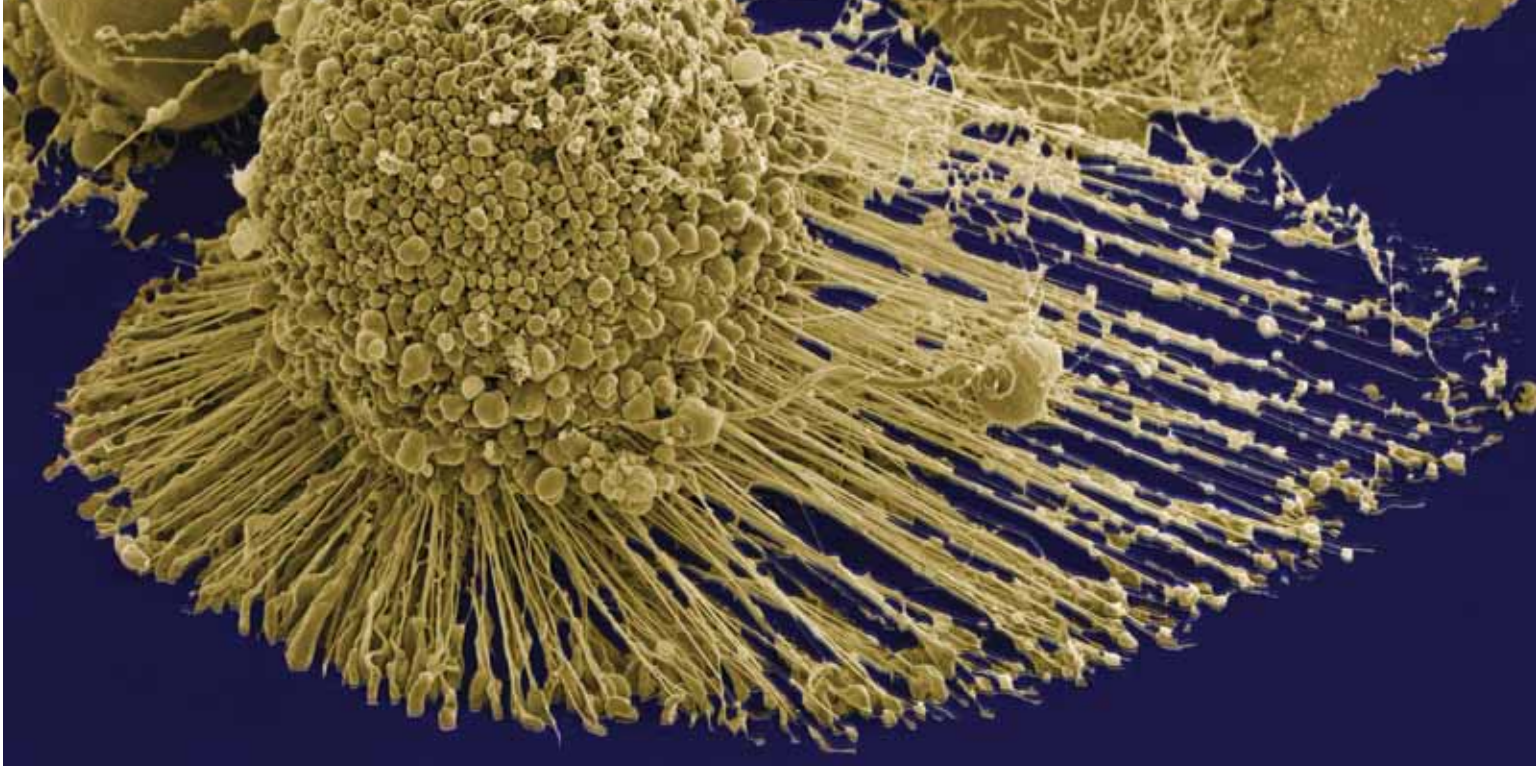
An effective exposure control plan is comprehensive, clearly written in concise terms, well organized, distributed to all people who must enter or work in the containment lab, and, most important, read and understood by all. A good comprehensive exposure control plan will contain at least seven main sections. These are general laboratory function, specific facility design and operational procedures, special laboratory safety equipment and personal protective equipment (PPE), laboratory research practices and procedures, health and medical monitoring requirements, emergency procedures, and employee training. Let's take a look at each of these chapters to see what they should include.

General laboratory function

The opening section will provide a clear organization of personnel and assign responsibilities for all who work in and support the containment laboratory. How access is controlled is of primary importance. The laboratory director has ultimate responsibility. Access should be restricted to only certified people who are absolutely necessary. Certified means they understand the potential biohazard, have demonstrated proficiency in the laboratory's procedures, and have complied with the health and medical entry requirements. Proper entry and exiting procedures for staff, visitors, and maintenance/custodial workers are clearly established in this section as well. Finally, procedures for identifying, reporting, and correcting problems or violations of protocol are detailed.

Specific facility design and operational procedures

Specific laboratory layout and operations are described in this section. Included are security access mechanisms; self-closing, lockable doors; and other security



Hi

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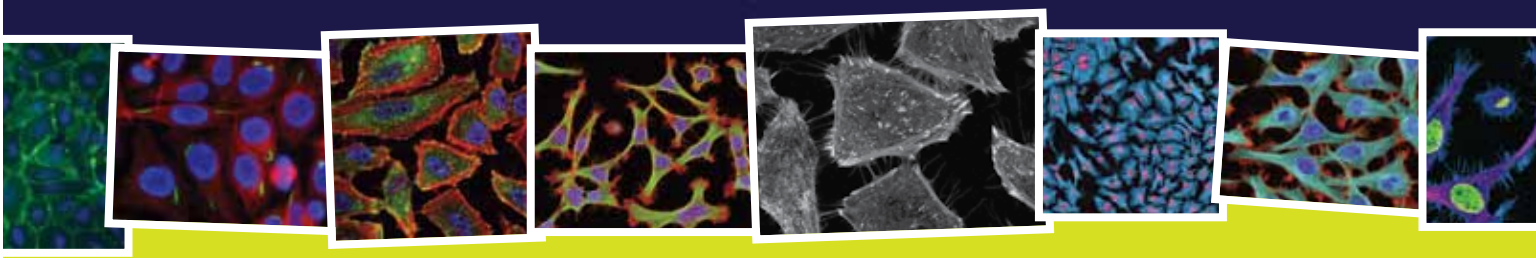
but you may also know me as Hep-2, or even as KB



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DEVELOP A PROGRAM FOR DATING STORED CHEMICALS AND FOR RECERTIFYING OR DISCARDING THEM

By James. A. Kaufman

Some chemicals have a short life expectancy. Others will remain good for a long time. Solvents that form peroxides are one example of substances requiring periodic testing. Ethers, vinyl compounds, alcohols, ketones, and aldehydes are some of the peroxide formers. Your chemical inventory system should provide reminder dates.

Bottles should be marked when they are received and when they are opened. In addition, draw a line on the bottle with a china marking pencil or other marker to indicate the full level. This mark will serve as a useful guide to indicate how rapidly the material is being used up and to gauge the remaining amount.

Peroxide formers need a special label to indicate the required interval for peroxide formers, the date the test is performed, and the initials of the individual performing the test and certifying that the test was successful (negative).

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

measures. Proper signage indicating agents present, contact information for the principal investigator and other responsible people, and any special requirements are posted at all access points. The design of directional airflow from clean areas toward contaminated areas is described, and procedures for checking proper operation by laboratory staff are outlined. Measures are included for checking and ensuring that the surfaces of all walls, floors, and ceilings are smooth, impermeable, and easily cleaned and that all penetrations are sealed. Pest management is addressed here as well, with an appropriate insect and rodent control program.

Special laboratory safety equipment and PPE

This is arguably one of the most important parts of the exposure control plan. It should explain the PPE that must be worn. Describe where PPE is stored as well as when and where it is used and how it is removed and discarded. It should cover the proper types of gloves, eyewear, and gowns or lab coats to be used. This section also addresses proper use and maintenance of the lab's safety equipment such as autoclaves, biosafety cabinets, eyewash stations, safety showers, ventilation alarms, and other specially designed containment equipment. Procedures for decontaminating equipment prior to maintenance work should also be included.

Laboratory research practices and procedures

The heart of the exposure control plan is contained in this section. It addresses safe handling and storing of viable material, including biological safety cabinet use, handling frozen samples, and use of secondary containers. Procedures for using and disposing of sharps, found in most containment laboratories, are paramount. Addressed in this section are waste handling and disposal, decontamination, and housekeeping (e.g., cleaning up at the end of the day or after finishing a research protocol).

Health and medical monitoring requirements

The purpose of this section is to provide another level of protection against laboratory-acquired illness by documenting necessary immunizations. Immune-suppressed individuals or persons at increased risk should be strongly discouraged from entering the facility. Depending on the agents present, vaccinations (hepatitis B), antibody testing (TB skin test), or serum storage may be required. The exposure control plan should clearly define with a well-documented rationale what is required and who is covered.

Emergency procedures

This segment describes procedures for an accident, spill, release, or exposure that contaminates or injures laboratory staff or the environment. A good reference for putting this section together would be the OSHA bloodborne pathogen standard, 29CFR1910.1030.[2] Everyone working in the facility should be thoroughly versed in the emergency procedures. Spill kits should be maintained and biohazard spills decontaminated and cleaned up as soon as possible by properly trained and equipped staff. Any incident should be completely documented with a written report.

Employee training

We wrap up our exposure control plan with the chapter covering employee training. The first step is to make sure everyone who will be working in the containment facility has read and understands this exposure control plan. They should be informed about each infectious agent present, the risks associated with these, and the signs and symptoms of infection or disease. This training, along with bloodborne pathogen training, should be renewed annually and written documentation kept on record.

There you have our quick outline for putting together an effective exposure control plan. We have just touched on each topic briefly in this article. Future articles will probe deeper into select sections, providing additional details as well as tips for success and traps to avoid. Watch this column for more helpful information. As always, the Safety Guys welcome your comments and questions, so we hope to hear from you. Until then, stay safe.

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1. *Biosafety in Microbiological and Biomedical Laboratories*, 5th edition, Centers for Disease Control and Prevention and National Institutes of Health, February 2007. http://www.cdc.gov/biosafety/publications/index.htm
2. OSHA bloodborne pathogen standard, 29CFR1910.1030. http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10051

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

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by Rachel Muenz

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THE CLEVELAND FIRE DEPARTMENT'S MOBILE LAB BEGINS AND ENDS WITH EQUIPMENT

by Rachel Muenz

Born of the anthrax mailing scare of 2002, the mobile lab in the hazardous materials section of the Cleveland Fire Department in Ohio deals with public health risks and the identification of unknown, potentially dangerous substances in the region. In early 2000, that meant going after white powders that could be anthrax.

"Going back to approximately 2002, when we started chasing all the white powders and there were a lot of unknowns, we decided [on] a better way, a better mousetrap if you will, of trying to find unknowns," said Lieutenant Terry Bindernagel of the department's hazardous materials section about how the lab got its start.

The fire department worked with the McCrone Group's Hooke College of Applied Sciences, based in Westmont, Illinois, to develop the lab, which has about eight employees and is fitted onto a 20-foot box trailer, making it easy to transport to sites in Cleveland and the surrounding counties the fire department covers. That vehicle was put into service in 2004.

> "The lab surprisingly has a lot of room for what we have."

"It's used not only for response, but it's also used at events, and [its use] varies," Lt. Bindernagel said about the number of calls the mobile lab responds to annually, adding that because of that variability it's tough to pinpoint an exact average number of calls the lab responds to. "It's based on perceived needs sometimes [as well]."

A typical request for the mobile lab can come from anywhere—either within Cleveland or the surrounding counties—and responding to that call can mean spending from one to eight hours at the site.

"It depends on the situation, how long it takes to get a sample, and [whether] you have to work with other agencies at a scene," Lt. Bindernagel explained. "Sometimes when I go to a scene it's a law enforcement issue—it varies. So you're sometimes working within other people's frameworks."

When the team arrives on-site, they meet with whoever is in charge. Sometimes the fire department itself is in charge, and other times law enforcement or the FBI has control over the situation.

The vehicle that houses the fire department's mobile lab and that transports the lab to various sites in and around Cleveland.

"We show up, and we assist on the scene," Lt. Bindernagel says of working with other agencies. "We work under them–whatever they ask for, whatever they request, we try to provide it."

Lab setup

Like most labs, the Cleveland Fire Department's mobile lab begins and ends with its equipment. "A typical day would be coming down, prepping the equipment, center[ing] the scope … We discharge and charge [the instruments] to try to keep the battery life up on all our equipment, checking out the vehicle; there [are] different things," Lt. Bindernagel said. "A lot of times it's just the maintenance of the lab and preparation."

That maintenance is typically done at least several times a week, he added. The main technology hardware used in the mobile lab includes microscopes, infrared equipment,

and GC-MS as well as radiation meters and meters that can detect volatile organic compounds, because of the response aspect of the facility. A specially designed glove box is also a key part of the lab.

"McCrone helped us develop a glove box; I can look at samples through the microscope, and it's entirely enclosed in the glovebox—I can manipulate [the sample in the glove box] ... and do everything that you could do on a bench," Lt. Bindernagel said. "To the best of our knowledge—McCrone and I have talked about this–this is very unusual; this is not something that I would call standard by any means."

> "The challenge is ... we don't always know what might be the exact best piece of equipment for us."

Though the lab is small, it's set up in such a way that the hazmat team has just the amount of room they need for the job. "The lab surprisingly has a lot of room for what we have," Lt. Bindernagel said. "We have a relatively small space that we can work in as far as bench space ... but outside of that, we planned what we were going to use around how we built the lab, so spacewise and everything, we actually have quite a bit of room."

Continuing education

As far as required education, members of the hazmat team who work in the lab not only have to train with regular firefighting equipment, but they must also be proficient with the specialized instruments in the mobile lab.

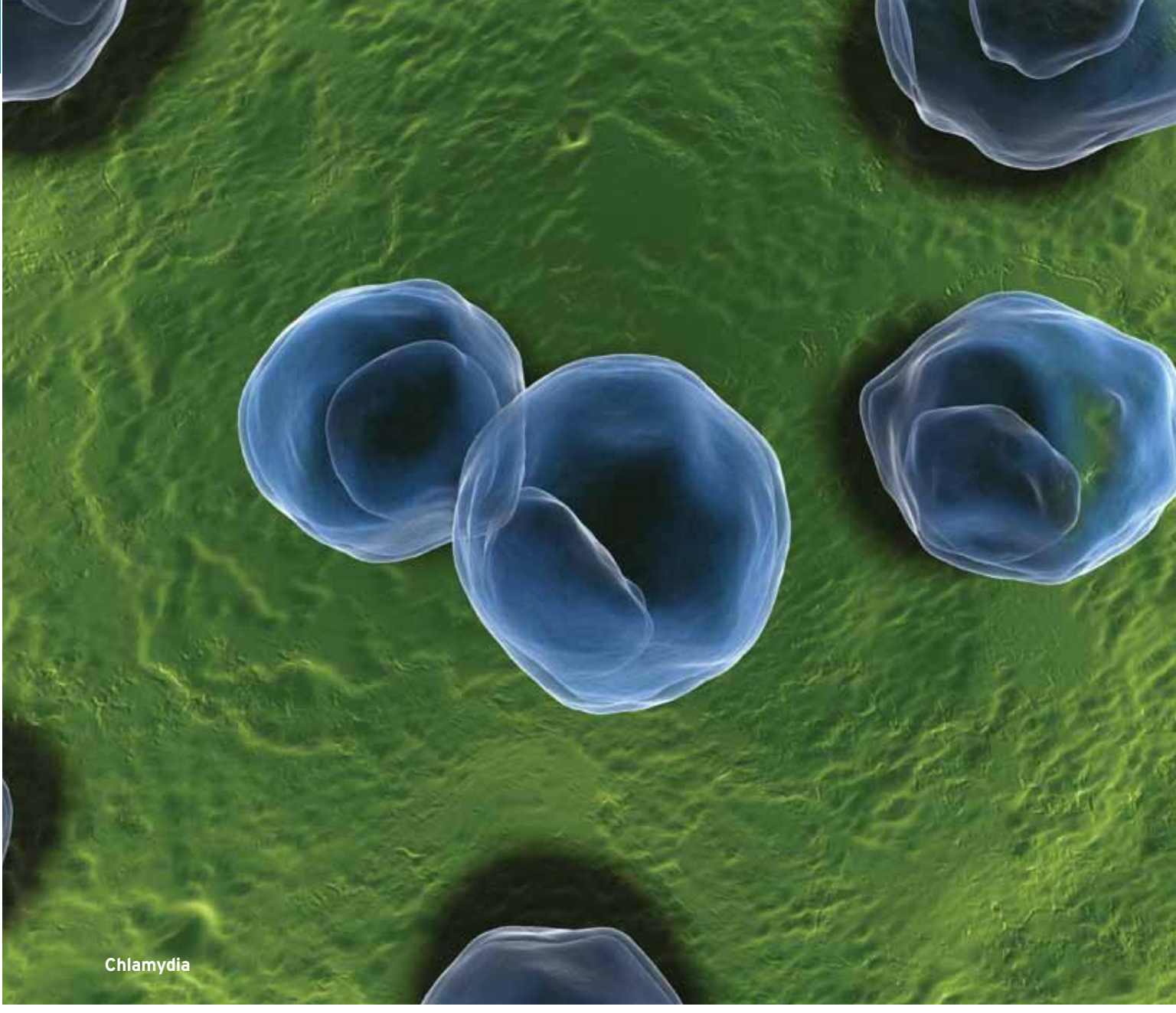
"The training revolves heavily around our normal response equipment, plus we've all gone to the McCrone College of Microscopy [now Hooke College]," Lt. Bindernagel said. "We've also [done work] based on [certain minimums of] the National Response System that we are now trying to meet; there's certain standardized training that a lot of our guys are going through, and surprisingly some of this standardized training actually covers some of the particular pieces of equipment related to the lab."

▲ *The entrance of the Cleveland Fire Department's mobile lab through the rear door of the vehicle.*

He added that some of the technology requires training from outside sources.

"There [are] just two or three pieces of equipment [that] are very specialized [that] require outside training, and one, of course, is the [microscope]," he said. "We get that [microscopy training] through McCrone."

One of the lab's biggest challenges, along with changing technology, is finding the time to make sure staff are up to snuff with all their training, Lt. Bindernagel said. In September



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▲ *The combined glove boxes used in the Cleveland Fire Department's mobile lab.*

alone the department expected to put in about 12 hours of training. "We just have to set aside training time," he said of how the hazmat division meets that challenge. "We have to tell guys that they're going to block off pieces of their schedule for x number of hours on this day, and then on that particular day we meet and we'll take a piece of equipment and we'll start to work at it." He added that Hooke College has continued to be a big help in keeping the mobile lab team's skills sharp.

"The Hooke College people have assisted me greatly from the standpoint that they offer things, like they'll send us an unknown and then they monitor us; for example, you can call them back and say 'We had trouble with this or trouble with that,' and they just walk us through it," Lt. Bindernagel said. "That's just one example."

Many of the hazmat division's equipment vendors also provide courses for the more complex technology featured in the hazmat lab.

"A lot of manufacturers, when you get into equipment that's either (a) technical or (b) it's expensive, or both, every other year they'll say, 'Hey, do you want us to come down and do some continuing ed for you?'" Lt. Bindernagel said. "So that's assisted us greatly—a lot more people are getting on board. [But] the people at McCrone have probably been head and shoulders above most of the other people we've worked with."

While outside agencies are a key part of keeping staff training current, Lt. Bindernagel said the team members also practice themselves while they are out on a call. "A lot of times, we'll actually be in response, we'll be working on something, and we'll think of [a piece of training]," he said. "So what we're doing in response [is] we're going back and revisiting some of the things and pulling out our old manuals and looking at things."

That means running extra tests, even if they aren't absolutely necessary. "Sometimes we go out of our way to run a test on something even though we know it won't give us the results that we need to make an ID, but we'll do it anyway to confirm it,"

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said Lt. Bindernagel, who has been a firefighter for 30 years. "It's just a way of keeping ourselves abreast of how to use that piece of equipment."

Apart from training and maintenance and a high changeover of lab personnel, choosing the best technology for the lab is also often a challenge.

"As equipment comes on [the market], we'd love to see it put into our environment, but it's not always that easy," Lt. Bindernagel said. "The challenge is … we don't always know what might be the exact best piece of equipment for us."

to say they've been very pleasantly surprised when they see the lab and they see its capabilities," he said.

The people he works with and the challenge and variety the job provide are other reasons Lt. Bindernagel loves his work.

"Working in a large city department like I do—Cleveland, Ohio—there are multiple opportunities, there [are] a lot of things you can explore, different areas you can work within, different bureaus–it's very much a great time," Lt. Bindernagel said. "It's been a great time for 30 years."

"Working in a large city department like I do—Cleveland, Ohio—there are multiple opportunities … It's been a great time for 30 years."

Best parts of the job

Lt. Bindernagel said using the equipment and getting the results needed are the things he likes best about being a part of the mobile lab's team.

"When you start to use the equipment, it's very much like the pieces start to fall in order and you start to see what's happening; when the equipment works in the manner where [the pieces] complement one another–that's what I find very satisfying," Lt. Bindernagel said. "Then you know things are working out the way that you anticipated them to."

Some of the most interesting calls he's dealt with have involved working with other agencies.

"When we work with outside agencies and they're not familiar with what we're trying to do, I would have

A robotic future

In the future, Lt. Bindernagel would like to see the mobile lab's use expanded to a larger portion of the state of Ohio.

"I think it's an asset," he said of the lab. "I'd like to invite people who, for example, work for the health department and [people] along those lines to become part of the response team. I think that would be very appropriate. To date, that hasn't happened, but I think a lot of that is because of logistics; just because of where we are located in the state, it's very hard."

Going robotic is another thing Lt. Bindernagel has been working on with NASA, with hopes of integrating robots into the Cleveland Fire Department's lab.

"We're actually now trying to work robotics into our lab; in other words,

A closer look at the unique glove box with built-in microscopy used by the Cleveland Fire Department's hazmat division.

we can send the robot in with certain pieces of our equipment to try to at least get readings," he said. "It's going to be somewhat limited on which equipment it can take in, but we're trying to work it out now where we can get remote readings—we [won't] have to commit personnel."

Aside from being safer, robotics will also provide another important benefit.

"We also think it's going to save time," Lt. Bindernagel said. "So we're just taking it from there."

Rachel Muenz, *assistant editor for* Lab Manager Magazine*, can be reached at rachelm@labmanager.com or by phone at 888-781-0328 x233.*

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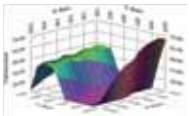

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Early last month, Bruker launched two LC-triple quadrupole (LC-TQ) mass spectrometers—the high-performance EVOQ Qube™ and the ultra-high sensitivity EVOQ Elite—at the 2012 Japan Analytical Scientific Instruments Show (JASIS).

These systems are setting new standards for analytical performance and quantitative robustness. Despite featuring several innovations, however, the EVOQ platform is simple to use.

"Our intention was to make the EVOQ LC-TQ very intuitive to use, whether the users are analyzing pesticides in water using our new Advance UHPLC with on-line extraction (OLE) capability for high volume injections, or quantifying peptides in plasma," said Bruker's EVOQ product manager, Jonathan McNally. "Our goal is to allow the user to focus on solving the analytical problem, and not be distracted by the instrument parameter operation."

He added the EVOQ simplifies MRM-based quantitation with Bruker's unique Compound Based Scanning (CBS), which makes MRM methods development simple, and MS-MS as easy to use and deploy as single quadrupole mass spectrometry.

The main advances in the new platform include the industry's first vacuum-insulated probe (VIP) heated electrospray technology, which preserves and ionizes thermally fragile molecules with excellent sensitivity. Novel PACER™ software which enables 'exception based data-review', a feature that significantly reduces the error rate for quantitative analysis, was another big innovation unveiled in Japan.

"Our customers need to run more samples, spend less time cleaning and re-tuning instruments, and use software to minimize errors associated with the daily review of thousands of chromatograms," said Bruker CAM division president Collin D'Silva. "The EVOQ with PACER software delivers significant value to a laboratory whose core focus is providing time-sensitive quantitative data."

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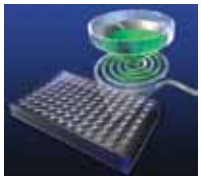

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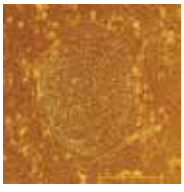

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DUCTLESS FUME HOODS; A REALITY FOR THE FUTURE OF SUSTAINABILITY AND STEWARDSHIP

Why go ductless and how Aura® can meet your safety and environmental stewardship objectives!

As the importance of environmental protection and operator protection grows so too does the need for advanced ductless fume hood technology. The ductless hood provides an environmentally sound, safe and energy efficient solution for most laboratory air pollution control needs. Bench space is at a premium as the trend toward flexible, smart laboratory space becomes standard. In a world of sustainability, green and flexible laboratories, filtration hoods are the best solution available.

The days of fixed, ducted hoods as the only solution are numbered. They simply cannot provide the operator and environmental protection necessary for the 21st century. The ductless fume hood is the way forward for the modern laboratory. For example, fixed, ducted hoods do not neutralize chemicals but merely disperse pollution it into the surrounding environment. In addition, ducted hoods protect the operator through cumbersome roof-mounted blowers, and maintenance heavy, problem prone ductwork. Advanced filtration hoods adsorb/absorb pollutants, pulling them out of the environment. They do so though laboratory tested filtration technology bypassing ductwork and blowers.

While fixed exhaust hoods utilize simple technology, their maintenance is ever in flux. Ductwork and blowers require constant and expensive upkeep, consuming thousands of dollars in maintenance. Ducted hoods pull air out of the laboratory stressing the HVAC system to constantly return new conditioned air into the room resulting in larger utility bills with ever shrinking budgets. Current technology found in today's modern ductless fume hoods require minimal maintenance and re-circulate conditioned room air. This vastly reduces the amount of electricity used, saving thousands of dollars on energy and maintenance bills.

With today's advanced technology almost any work situation involving the use of chemicals or particulate can be made safer utilizing capture and filtration systems. Utilizing gas phase filtration and recirculatory technology these systems adsorb and capture gases that occur in many laboratories worldwide.

Since 1959, Mystaire® Misonix® has designed, developed and manufactured exposure control equipment for operator safety. The Mystaire® Misonix® Aura® ductless chemical fume hood provides optimal operator protection while performing routine laboratory manipulations with liquid chemicals or powders. By incorporating the Aura® ductless fume hood into your laboratory design, you eliminate excessive installation cost and include maximum flexibility into the design.

Aura® establishes negative pressure at the opening pulling contaminates into the filtration zone. Aura® ductless fume hoods are ASHRAE 110 tested for containment and are designed to meet ANSI Z9.5, OHSA 1910.1450 and SEFA 9 standards and guidelines. The filtration zone media configuration will depend on the application performed within the enclosure. Mystaire® Misonix® offers a wide variety of activated and chemisorptive specialty carbon blends as well as HEPA and ULPA filtration to meet your application needs. Mystaire® Misonix®'s qualified technical staff will review the application and recommend the proper media package for your chemistry.

Aura® ductless fume hoods not only provide superior operator protection but promote environmental stewardship. The Aura® ductless fume hood simply recirculates the filtered air inside the laboratory space while removing harmful toxins from the airstream. Unique to Aura® is the Filtrak™ positive sealing system which ensures the main filters have an airtight seal. This exclusive feature prevents toxic gases from bypassing the filtration media.

Advanced monitoring and control is critical to operator safety. Aura® ductless fume hoods come standard with the EverSafe II™ microprocessor safety controller. EverSafe II™ uses sophisticated control methods to determine chemical breakthrough. In addition, EverSafe II™ monitors fume hood face velocity and maintains user set value without operator inaction. Visual and audible alarms signal to the operator if airflow reaches an unsafe level or if the filters approach saturation, allowing sufficient time for main filter replacement.

Mystaire® Misonix® ductless fume hoods are a safe, environmentally friendly and cost-effective alternative for laboratory personnel protection. Mystaire® has designed and developed advanced environment safety and pollution control products since 1959. For more information on Aura® ductless fume hoods and other products please contact Mystaire Misonix at+1 919-229-8511 or visit www.mystaire.com.

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Selecting a Quality Antibody, Every Time

Problem: Poor quality antibodies are a major stumbling block for scientists detecting new protein targets in immunological applications. The prevalence of such antibodies is significant; reactions to recent, high-profile retractions of several papers containing disingenuous Western data support this. Judging by responses to these events, it is evident most scientists have crossed paths with an inferior antibody at some point. A perceptible hint of distrust lingers over these reagents, and understandably so–immunological applications such as Western blotting and immunohistochemistry (IHC) can fail simply because of a substandard antibody. Direct consequences usually take the form of non-specific bands and staining patterns, but the real damage is often done to scientists' time and resources.

Not all antibodies, however, are created the same. There are plenty of high-quality antibodies out there, in addition to companies that care about producing ones that work. Steps can and should be taken, where appropriate, to avoid inferior antibodies and eliminate them from the selection process *before* they make it to your bench.

Solution: In addition to your usual literature search, use antibody comparison sites and search engines when sourcing antibodies to fit new scenarios in the lab. Comparison sites allow you to weigh up cost and application data of multiple vendors in one place, and search engines maximize your results. Cross-reference the literature for products that have a good track record in publications.

When you begin your search keep in mind your basic criteria: which application is your top priority? Is a polyclonal or monoclonal antibody better suited? Where is your protein or epitope of interest located? Is it subject to post translational modification? Being clear on the answers to such questions will help you conduct your antibody search more objectively.

When you've identified a potential antibody, look at the validation data provided by the vendor; check depth and quality. Is there simply a verification of antigen recognition by ELISA testing or are there Western and IHC data too? (The more validations, the better.) Check the types of samples used for validation. Make sure you're viewing data obtained with whole tissue or cell lysates as opposed to those prepared with purified recombinant proteins–the latter are not accurate representations of antibody performance.

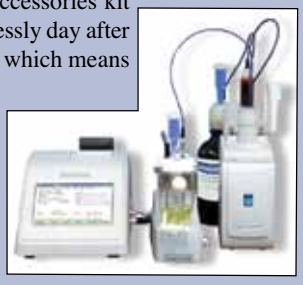
▲*Western blot validations hanging up in the Proteintech lab.*

If your only options lie in under-evaluated antibodies you can still find a diamond among the antibody rough–and in a risk-free environment with the right company. Look for vendors offering trial samples or covering their products with a money-back guarantee. (With the latter you can try larger volumes, still confident that you're not wasting any of your grant money.) Guarantees should be 'no-quibble' and the best ones will offer the option of your full money back as opposed to credit.

Seeking out companies producing their own antibodies, as well as the larger antibody 'supermarkets,' has its merits. The former know their products inside and out, and can detail everything about an antibody's production process. They can often perform validations at your request and can send you hard copies of their original validation data. These companies are also more likely to offer comprehensive and guaranteed custom production services in the event your search for a reliable pre-made antibody is unsuccessful.

For more information, visit www.whyitworks.ptlab.com

KF Volumetric Titrator - Rugged, Long Lasting and Eco-Friendly. The **AQUACOUNTER® AQV-2200S** is designed with small volume titration cells requiring only 20mL of titration solvent for accurate measurements. Less reagent volume reduces waste and makes it easy to replace fresh solvent for the next series of measurements. This unit has a superb accessories kit and performs flawlessly day after day, year after year which means long-term value for the money spent.



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The **AQUACOUNTER® AQ-2200S KF Coulometric Titrator** is ideal for the trace level water content determination with excellent capability and upgraded performance. It will be of interest for users who have many kinds of samples to be analyzed, exchange KF reagents frequently or after each measurement, and are eco-minded and budget-conscious.

This titrator allows two titration stations to run parallel with various coulometric/volumetric combinations. With both a volumetric and coulometric channel, one can measure moisture over the entire range from 2 ppm to 100% or double your sample throughput with 2 identical KF stations.
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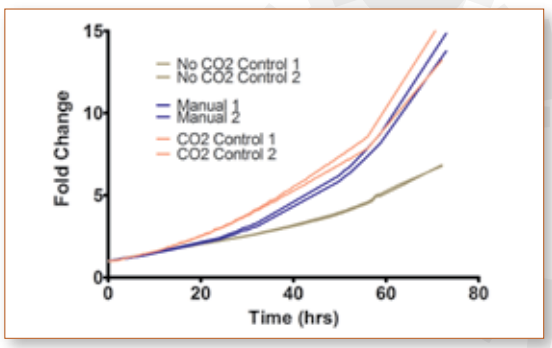
A Microplate Reader with Environmental Control

Problem: There is little doubt that cell-based assays are becoming a mainstay across the pre-clinical drug discovery process. Many of these assays are end-point based, where live cells are cultured in microplates, incubated with compounds of interest and then lysed to release the contents of the cell such that they can be assayed with reagents subsequently added to the wells. Often, the incubation times required for the assay can be counted in the minutes to decades of minutes, such that maintaining a controlled environment for cell health is not a significant concern. For those end-point assays that require longer incubation times of hours to decades of hours, controlled environments become a substantial concern and requirement. Depending on sample throughput required, this can be accomplished by manual intervention and placing the microplate(s) in a standard CO_2 incubator or by robot into a microplate hotel.

Yet there is a growing trend in the use of live cell assays, where the cellular response to compounds is monitored kinetically through the use of non-toxic, cell membrane permeable reagents or phenotypic methods. This real-time response gives researchers an additional level of information that may be missed in single time point, end-point assay. While these live cell assays are easily incorporated into workflows for assays conducted over an hour or so, longer term responses can be problematic to obtain due to the difficulty in maintaining a controlled environment over the microplate to maintain cell health while kinetically reading the cellular response.

Solution: The addition of an atmosphere control unit to a microplate reader offers a solution to this problem by providing a controlled environment within the microplate reading chamber in which live cells can be nurtured. BioTek's Synergy H1, for example, has a number of features that are important for successful live cell assays, including precise temperature control up to 45°C, controlled shaking of the microplate, and a gas controller module that allows control and monitoring of CO_2 and O_2 within the reading chamber. The precise control of both CO_2 and O_2 allows adjustment to the optimal physiological conditions up to 20 percent and down to nearly 0 percent for hypoxic and nearly anoxic conditions that many live cell assays require. Microplate readers with these features combined are ideal for kinetic live cell assays.



▲ *Comparison of mouse NIN3T3-GFP cell growth conditions.*

In particular, the Synergy H1 microplate reader has quadruple grating monochromator optics for fluorescence intensity measurements from the top or bottom of the microplate. UV-Vis and luminescence measurements can also be made with the system. The reader's optics are modular, with an option to add filter-based fluorescence along with monochromator-based fluorescence.

To confirm the efficacy of the Synergy H1 system for live cell assays, mouse NIH3T3-GFP cells were compared using three microplate-based growth conditions:

- incubation in a dedicated tissue culture chamber with a manual transfer of cells to the microplate for analysis,
- incubation in the microplate reader chamber without CO_2 control, and
- incubation in the microplate reader with 5 percent CO_2 control and monitoring

Cell growth was monitored by GFP fluorescence detection, with readings taken every two hours for the manual method and every 30 minutes for the reader incubated methods over a total 70-hour runtime. As seen in Figure 1, data is expressed as a fold increase over time and shows comparable growth rates for manual and Synergy H1 equipped with the gas controller. The microplate reader method where CO_2 was *not* used shows significantly lower cell growth.

For more information, visit http://www.biotek.com/products/microplate_detection/synergyh1_hybrid_multimode_microplate_reader.html

A Gas Control Module in a Multimode Microplate Reader

Problem: Performing long-term, cell-based applications with living cells using a multimode microplate reader is becoming more and more popular in life science research. There are various absorbance-, fluorescence- and luminescence-based assays that require alternating cell incubation and signal detection over a long period of time–from several hours up to several days–including reporter assays, proliferation and viability studies, cytotoxicity and cell death studies, and many more. Besides optimizing the optical properties of the detection device, the major requirement for these applications is to keep cells viable and proliferating throughout the whole experimental period.

At present, a tedious transfer of the microplate between a common cell incubator and the microplate reader is the standard procedure, but has critical drawbacks. Without costly robotic solutions, the user has no choice but to manually transfer the plate for each detection step, increasing the risk of contamination and resulting in the loss of data, especially for overnight experiments. Furthermore, when incubating at low oxygen levels, transferring a plate from the incubator to the reader results in a change of environmental conditions, which can critically affect the outcome of the study.

Solution: The simplest solution to this problem is a microplate reader offering rigorous environmental control inside the measurement chamber, particularly the regulation of atmospheric gas concentrations.

For example, the Infinite® 200 PRO multimode reader is the first fusion of a microplate reader and a cell incubator on the market. Tecan's patent pending Gas Control Module (GCM™) allows independent and simultaneous control of oxygen (0.1-21 %) and carbon dioxide (0-10 %) concentrations inside the reader's measurement chamber, with an altitude correction function to allow automatic compensation for variations in the atmospheric partial pressure of CO_2. This ensures greater biological relevance for a wide range of studies, extending the experimental window for microplate-based investigations in proliferation studies (especially with anaerobe and facultative anaerobe bacteria), and allowing close replication of hypoxic and physiologic conditions for eukaryotic cells.

The GCM can also be used with pre-mixed gases, enabling flexible environmental control for a broad range of cell biology applications and ensuring excellent viability and proliferation for various cell types, throughout the whole period of analysis. The system's process security features include both audible and visual warnings to alert the user of changes in gas pressure or flow, as well as continuous monitoring to easily identify if the target concentration will not be reached or deviates significantly during incubation.

◀*The Infinite® 200 PRO multimode reader from Tecan.*

Tecan has conducted several studies to evaluate the Infinite 200 PRO's GCM-related functions, including proliferation of GFP-transfected human epithelial carcinoma cells inside the microplate reader over a period of 75 hours. In this study, cells incubated at five percent CO_2 stayed viable and kept proliferating throughout the experiment, whereas cells incubated without CO_2 regulation ceased proliferation and began to die within 24 hours. In a second experiment, it was demonstrated that hypoxia could be induced as efficiently in the Infinite 200 PRO as in a common CO_2/O_2 cell incubator, eliminating the need for a separate O_2 incubator and offering complete workflow automation. Finally, it was demonstrated that growth studies with facultative anaerobe bacteria, such as *Helicobacter pylori*, can be quickly and conveniently performed. *H. pylori* cells were grown inside the reader at five percent O_2, ten percent CO_2 and 37°C for 27 hours, with OD_{60} measurements every hour.

To minimize evaporation during long term incubation periods inside the reader, Tecan recommends using Thermo Fisher Nunc™ Edge plates. The evaporation moats built into these plates provide passive humidity control, reducing evaporation to insignificant levels for incubation periods of up to three days. Cell biology-oriented functions, like those included in the Infinite 200 PRO, such as enhanced fluorescence bottom reading with Optimal Cell Reading (OR), for a better sensitivity and reproducibility in applications with adherent cells; efficient shaking capabilities, for a better optimization of the growth of suspensions cells; automated Z-focusing for top reading fluorescence measurements, to maximize signal-to-blank ratios when working with colored cell media; and precise temperature control can help users set new standards for cell based assays.

For more information, visit http://www.tecan.com/gcm

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The new PRESTO® from JULABO represents the state-of-the-art in liquid temperature control for modern laboratories. Models in this redesigned line of temperature-control instruments are the air-cooled A30, A40 and the water-cooled W40. These instruments cover a working temperature range of -40 to +250 °C with 1.2 kW of cooling capacity and 2.3 kW of heating capacity.

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The A80 and W80 have an operating range of -80 to +250 °C with 1.2 kW of cooling capacity and 1.5 kW of heating capacity. Related A80t and W80t models provide additional heating power: 2.8 kW. The newest models, W91 and W92, supply 11 or 31 kW of cooling with options for heating (12, 24 or 36 kW) and pump capacity over a temperature range of -92 to +250 °C. Maximum heating capacity can be adapted to fluctuations in the main power supply. Highly efficient components give these instruments the ability to compensate for exothermic and endothermic reactions with extraordinary speed. The new PRESTO® units are extremely robust and work reliably even if the ambient temperature climbs as high as +40 °C.

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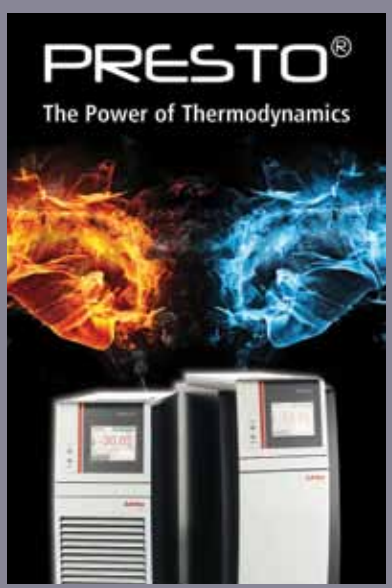
JULABO is a manufacturer of liquid temperature control systems for research, science, laboratories, pilot plants, and industrial processes. Since its founding in 1967, JULABO has been a driving force in the development of instruments for liquid-based temperature control. The company offers an extensive range of solutions covering a temperature range of -95 to +400 °C. JULABO's product line includes temperature-control instruments for a wide range of applications. Heated and refrigerated circulators are ideal for virtually any application within the range of -95 to +400 °C and are available with an extensive selection of features and capabilities. JULABO water baths are high-quality and robust products that utilize the latest microprocessor technology. They are designed for the temperature range of +20 to +99.9 °C. Advanced heating and cooling systems from JULABO control the temperature of more complex systems, such as jacketed reaction vessels. They offer scientists tremendous flexibility across a temperature range of -92 to +250 °C. JULABO recirculating chillers are used for a wide range of cooling tasks in industrial environments. Users can choose from an extensive product line, including air- or water-cooled refrigeration units and cooling capacities ranging from 0.3 to 20 kW. JULABO also offers instruments designed for highly specific tasks and an extensive selection of accessories.

For more information, visit www.julabo.com



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16. Publication of Statement of Ownership for a Requester Publication is required and will be printed in the October 2012 issue of this publication.

17. Signature and Title of Editor, Publisher, Business Manager, or Owner: Mario G. Di Ubaldi — Date: 09-20-12

I certify that all information furnished on this form is true and complete. I understand that anyone who furnishes false or misleading information on this form or who omits material or information requested on the form may be subject to criminal sanctions (including fines and imprisonment) and/or civil sanctions (including civil penalties).

PS Form **3526-R,** September 2007 *(Page 2 of 3)*

ADVERTISER INDEX

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Agilent Technologies	www.agilent.com/chem/selectcrosslab	7 & 100
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BINDER, Inc.	www.binder-world.us	76
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Brandtech Scientific, Inc.	www.brandtech.com	74
Buck Scientific	www.bucksci.com	41
CEM	www.cem.com	45
Conquer Scientific	www.conquerscientific.com	97
ELGA LabWater / Veolia Water	www.vwr.com/elga	3 & 19
EMD Millipore	www.millipore.com/ultrapure	11
Environmental Express	www.environmentalexpress.com	71
Eppendorf North America	www.eppendorfna.com	5
Equipnet, Inc.	www.equipnet.com	97
GenTech Scientific, Inc.	www.gentechscientific.com	97
HEMCO Corporation	www.hemcocorp.com	23
International Equipment Trading, Ltd.	www.ietltd.com	97
JM Science Inc.	www.jmscience.com	90
Julabo	www.julabo.com	29 & 94
KNF Neuberger Inc.	www.knflab.com	55
Labconco	www.labconco.com	43
LabX	www.labx.com	96
Lancer USA Inc.	www.lancer.com	73
Mettler Toledo, Inc.	www.mt.com/us-glantleap	49
MIDSCI	www.midsci.com/TPP	79
Miele, Inc.	www.labwasher.com	33
Mystaire Inc.	www.mystaire.com	88 & 89
NuAire Inc.	www.nuaire.com	9
Panasonic Healthcare	www.twinguardseries.com	99
Pittcon	www.pittcon.org	95
Pro Scientific Inc.	www.proscientific.com	65
Pronton Onsite	www.protononsite.com	47
Puritan Medical Products, LLC	www.puritandiagnostics.com	75
Quadrex Corporation	www.quadrexcorp.com	37
RADWAG USA L.L.C	www.radwagusa.com	69
RDM Industrial Products, Inc.	www.labspacesolutions.com	27
Supelco / Sigma-Aldrich Co.	www.sigma-aldrich.com/express5	13
Thermo Fisher - Unity Lab Services	www.unitylabservices.com/smartcapture	77
Thermo Scientific	www.thermoscientific.com/tc	25
Thermo Scientific NanoDrop	www.thermoscientific.com/nanodrop	2
Universal Electric	www.starlinepower.com	39
USA Scientific, Inc.	www.usascientific.com/ergoone	21
Vacuubrand, Inc.	www.vacuubrand.com	78
W.A. Hammond Drierite Company	www.drierite.com	64
Wyatt Technology	www.wyatt.com/	17

PRE-OWNED EQUIPMENT MARKETPLACE

PARTING POINTS

Takeaways from this month's issue:

WINNING THE TALENT WAR

Since the end of the recession, the war for talent rages anew in some laboratories. However, simply screening large numbers of résumés will not enable your laboratory to win the talent war and hire the best candidates, you must also:

- Guide candidates to your website where they must answer questions related to the job
- Avoid advertising on big job boards but post on your own website and science job sites
- Clearly define the skills, experience, and personal characteristics you are looking for
- Find passive candidates

10

20

THE SIXTH ANNUAL SALARY & EMPLOYEE SATISFACTION SURVEY

This year's results continue to reinforce the idea that laboratory professionals are for the most part happy in their careers and derive meaning and satisfaction from the work they do. Some of the main findings include:

- Longevity is the hallmark of the scientific research profession
- Three percent more respondents now had managerial responsibilities than did in 2010
- Compared with 2010, there has been very little change in compensation
- Respondents seem to be more certain in their futures within their organizations

24

CAREER COUNSELING

The era of the one-company, 40-year career is over. To succeed in this constantly changing career environment, it is best to focus on six lifelong competencies that are transferable from one job to another and from one career to another. Four of these include:

- Having a long-term perspective on your career
- Satisfying your customers' ever-changing needs
- Becoming and remaining a creative, effective, and efficient problem solver
- Developing a global perspective

30

THE CHALLENGES OF HIGH PERFORMANCE COMPUTING

The unrelenting increase in the daily volume of data generated in modern scientific laboratories poses tremendous challenges for managers and directors tasked with facilitating optimal performance while simultaneously minimizing power usage by computing systems. Some tips to deal with this include:

- Get together with lab management teams to assess the budget of the system
- Once equipment is ordered, will it be set up and running in 6 weeks or 6 months?
- Keep researchers involved in the procurement and management of computing systems
- Containers or pods are an alternative to data centers as they are smaller/more efficient

62

CHOOSING THE RIGHT IT SYSTEM AND DATA INFRASTRUCTURE

Alexander Sherman discusses why the right choice and setup for data collecting, data handling, and data sharing infrastructure is important to help establish successful research collaborations. Some of his key points include:

- Think first about all the different types of data labs can possibly collect from patients
- Consider whether and which data can be shared
- The need to agree on the common data elements (CDEs) to capture and the nomenclature of biosamples to be used, as well as what to put on the vial
- Careful planning is a must

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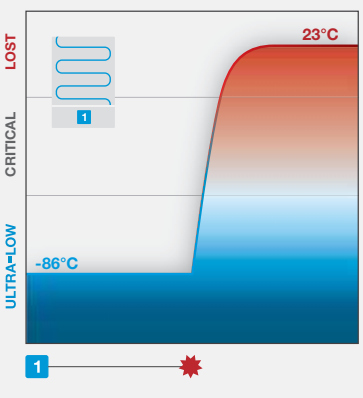

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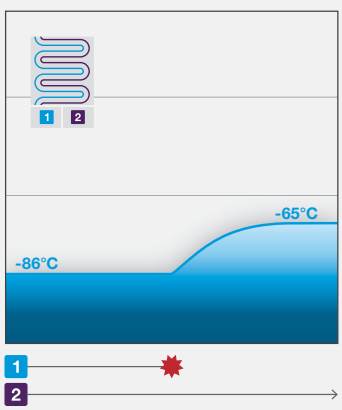

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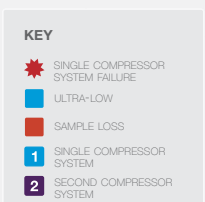

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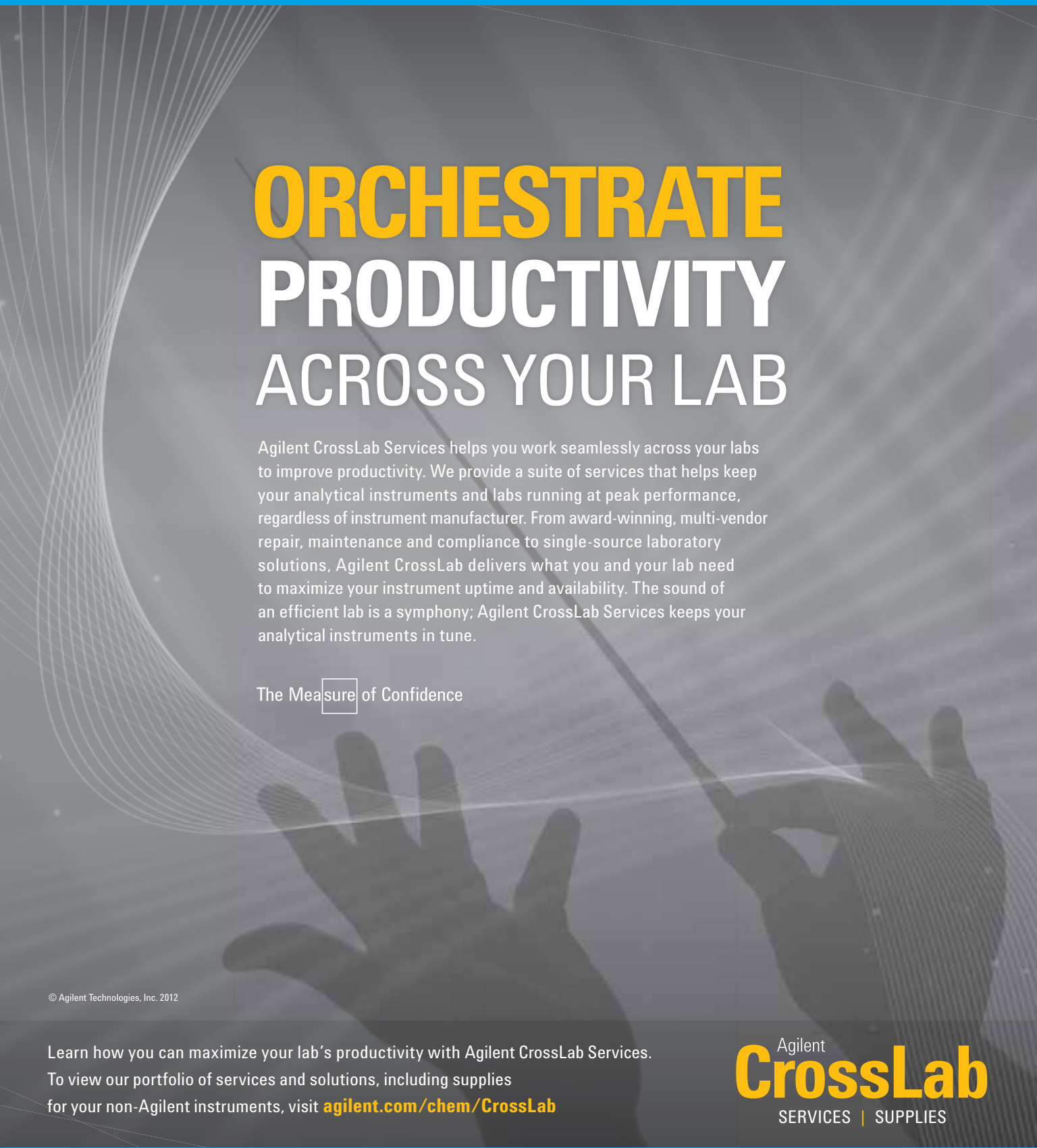

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