June 2019
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June 2019

contents

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feature

10 AI & IoT: A Powerful Combination
How two broad technologies are influencing life in the lab.
John Joyce

14 Purchasing Trends Survey
Growth seen in research activities and investments.
Catherine Crawford-Brown

labs less ordinary

18 The University of Rhode Island's AI Lab
Artificial Intelligence Lab is first to be housed within a library.
Lauren Everett

business management

22 Lab Accreditation
How to ensure a smooth transition to ISO/IEC 17025-2017 accreditation.
Prashant S. Umare

asset management

28 Maintenance and Repair Services for Sophisticated Instruments
Multi-vendor service providers must adapt to meet their customers' needs.
Michelle Dotzert

leadership & staffing

32 Change Management
Consulting experts offer tips on the change-management process.
Donna Kridelbaugh

health & safety

36 Maintaining Control
Guidelines for handling controlled substances in research labs.
Vince McLeod

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TRENDS AND FUTURE VISION

This month's issue features the results of our Purchasing Trends Survey. Nearly 800 readers responded to this year's survey to help reveal trends in the types of purchases lab managers are currently making, as well as insight into what changes they expect to see to their budgets in the upcoming year. Overall, results show healthy growth in research activities and investment, but as expected, limited funding is still having an impact. See more detailed results and analysis of the results on page 14.

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DEPARTMENTS

industry insights

40 Assay Development: Vaccines
Developing specialized assays to assess vaccine efficacy, exposure, and safety.
Michelle Dotzert

ask the expert

44 Ask the Expert
Developments in cell engineering and therapy.
Tanuja Koppal

product focus

46 Next-Generation Sequencing
Library preparation is a critical step in the workflow of several NGS paradigms.
Brandoch Cook

48 PCR/qPCR
Deciding on a PCR detection method.
Mike May

50 Robotic Workstations
Automation in drug discovery.
Angelo DePalma

51 Shakers
A primer on digital shakers.
Brandoch Cook

in every issue

23 Infographic Optimizing Ion Exchange Chromatography Buffers

54 Technology News The latest equipment, instruments, and system introductions to the laboratory market.

60 ASK LINDA Automated lab instruments.

61 Pre-owned Equipment Marketplace

61 Advertisers Index

62 Lab Manager Online

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innovative lab solutions

What measures do you take to drive innovation in your lab? From installing new "smart" equipment to simply encouraging a collaborative work environment, innovation promotes new discoveries and breakthroughs. This month's issue threads the theme of innovation throughout our articles.

The cover story, "AI and IoT: A Powerful Combination" provides an informative overview of artificial intelligence and Internet of Things devices and how they can be best used to connect instruments and provide data in laboratories. As author John Joyce, PhD, notes, both AI and IoT are viewed as "umbrella" terms, meaning they are very broad, and numerous other terms such as "machine learning" can fall under one or both of these categories. Joyce breaks down the true definitions of AI and IoT for us, what purposes they serve, and how they complement each other for use in laboratory settings. Turn to page 10 to learn more.

The AI Lab at the University of Rhode Island is also working to demystify the field of artificial intelligence by offering resources, educational programs, and events that help answer questions of AI in both science labs and the real world, as well as address the ethics behind the use of this technology. URI's AI Lab is the first in the nation to be located within a library, a strategic decision made by Harrison Dekker, interim lab director, and Karim Boughida, dean of libraries at URI, to promote an open-door environment for anyone who is interested in learning more about AI and its potential applications. "People have a stereotypical view of what librarians do or what goes on in a library. It's important for more libraries to be involved with these new, emerging conceptual spaces," says Dekker. Read more about the AI Lab on page 18.

As research evolves and lab instruments become more advanced, service providers also need to keep up and adapt to the latest technologies. This month's Asset Management article (page 28) discusses how multi-vendor service providers are shifting their focus to better resolve clients' needs. "We see greater needs in areas such as training, applications consulting, and a desire for capabilities such as predictive diagnostics to help with workflows," explains Agilent's Kristin Giffin, VP and GM, Services and Support Division, and Marc Boreham, VP and GM, Laboratory Enterprise Services Division.

An additional special feature included in this issue is the results of our Purchasing Trends Survey. We asked our readers a series of questions regarding their lab's budget, in what areas they plan to increase or decrease spending, plans for expansion, and adopting new technologies, among others. Regardless of the type of lab you run, most managers would agree that financial limitations are a top concern. Take a look at our survey results to see how our key takeaways from the survey relate to your lab.

Best,

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AI & IoT: A POWERFUL COMBINATION

HOW TWO BROAD TECHNOLOGIES ARE INFLUENCING LIFE IN THE LAB

by John Joyce, PhD

Two informatics fields that are currently undergoing rapid evolutionary development are artificial intelligence (AI) and the Internet of Things (IoT). As a result of AI and IoT being complementary fields, with the synergy between them greatly enhancing the capabilities of each entity, you don't see the competition for resources that you might normally expect. The key to understanding this is to realize that AI functions best with vast amounts of data, while IoT devices are ideal sources for supplying the required information streams.

> "A number of instruments that take advantage of the power of AI are already on the market."

Artificial intelligence

AI is an umbrella term that is frequently used but often misunderstood. It is also a term that many people are reluctant to use, in part because past AI revolutions had been vastly overhyped. Frequently, AI terms are categorized by their capabilities:

- **Type I—Reactive AI:** This is one of the most common and basic types of AI. It performs very well in the specific field that it is trained in. IBM's Deep Blue is an instance of this AI type.
- **Type II—Limited Memory AI:** In this type of AI, the limited memory refers to the limited retention time of memory. Think of it like the short-term working memory in a human. This is the type of AI employed in autonomous vehicles, as the data stored provides a reference point against which it can control.
- **Type III—Theory of Mind AI:** Reflecting what cognitive scientists refer to as a "theory of mind," this type of AI cannot only form representations regarding what it senses, but it can also recognize that other entities, such as people, will have their own contrasting representations.
- **Type IV—Self-Aware AI:** This is an extension of Type III AI to the point that it is self-aware. The android Commander Data from *Star Trek: The Next Generation*, could be considered an example of this AI type.

When most people inquire as to the type of AI in a system, what they are really wondering about is "how does it work?" In most of those instances, they are probably dealing with a Type I AI, and a rough explanation would be based on what approach or algorithm[1] it uses. Some of the most common approaches are:

- **Machine Learning:** An iterative procedure that uses one of a variety of algorithms to automate the building on an analytical model.

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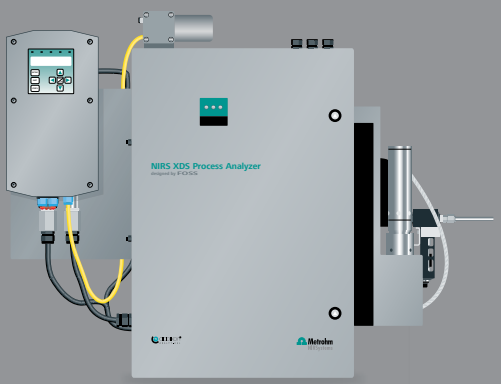

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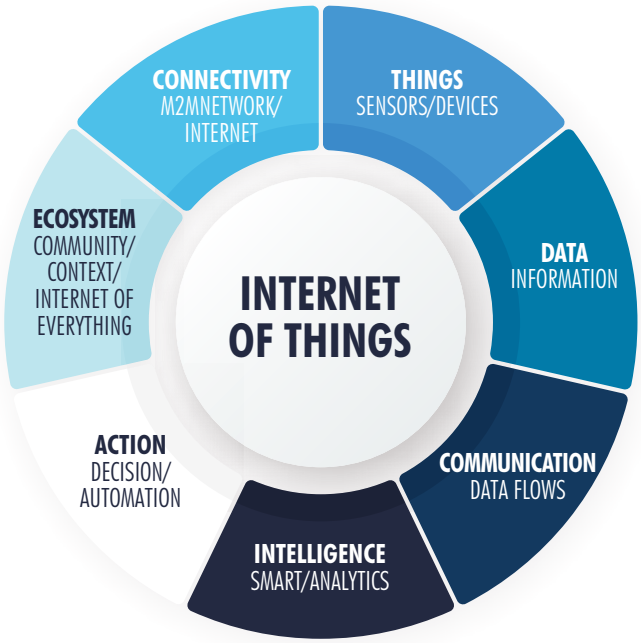
- **Deep Learning:** A form of machine learning that uses multiple layers of a selected algorithm to model highly abstract data. Each processing layer is responsible for extracting a single feature, then feeding the information onto the layer above it, with the top layer being a classification layer.

DEFINING IoT: 7 CHARACTERISTICS



Internet of Things

In somewhat simplistic terms, the IoT consists of all devices connected to the internet. Various estimates project that by 2020 there will be 50 billion IoT devices connected to the internet.

As a result of this definition being so broad, you will sometimes hear IoT referred to as a field rather than as a specific topic. One of the downsides of it being an umbrella term—similar to AI—is that it has become something of a buzzword that's frequently included in marketing hype, whether appropriate or not. While many have attempted to devise a more specific definition, this resulted in a plethora of definitions, making many definitions context sensitive. Just a partial list of the definitions that have been developed would be longer than this entire article.

The complexity of the device has nothing to do with its classification as belonging to the IoT. The device could be something as simple as a thermometer or a float switch, or as complex as a Tesla electric car or a gas chromatograph. The critical factor is that it is connected to the internet—either directly or indirectly. Directly connected is fairly obvious—it might connect via a standard Ethernet cable, wifi, or any other standard internet interface. Indirectly connected devices can be somewhat more enigmatic, in that the device might use a technology such as Bluetooth or Zigbee to connect to a gateway, which is then connected to the internet.

This concept can be extended further, as a specific device need not be directly connected to the gateway. Instead, it can traverse a local network composed of an arbitrary number of devices in order to link to the gateway. This latter situation is most commonly found in a mesh network of devices. This allows the connection to follow any arbitrary path through this mesh, a very useful characteristic in the event that one or more devices is somehow damaged. Normally, the practical limitation to the number of IoT devices comprising the mesh is determined by the amount of transmission delay that the particular application can tolerate, as there is an additional transmission delay for each device the message has to go through, even if we ignore the possible delay from network collisions between devices or the gateway.

Depending on how our arbitrary IoT device is engineered, it may be powered from standard line voltage or a battery; in some instances, it may not have an attached power supply at all. With the advances made in low-power processors and other electronics, it is quite feasible to

THE TECHNOLOGICAL CHALLENGES FACING IoT

design an IoT device to be powered by harvesting energy[2] from its environment. It is quite feasible for devices to harvest sufficient energy to power both the device and its communication interface.

The synergy of it all

It is by combining AI with IoT that we observe a multiplier effect, allowing these technologies to display capabilities that neither could exhibit on its own. There are two primary ways of accomplishing this. Currently, the most common is installing appropriate sensors in the IoT device and using them to provide a data stream back through the internet to be processed on a remote AI system. Depending on what you are trying to monitor, you might have single or multiple data streams from one sensor type or a variety of sensor types. We are already seeing a migration of this data processing onto the IoT device itself as the processors and memory within the devices become more capable.

There are a number of reasons to perform this migration. One is to help reduce the amount of network traffic, as an IoT device can generate a prodigious amount of data. What we currently think of as "big data" will seem minuscule in comparison to the data streaming from all of the IoT devices being monitored. Another justification for migrating the processing to the IoT device is that in many instances, the value of the data is extremely transient. In other words, the data must be processed immediately or its value drops to nothing. A good example of this is when the extracted data is being used in a process control loop. If you have a continuous flow reactor, to optimize the quality of the product produced, you must apply feedback continuously. Any significant delay, which in some systems may be seconds or less, results in either an inferior/low-yield product, or worse, a runaway exothermic reaction.

By installing IoT devices to monitor all reactor conditions that could affect the process, such as temperatures, pressures, flow rates, etc., the AI system can be used to optimize the product yield. On the scale that many industrial processes work, even a fraction of a percent improvement in product yield could result in a significant financial return.

AI can be applied to the analysis side in a laboratory as well. A number of instruments that take advantage of the power of AI are already on the market. You can find gas chromatographs, infrared spectrometers, Raman spectrometers, etc., that include AI in their control software. This makes the machines much "smarter" when it comes to analyzing the data being collected. In all but rare cases, this eliminates the need for specialists to run the machines and analyze the data. Another significant use of AI would be in multi-omics, where it can be used to analyze data from gas chromatograph mass spectrometers and liquid chromatograph mass spectrometers or other instrument combinations to visualize the enormous volume of data produced in proteomics, metabolomics, and flux analysis testing. While various vendors have added their own extensions, called gadgets, an open source software platform to enable the connection of data sources, analysis packages, and viewers, called the Garuda Platform, is available from the Garuda Alliance (www.garuda-alliance.org).

An AI system could also be used to track the movement of personnel in and out of, as well as around, the lab. Note that the goal here is not to micromanage your personnel but rather to ergonomically understand the movement of personnel through the building. This would provide information for altering the arrangement of the lab and placement of offices, or even could be used to design an entirely new laboratory.

Combining the umbrellas of IoT and AI shows how one can accelerate the analysis of complex data without the constant need for an expert in the field, at the same time processing massive amounts of experiment data to extract meaning from all of those data bits in order to provide multiple ways of imaging the data. The complement of this is that it also can provide data for optimal laboratory design, as well as afford more effective control of the laboratory environment.

Dr. John Joyce *is a laboratory informatics architect based in Richmond, Virginia. His background includes extensive work in instrument design and automation for industry as well as engineering the data flows from instruments to and between data systems. He can be reached via email at jrj_sci@yahoo.com or by phone at 804-601-0211.*

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Purchasing Trends and the Future of Laboratories

LAB MANAGER'S PURCHASING TRENDS SURVEY REVEALS GROWTH IN RESEARCH ACTIVITIES AND INVESTMENTS, BUT ALSO FUNDING CONCERNS **by Catherine Crawford-Brown**

We asked *Lab Manager* readers to tell us about their current lab purchasing trends, their motivations behind purchases, and what changes they have seen or anticipate seeing in their lab's budget. A total of 774 individuals responded, with almost 60% of these individuals holding managerial roles.

Looking at the demographics of survey respondents, almost one-third are in roles focused on research and development. Other major categories include quality assurance/validation and operations. Almost all research industries are represented, including biological science, chemistry, environmental science, engineering, and many more. Interestingly, approximately one-third of survey respondents work for colleges or universities. A further 15% work for hospitals or medical centers.

Job titles of survey respondents *Denotes managerial positions	
Lab Manager/Supervisor/Director*	**46.16%**
Research Scientist	**11.70%**
Technician	**6.24%**
Academic Professor	**5.59%**
Chemist	**4.68%**
QA/QC Manager/Director*	**4.16%**
Corporate Manager*	**4.03%**
Principal Investigator	**2.86%**
Academic Student	**2.47%**
Facility Manager*	**2.08%**
Project Manager/Director*	**2.08%**
Consultant	**1.82%**
Engineer	**1.30%**
Safety/Risk Manager*	**0.52%**
Purchasing Agent	**0.52%**
Other	**3.77%**

Types of facilities in which survey respondents work	
University or College	**30.74%**
Hospital or Medical Center	**15.95%**
Industrial Research Lab	**11.67%**
Government	**6.36%**
Environmental Lab	**4.93%**
Private Research Institution	**4.67%**
Contract Research Lab	**3.76%**
Consulting Firm	**2.98%**
Clinical Research Lab	**2.20%**
Forensic Lab	**1.04%**
Other	**15.69%**

Fields of research or industry of survey respondents	
Biological Science	**11.66%**
Medical/Clinical	**11.66%**
Chemistry	**8.55%**
Molecular/Cell Biology or Genetics	**7.90%**
Environmental Science	**6.35%**
Biotechnology	**6.22%**
Clinical Diagnostics	**5.96%**
Pharmaceuticals/Biopharmaceuticals	**4.92%**
Microbiology	**4.27%**
Biochemistry	**3.63%**
Chemicals/Plastics/Polymers	**3.37%**
Engineering	**2.98%**
Foods/Beverages	**2.46%**
Agriculture	**2.33%**
Animal Science/Veterinary Medicine	**2.20%**
Energy/Petroleum	**1.81%**
Pathology	**1.30%**
Forensics	**1.17%**
Instrumentation Design/Development	**1.17%**
Informatics/Bioinformatics	**0.78%**
Consumer/Durable Goods	**0.52%**
Other	**8.81%**

Overall, the results of the survey show better business conditions for labs, more spending on all categories of lab budgets, expansion of existing labs, and initiation of new labs. However, the survey results also emphasize the limitations in spending and innovation faced by labs because of funding challenges.

Business conditions and laboratory spending

Survey respondents were asked to compare their business conditions from the first quarter of 2019 to the first quarter of 2018. Approximately one-third of those surveyed reported better business conditions in 2019 compared with 2018. Only 11% of respondents reported worsening conditions.

Looking at overall laboratory spending, 41.5% of respondents reported increased spending in the current year compared with previous years. In contrast, about 18% of those surveyed reported decreased spending. A further 34.6% saw no change in funding this year compared with previous years. These results indicate that most labs are either in a growth phase with increased spending, or a maintenance phase.

We asked survey respondents to tell us about how their budgets have changed for different categories of laboratory spending. A net change in spending for all survey respondents was calculated by subtracting the percentage of individuals who reported a decrease in spending from the percentage of individuals who reported an increase in spending.

Net changes in spending over the previous year and in the next 12 months	Compared to last year	In the next 12 months
Commodity/Consumable products (glass & plasticware, filtration membranes, pipettes, gloves, etc.)	13.28%	14.33%
Constructing/Setting up a new lab facility	8.00%	7.42%
Educating (training, industry meetings, information databases, etc.)	4.30%	7.30%
Funding for new research projects	2.10%	10.03%
Hiring additional and replacement staff	3.14%	9.78%
Investing in existing research projects	4.56%	7.31%
Investing in new and pre-owned lab technology	5.34%	10.55%
Management & staff compensation/benefits, etc.	4.82%	6.27%
Modernizing existing lab facility (new lab furniture, etc.)	4.55%	5.35%
Outsourcing services	-2.23%	1.45%
Raw materials (chemicals, reagents, metals, other materials)	14.57%	13.82%

Net increases in spending over the last year and in the next 12 months were reported for every category except outsourcing. The largest net increase in spending was seen for commodity/consumable products and for raw materials. These increases were consistent from last year to next year.

> "Overall, the results of the survey show better business conditions for labs, more spending on all categories of lab budgets, expansion of existing labs, and initiation of new labs."

Interestingly, more labs are increasing their budgets for certain categories in the coming 12 months compared with the last year. Categories showing increased spending include education, new research projects, employees, existing research, new lab technology, and staff compensation. These results demonstrate the anticipated growth in the industry over the next 12 months.

Decline in outsourcing

The only category that saw a net decrease in spending among survey respondents over the last year was outsourcing. This category also saw the lowest predicted net increase in spending over the coming year. Approximately 65% of those surveyed outsource laboratory activities and the most commonly outsourced services include information technology, quality and assurance testing, and accounting and payroll.

Percentage of respondents who outsource specific services	
Information Technology	19.64%
Quality and Assurance Testing	18.22%
Accounting and Payroll	17.31%
Research	14.60%
Facilities Management	12.40%
Human Resources	11.37%
Production	9.43%
Development	8.79%
Purchasing	8.53%

Interestingly, respondents noted in the comments section that they are actually looking to purchase new equipment to eliminate outsourcing. The ability to conduct assays in-house saves on expenses such as labor costs and decreases turnaround times. Having the capacity to conduct analyses in-house could also provide a source of revenue for labs, as they could become a site for outsourced experiments.

Making purchasing decisions

The financial concerns of respondents were evident throughout the *Lab Manager* purchasing trends survey. More than half of those surveyed noted cost reduction as a significant concern when purchasing products for their lab. Looking at the top factors considered by respondents when making purchases, more than 75% marked the price and value of vendor's products as well as the long-term efficiency and operating costs as being very important.

Percentage of respondents who ranked factors as "very important" to consider when purchasing products or services	
Price/value of vendor's products	78.80%
Long term efficiency and operating costs	75.23%
After sale support, maintenance, and warranty	74.02%
Compatibility of vendor's products with current systems	72.92%
Vendor representative's knowledge of industry and technology	66.28%
Vendor reputation and brand awareness	63.05%
Current or previous relationship with vendor	52.02%
Vendor's ability to innovate and expand on lab product as requirements change	48.37%
Vendor's online presence	25.66%

The other top considerations when purchasing also point to this resource-saving attitude. Almost 75% of respondents agreed that after-sale support, maintenance, and warranty are very important to consider when purchasing new equipment. These features ensure the longevity of equipment and limit the need for out-of-pocket replacements and repairs.

A similar number of respondents also consider compatibility with current equipment to be very important when making purchases. Compatibility limits the amount of new equipment that must be purchased and therefore the amount required from a lab's budget for new equipment. Compatibility also lessens the learning curve required when using new equipment as lab workers will be using other components that they are already familiar with.

Addressing financial limitations

Being that so many labs are concerned about cost reductions, purchasing used lab equipment makes sense. It is therefore unsurprising that nearly 39% of survey respondents purchase used lab equipment, with almost all of these individuals citing the main reason as wanting to save money. Other reasons for purchasing used equipment include limited use of the instrument, short term need, and not requiring the features that come with newer equipment.

Respondent reasons for purchasing used lab equipment	
Seeking to save money/stretch our budget	88.94%
Small or moderate level of usage for the equipment/instrument	42.31%
Short term need for the equipment/instrument	19.47%
New equipment/instruments come with features we don't need	14.18%
Other	2.16%

Based on respondent comments, labs appear to be in one of two phases: a maintenance phase or an expansion phase. Labs in a maintenance phase are focused on replacement only as necessary. For example, more than half of survey respondents are very likely to spend money on chemicals and biochemicals in the next year, but they are much less likely to purchase other equipment or materials.

Respondents indicated in the comments section that this is because of funding limitations rather than lack of need. For this reason, equipment purchases are limited to replacing broken or obsolete equipment rather than adopting new technologies. This is an unfortunate indication of the poor funding climate in certain research sectors.

Expanding laboratories

Of those who responded to the survey, 25% listed that their lab is in expansion or growth mode. Several other survey indicators point to this pattern of growth. For example, 22% of respondents said that they had increased their lab's research budget for hiring additional and replacement staff. Additionally, 24% of respondents said they anticipated an increase in their lab's research budget for this category in the coming year.

Other areas of growth include infrastructure, as about 20% of respondents said their lab budget for building or setting up new facilities had increased in the last year. Similarly, 19% of survey respondents anticipated an increased budget in this area for the coming year.

Potentially the most exciting finding is the investment in new research projects. Of those surveyed, nearly 19%

reported an increased investment in new research projects over the last year and 19% predicted an increased budget for this category in the coming year. These results indicate that not only are labs physically expanding, but they are also growing into new research areas.

Looking at respondent's comments, labs in this state of growth are making purchases to expand into additional areas of research and expertise. They are also interested in technology that will increase their throughput and efficiency. This might also include upgrading or modernizing to faster instruments.

"The financial concerns of respondents were evident throughout the *Lab Manager* purchasing trends survey."

Adopting new technology

A total of 20% of survey respondents reported that their laboratory is among the most innovative compared to other labs of the same type. Looking at technology, 18% of those surveyed reported that their lab is among the first to adopt new technologies. These results correspond with the number of survey respondents who reported that their labs are in growth mode.

One way to increase lab throughput and efficiency is to adopt automation. Approximately 11% of survey respondents reported that they are very likely to purchase lab automation such as auto liquid handling systems, robotic systems, and autosamplers in the next 12 months. Several individuals specifically mentioned in the survey comment section that their labs were interested in automation. Employing this type of technology can lead to increased throughput because of increased instrument uptime. Using automation can also lead to increased efficiency while freeing up lab workers for more skilled tasks.

Conclusions

Even in this challenging research and funding climate, a pattern of growth can still be seen, with labs expanding and new labs starting. However, funding limitations are also having an impact, preventing researchers from purchasing new equipment, and instead forcing them to prioritize some research activities over others.

Based on survey results, labs that are decreasing their budgets for spending categories are actually in the minority, indicating a healthy research environment. With the expanding lab industry, we can expect to see exciting results and innovations over the coming years.

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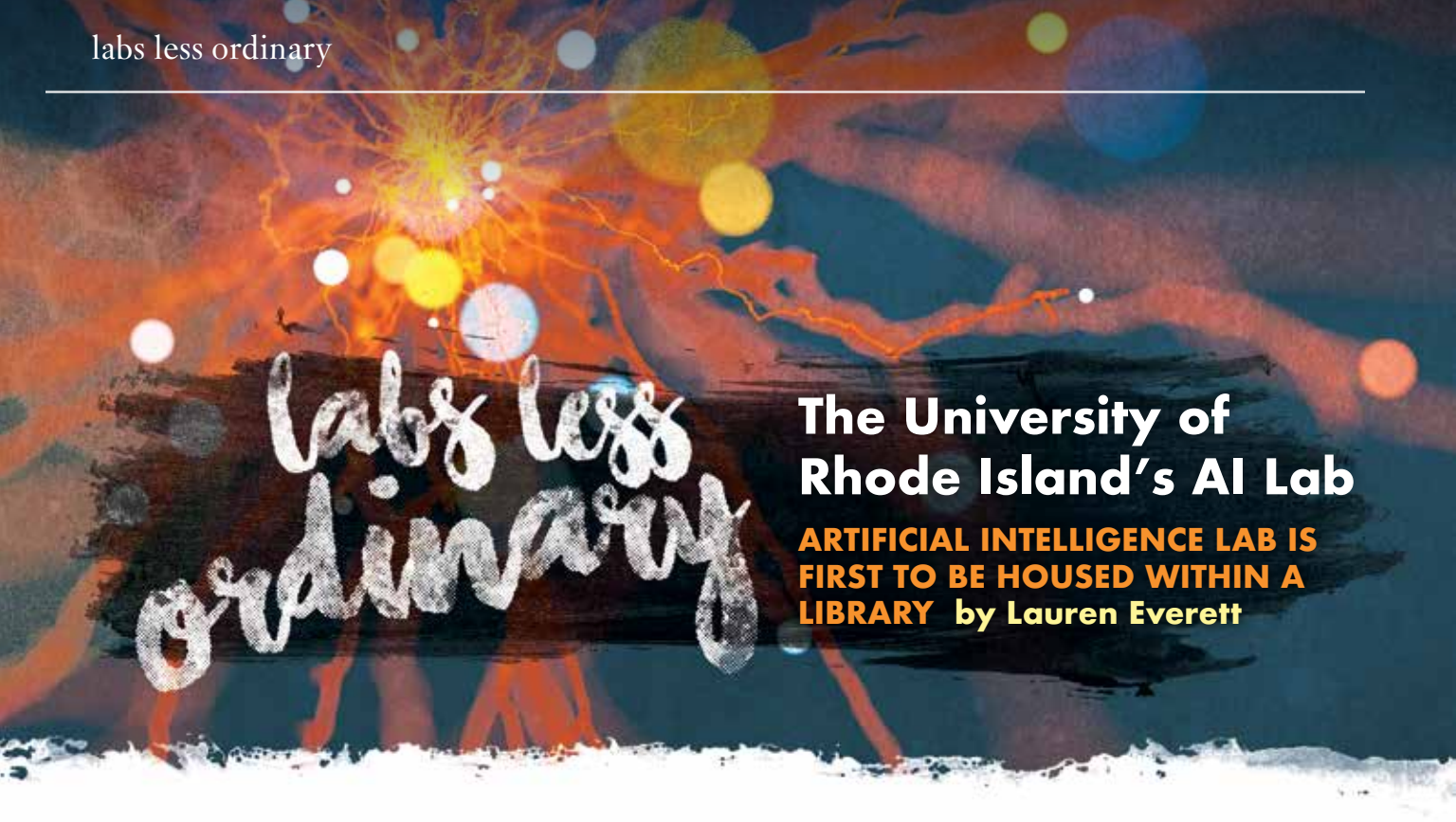

The University of Rhode Island's AI Lab

ARTIFICIAL INTELLIGENCE LAB IS FIRST TO BE HOUSED WITHIN A LIBRARY

by Lauren Everett

The AI Lab at the University of Rhode Island (URI) has been open only since September 2018, but it is already sparking a potential wave of similar facilities across the US and the world.

The lab is located within the university's Robert L. Carothers Library and Learning Commons, making it the first lab of its kind to be housed in a college library. The location provides easy access for students, faculty, and even the local community to learn about both the technical and nontechnical aspects of artificial intelligence (AI). Some of the equipment available includes an AI supercomputer, six specialized laptops for running large data sets and open-source software, 3D printers, and virtual reality technology.

"Why in a library?" asks Karim Boughida, dean of libraries at URI. He promptly continues: "Because the library is the common space for people to explore or create new things."

> "Other universities and research institutions are looking at us to lead this trend."

According to Boughida, the mission of the lab is threefold. Currently, the first priority is education, followed by research and then community building. The lab encompasses 600 square feet of space on the first floor of the library and has three "zones." Zone 1 is equipped with the supercomputer, where individuals can test out basic exercises and prepare to transition to more complex projects. Zone 2 provides hands-on opportunities for students to develop lab projects based on robotics, the Internet of Things, "smart" cities, wearable technology, and big data analysis. Zone 3 is dedicated as a brainstorming hub where groups are encouraged to collaborate and discuss challenges or potential opportunities with AI technology. In addition to the more freeform style of Zone 3, part of the educational program of the AI Lab involves discussions around the ethics and social justice of AI technologies. The lab hosts a series of workshops and "AI Meetup" events, where attendees are invited to join discussions and presentations on a variety of topics surrounding AI development, ethics, data bias, and fairness.

"I'm interested in providing a space where student-centered learning can go on. I want the students to drive the progress and determine what the programs or activities will be," says Harrison Dekker, interim director of the AI Lab. "There's a whole set of skills that are emerging that aren't necessarily provided in the curriculum. So by having these sorts of training spaces, it helps fill the gaps in the curriculum, and also helps students take what they're learning in the classroom on a theoretical level and then apply it to material things, code, or an actual project," he adds.

A nearly $150,000 grant from the Rhode Island-based Champlin Foundation provided much of the support to jump-start the lab. An interdisciplinary effort from faculty

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STIRLING ULTRACOLD

within the library and the computer and biomedical engineering and philosophy departments, as well as computer science statistics and URI's Big Data Initiative, enabled the lab to get up and running at the start of the fall 2018 semester. Getting representation from multiple fields and departments from the start of the lab launch drives home the message that the lab's resources are available to anyone with an idea or concept that they want to carry out, and aren't restricted to those in a specific field or major.

Finding a home in the library

Incorporating this type of lab into URI's library had been a long-time dream of both Boughida and Dekker. As AI has become more of a trending "hot topic" in the news and among researchers, Boughida thought it was the perfect time to bring the vision to reality. The students at URI agreed. A recent survey that asked URI students about the topics they would like to see in their curriculum showed that AI was among the top requests. Housing the lab in the library—a central, welcoming location for all students and faculty—was a natural fit.

> "It's important for more libraries to be involved with these new, emerging conceptual spaces."

"People have a stereotypical view of what librarians do or what goes on in a library. It's important for more libraries to be involved with these new, emerging conceptual spaces," says Dekker.

Some examples of the groups working, and the work being done, in the AI Lab include engineering students

1. The AI Lab at URI officially opened in September 2018. **2.** AI Lab interim director Harrison Dekker (left) talks with AI Lab staff member Angelica Ferria and URI students Jaime Jaramillo and Sydney Cirone. **3.** From left to right: Indrani Mandal (AI Lab instructor), Brinn Van Denburg (URI student), and Avi Shrivastava (URI student) work with robots in the AI Lab. **4.** From left to right: Harrison Dekker, Jaime Jaramillo, Angelica Ferria, and Sydney Cirone. **5.** URI's provost and members of the AI Lab team gather at the lab's entrance. *Credit for all photos: Michael Salerno, URI*

applying machine and deep learning algorithms to enhance designed wearable items that collect data on health; a group of students using the lab's processing power to gain a deeper understanding of using brain electrical activity to control robots; and a philosophy class conducting programming exercises to engage in discussions related to relationships between humans and machines. The lab will also serve as a generator of brand-new courses that can explore and incorporate AI.

"When you're the first, some people will question why," says Boughida. "We believe people aren't [fully] aware of the impact AI will have on our daily lives, and since we see ourselves as a service to the community, we need to do something about it in terms of educating students, the public, and faculty." He also notes that AI has become more of an "umbrella" term now and a lot of different technologies fall under the AI label, such as machine learning, natural language processing, and robotics, among others, which is why it is important to learn the various applications and their impact. "Other universities and research institutions are looking at us to lead this trend," Boughida says.

When asked what the future vision of the AI Lab is, Boughida says that he is "thinking big." He hopes to develop a long-term plan to allocate and train more individuals to join the lab, expand its services, establish more relationships with industry partners, and work with other libraries on data projects. Dekker echoed Boughida's vision, adding that he would like to leverage the existence of the lab for fundraising efforts, to earn grants, and create more opportunities for students to get paid work experience. "I'd also like to have more of an applied research focus—where we can do more library-centric applications of artificial intelligence."

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Lab Accreditation

HOW TO ENSURE A SMOOTH TRANSITION TO ISO/IEC 17025:2017 ACCREDITATION

by Prashant S. Umare, PhD

All laboratories involved in testing and calibration strive to produce valid results for their customers, and it is a significant key performance indicator (KPI). Laboratory accreditation as per the globally accepted standard, ISO/IEC 17025, "General Requirements for the Competence of Testing and Calibration Laboratories," plays a vital role to meet this KPI. The fundamental objective to develop this standard was to promote confidence in the operation of laboratories and contains requirements for laboratories to enable them to demonstrate their competency and generate valid results. Implementation of this standard requirement in laboratories does not only facilitate the development of a robust structure of a laboratory management system (LMS), but also lays down a strong foundation for the operational excellence model. As of 2017, standard requirements encompass a complete supplier-input-process-output-customer (SIPOC) cycle and end-to-end laboratory processes. It is the single most widely employed standard by calibration and testing laboratories throughout the globe to obtain the accreditation. This is a generic standard for any laboratory and can be implemented in any laboratory regardless of the nature of testing and number of people. It covers testing, calibration, and sampling performed using standard, nonstandard, and laboratory-developed methods and sampling associated with subsequent testing and calibration. Additionally, this standard is being used by various stakeholders in different ways. A laboratory uses this standard to develop a LMS, the accreditation body uses it in confirming or recognizing the competence of laboratories, and customers use it as a reference to ensure the competency of the laboratory.

> "The fundamental objective to develop this standard was to promote confidence in the operation of laboratories."

History and transition

The third edition of the standard was published in November 2017 as ISO/IEC 17025:2017. Historically, ISO/IEC 17025 was first released in 1999 to replace ISO Guide 25. The second edition was released in 2005 to include management requirements in line with ISO 9001:2000, which was subsequently reaffirmed in 2010. A three-year transition period has been given for accredited laboratories to transition to the 2017 version of ISO/IEC 17025. During this transition period, ISO/IEC 17025:2005 and ISO/IEC 17025:2017 will be equally valid and applicable. At the end of the transition period, accreditation of a laboratory to ISO/IEC 17025:2005 will not be recognized under the International Laboratory Accreditation Cooperation arrangement. The standard is developed by ISO's Committee on Conformity Assessment (CASCO). Primarily, in the 2017 version, there are obligatory changes as per the ISO/CASCO Chairman's Policy and Coordination Group, philosophical changes, structural changes, and the addition of new definitions. High-level changes can be summarized as follows:

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A new definition of laboratory is introduced by virtue of which laboratory accreditation scope has been expanded to cover testing and/or calibration laboratories, which are only involved in the sampling associated with subsequent calibration and testing.

The format of the third edition has been profoundly changed and the current version is similar to the 17000 series standards from CASCO, such as ISO/IEC:17020 and ISO/IEC:17065, and aligned to the ISO 9001:2015 principles on resources and processes. The structure of the new standard is as follows:

1. Scope
2. Normative references
3. Terms and definitions
4. General requirements
5. Structural requirements
6. Resource requirements
7. Process requirements
8. Management requirements
   - Annex A—Metrological Traceability (Informative)
   - Annex B—Management System (Informative)
   - Bibliography

There is a significant shift from prescriptive requirements to performance-based requirements by the introduction of the concept of risk-based thinking. In the new version, more focus is given to the outcomes of processes than merely having policies and procedures. As a result, there is greater flexibility, considering its own opportunities and risk to the laboratory than the previous edition in the requirements for processes, procedures, documented information, and organizational responsibilities.

Terms such as "quality manager," "technical manager," and "quality manual" have been removed. As per the new requirements, there is no obligation to formally appoint a quality manager or technical manager. Additionally, there is no explicit requirement to develop a quality manual.

A few terms are replaced with new ones, such as "accommodation by facility" and "preventive actions by risk and opportunities." In most cases, "test and/or calibration" is replaced with "laboratory activities."

Purchasing services and supplies and subcontracting is combined and considered as an externally provided service. New definitions are added, such as those for laboratory, intra-laboratory comparison, decision rule, and impartiality. Most of the nonvalue-added notes from the older version are either removed, moved to an annex, or added to the standard requirement. The new standard has a stronger focus on information technologies to address the increasing use of information technology to handle documents and records in the laboratory. The new version clearly acknowledges the use of ISO 9001 as a basis of use for conformity to ISO/IEC 17025.

Equal weighting has been given to internal and external processes. Replicate tests/calibrations, intra-laboratory testing, and blind tests are introduced in addition to proficiency testing and inter-laboratory testing. Requirement of a decision rule is added in the newer version, while providing a statement of conformity to a specification or standard for the test and/or calibration. Customer focus is emphasized by introducing new requirements under complaints, agreement on a decision rule, and approval on externally provided services to the customer.

Risk-based approach

Basically, "risk-based approach" means to evaluate the potential risk as well as the opportunities. Risk-based thinking is not a new concept and was implicitly addressed in the 2005 version, whereas in the 2017 version of the standard, it became very prominent and incorporated throughout the standard. Therefore, the laboratory should apply risk-based thinking from the conception of the LMS and spread it out over the planning, execution, and performance-monitoring phases. In fact, risk-based thinking replaced preventive action, which had a special clause in the 2005 version. The standard does not require any formal method of risk management or a documented risk management procedure; rather, it is expected to be an integral part of all laboratory processes. Moreover, the standard does not state how to determine and analyze potential risks. However, ISO 31000, "Risk Management Guidelines," is a very useful reference for understanding. To address this requirement, the laboratory should identify the risk proactively in the planning phase, understand the consequences, and implement effective preventive measures to eliminate or reduce the adverse impact on the laboratory operation. There are several formal and advanced tools available to identify the risk; however, a less formal approach that considers the frequency of occurrence, the severity of a situation, and a risk category can be adopted in the laboratory. For example, one of the potential risks to impartiality is financial pressure from customers to provide results in their favor. In this case, the source of risk would be

laboratory personnel involved in testing or decision-making. Preventive measures to eliminate or minimize risk can include signing a conflict of interest declaration form on a yearly basis to reiterate the commitment to impartiality, evaluating employee background history prior to recruitment, and executing a laboratory ethics policy. The likelihood of occurrence can be decided on the historical frequency and severity can be decided on the gravity of adverse impact. A similar approach can be adopted to evaluate the potential risk in other contexts related to laboratory operation.

Process approach to the standard requirements

The paradigm shift of ISO/IEC 17025 from the 2005 version to the 2017 version is a prescriptive approach to the performance-/process-based approach. If the laboratory is considered as a process, principle process input would be a sample and customer requirements and expected output would be results/reports. When it is viewed through the SIPOC window, secondary processes could be man, machine, method, environment, or supplier. This approach will facilitate stakeholders to understand and interpret the standard requirements to design and develop the LMS for seamless implementation and further improvement. Additionally, an amalgamation of process requirements and system requirements can be screened.

Conclusion

This is the first change to ISO/IEC 17025 in 12 years. Though there is a significant structural change in ISO/IEC 17025:2017 compared to ISO/IEC 17025:2005, the technical changes are comparatively less in magnitude and the content of the standard is very similar to the old version. The introduction of a risk-based approach and process orientation has shifted the prescriptive approach of the standard to the performance-based approach, which brought more flexibility in implementation and subsequent improvement. To ensure a smooth transition to ISO/IEC 17025:2017, each laboratory will prepare a transition plan compatible with the accreditation body's policy on transition and time frame. The laboratory should identify the gaps, revise policies and procedures to accommodate new requirements, train laboratory personnel, and approach the accreditation body for assessment within a transition period of three years. While working on the transition to the 2017 version, the laboratory needs to continue to conform to the 2005 version requirements.

***Prashant S. Umare**, PhD, CQM-ASQ, NEBOSH-IGC, Quality Coordinator, Ras Tanura Area Laboratory Division, Saudi Aramco, can be reached at prashant.umare@aramco.com.*

AUTOMATED SOLUTIONS SIMPLIFY NEXT-GENERATION SEQUENCING LIBRARY PREPARATION

Library preparation is fundamental for NGS success. Automating the process increases efficiency and generates high-quality data

DNA sequencing was an enormous scientific breakthrough that enabled investigation into various biological processes pertaining to human disease, genetic inheritance, immunity, and cancer, among countless others. The first rapid DNA sequencing technique was developed by Nobel Laureate Frederick Sanger and his colleagues in 1977. The chain termination method, now termed Sanger Sequencing, relies on a DNA polymerase to produce copies of a single stranded DNA template. Labeled deoxynucleotides are incorporated and the resulting DNA fragments of various lengths are electrophoresed and laser excitation is used to read the sequence and produce a chromatogram. While the Sanger technique was widely used, it has several weaknesses including low throughput, scalability, cost, speed, and resolution. More recently, the development of next-generation sequencing (NGS) has markedly improved on the limitations of Sanger sequencing. NGS enables millions of sequencing reactions simultaneously, reducing the cost and increasing the speed of DNA sequencing. NGS depends on a high-quality library prepared from genomic DNA and RNA, a process that involves copious amounts of pipetting and attention to detail. Such tasks may consume large portions of a working day that would otherwise be spent writing papers and grant applications, or staying up to date on new literature. Innovative automated solutions simplify NGS library preparation, increase productivity, and eliminate time lost to tedious tasks such as pipetting.

PRECISE AND ACCURATE LIQUID HANDLING FOR BETTER DATA QUALITY

NGS library preparation requires DNA fragmentation and addition of adapter sequences, polymerase chain reaction (PCR) methods for amplification, followed by gel purification. The process is labor-intensive, mainly due to the enormous amount of time spent pipetting. There is also a high risk of error when pipetting manually due to inconsistent technique, pipetting into the wrong well, and even skipping wells. Automating the process saves the operator countless hours of bench work and improves accuracy and precision to ensure high quality data and prevent costly errors.

Well-designed automation software can automate a pipetting protocol into a ready-to-run procedure and accounts for dispensing speed, aspiration, and blow-out parameters based on liquid characteristics. More viscous liquids, for example, should be dispensed slowly compared to more aqueous liquids and a longer blow delay will allow the liquid to flow down the tip completely. An automated alternative, such as an Eppendorf epMotion NGS solution offers settings for different liquid types, and the ability to modify individual parameters to ensure optimal liquid dispensing. Kits for NGS library preparation workflows are also available, and have been qualified by reagent manufacturers to ensure accurate results. Software should also be intuitive and easy to use, so that multiple users are able to operate the system implementing their own methods. For NGS applications, hiring a

specialist to develop a method can save time and expense spent optimizing hundreds of different steps.

For laboratories that need to process multiple different library preparation workflows, flexible open platform instrumentation is essential. Automated solutions with multiple deck positions, gripper options, and automatic exchange between single or multi-channel dispensing, and 96 or 384 well plates are suitable for a wide range of workflows.

PREVENTING CONTAMINATION

It is critical to avoid contamination during library preparation, especially during PCR processes. This often requires separating pre- and post-PCR processes spatially, and working with great care and attention to detail. It is recommended that pipette tips be changed between each sample, and between each row and each column when adding adapters. Automated Eppendorf systems offer contact-free dispensing, eliminating any potential cross contamination between liquids and samples and prevent user errors such as neglecting to change a pipette tip. Prior to a run, the automated epMotion system checks the deck to ensure the appropriate type and number of pipette tips are present, and reliably performs otherwise tedious pipetting tasks.

Automated systems may be equipped with ultraviolet lights and HEPA air filters to ensure sterility and prevent contamination. It is also important to work with low binding consumables to prevent sample loss due to adsorption to the plastic.

MAGNETIC SEPARATION, MIXING, AND TEMPERATURE CONTROL

Bead-purification steps and temperature controlled enzymatic incubations are part of the DNA and RNA purification process for NGS workflows. For optimal results, powerful magnets, variable mixing speeds, and precise temperature control are required. epMotion technology incorporates magnetic fingers that draw in and out of the sample rack to facilitate mixing, washing, and separation of magnetic beads. Mixing frequency has been optimized for specific labware and applications, and the system delivers stable temperature with precise control. It is also essential to avoid disturbing the magbead pellet, which is a risk associated with manual pipetting, especially when working with a multichannel pipette. Automated pipetting eliminates this risk and saves time compared to careful manual pipetting.

In addition to hours spent pipetting, the combination of bead purification steps and temperature controlled enzymatic incubations necessary for NGS library preparation can leave the operator feeling tethered to the bench for hours at a time. A reliable automated system provides the peace of mind necessary for the operator to step away from the bench during the process.

AUTOMATED SOLUTIONS ELIMINATE BOTTLENECKS

NGS systems continue to evolve, offering greater throughput, shorter run times, and better analytical techniques. Improved technology is matched with growing demand for fast answers, more affordable sample analysis, and better data. NGS library preparation remains the bottleneck between new technology and research demands, as it is a specialized, time-consuming process crucial to ensure data quality. Automated solutions can eliminate this bottleneck, as they perform otherwise tedious and time-consuming tasks with high accuracy and precision. When investing in an automated system, it is important to select a reliable, industry-proven manufacturer such as Eppendorf.

Maintenance and Repair Services for Sophisticated Instruments

MULTI-VENDOR SERVICE PROVIDERS MUST ADAPT TO MEET THEIR CUSTOMERS' NEEDS

by Michelle Dotzert, PhD

The ongoing evolution of laboratory instrumentation and technology makes powerful analyses possible. While new technology enables exciting techniques and discovery, these instruments still require maintenance and repair. Routine maintenance is essential to keep laboratory operations running smoothly, and a service agreement with a multi-vendor service provider can prevent costly downtime. However, as instruments become more sophisticated, service providers must stay up to date on the latest technologies and ensure their technicians are trained to service state-of-the-art equipment.

A service agreement with a multi-vendor service provider can offer more rapid response times at a lower cost. Prior to committing to a service contract, it is essential to ensure staff have the necessary technical expertise to work with equipment from various manufacturers. John Martin, VP of marketing at Full Spectrum Analytics (Pleasanton, CA), understands the importance of a knowledgeable staff. "We hire applications chemists, bench chemists, and engineers, some of whom are highly trained and qualified and have gone through a robust training program with the OEM," says Martin. "We have created a series of training programs internally for cross-training our staff to work on multiple types of instruments. We are a full-spectrum, ISO-certified company, so training is a really important part of what we have in place. We invest a lot to become a better and more educated workforce."

> "We are excited to bring our technical expertise to our clients...to enable them to be more resourceful and give them ownership of some basic problems."

Laboratories are constantly facing new demands and challenges. Agilent Technologies' (Santa Clara, CA) Kristin Giffin, VP and GM, Services and Support Division, and Marc Boreham, VP and GM, Laboratory Enterprise Services Division, are well aware of how new challenges have changed client and laboratory needs: "We see greater needs in areas such as training, applications consulting, and a desire for capabilities such as predictive diagnostics to help with workflows." As such, it would seem that the theory of operation has not changed dramatically, but the software and the way scientists interact with devices are changing. "Overall, I haven't seen any major revolutionary changes to the equipment, although sensitivity has greatly improved, but it still performs the same basic chromatography functions," says Martin. "It does have a lot more advanced, built-in protocols such as validation and qualification programs to meet ISO and FDA requirements. Software has advanced significantly and can also allow remote access and generate messages that can alert the client to potential issues with the instrument," he explains. Agilent *Smart Alerts* is a perfect

example of this advanced functionality: "The *Smart Alerts* subscription diagnostics service offers predictive maintenance and consumables replacement notifications, leveraging smart, built-in instrument-diagnostic capabilities," explain Giffin and Boreham.

There is also a shift in multi-vendor services toward offering greater autonomy for the user. Full Spectrum Analytics has plans to run courses for laboratory staff at a new training center in San Diego, offering customers the ability to "learn from a technically strong training crew," says Martin. "We can bring people in and give them some basic troubleshooting skills, show them what to look out for, parts to order . . . things of that nature. We are excited to bring our technical expertise to our clients—to educate them, enable them to be more resourceful and give them ownership of some basic problems." Remote access also offers users a sense of autonomy and can be used to provide assistance from off-site locations. According to Giffin and Boreham, "Agilent instruments, such as gas chromatographs, are supported by a mobile browser interface, providing remote access to the instrument for monitoring of system status and modification of system settings, if necessary. The remote mobile interface provides a suite of diagnostic tests that can be used to assist remote experts with troubleshooting and remediation of issues even while off-site."

Chromatography may operate on the same principles as it did many years ago; however, the technology driving this and other instruments is rapidly advancing. Multi-vendor service providers must continue to educate their staff and adapt their services to meet current customer demands.

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CREATE A SOLUTION FOR EVERY LABORATORY WITH MODULAR BALANCES

A completely modular design enables scientists to configure a balance specifically suited to their applications

No two laboratories are alike, and this uniqueness is essential for new ideas, discovery and innovation. Unfortunately, despite the variability of sample types and protocols used across hundreds of different fields, many of the instruments used on a daily basis are only available in standard configurations. The same instrument used in pharmaceutical research for example, may be used for food science or environmental applications. While standard protocols and metrics are the foundation of scientific investigation, instruments that are customizable for the specific needs of a laboratory may improve functionality and ease of use. The laboratory balance is ubiquitous, and a newly developed modular version offers laboratories the power to configure a solution specific to their needs.

While it may seem like a simple device, the balance is a sophisticated instrument. The right solution should integrate a weighing module, user interface, draft shield, software and communication capabilities best suited to the laboratory. The Sartorius Cubis® II and QApp software are completely modular, allowing the operator to design a perfect fit for the laboratory.

HARDWARE MODULES FOR CUSTOM SOLUTIONS

Weighing modules are available to suit every application from weighing micrograms of chemical compounds to kilos of ingredients for adhesive formulation, and it is important to select a module with a suitable capacity and readability. For an ultra-micro balance, this may translate to a maximum capacity of as little as 2 grams and a readability of 0.1 microgram. Alternatively, for larger scale applications with substances measured in kilograms, a high-capacity balance is required. Regardless of size, the weighing pan should have non-magnetic features, and the balance should be easy to disassemble and clean to prevent cross-contamination.

The user interface is essential for proper operation for any application. Configuring a balance with an intuitive touchscreen display is a simple way to improve functionality. The draft shield is also an important consideration, and different options can improve accuracy and safety. Glass panels coated with a conductive layer eliminate potential external transfer of electrostatic charge. Integrating a high-efficiency ionizer that eliminates electrostatic

charges from samples and containers in seconds further improves accuracy. For laboratories working with toxic substances, configuring the balance with an infrared sensor enables touch-free manipulation of the draft shield to eliminate a potential point of contamination.

Working with an unlevelled balance is critical for accurate weighing. In a busy laboratory, even a small accidental movement of the scale can affect calibration. A balance designed with built- in sensors can alert the operator if re-leveling is required and built-in motors allow for automatic adjustments to ensure consistent, accurate results.

FLEXIBLE SOFTWARE FOR EVOLVING LABORATORY AND REGULATORY NEEDS

Software needs vary significantly between laboratories. Security and compliance may be essential for some laboratories, while density determination, residual dirt analysis, and percentage weighing may be more important functions for other laboratories. Sartorius QApp software can be installed based on theme, such as pharmaceutical, or as an all-inclusive solution. To keep up with constantly evolving laboratory and regulatory requirements, software must adapt and QApp software can be easily extended or updated as needs change.

When regulatory compliance is a primary concern, especially among pharmaceutical laboratories, instruments must be configured to protect data. Software configurations enable complete traceability, and support the requirements to achieve 21 CFR part 11 and EU Annex 11 compliance. Using time-stamped, tamper-protected audit trails, password rules, electronic signatures and safe data transfer, the Cubis® II with pharma software package is a fully compliant solution.

EASY INTEGRATION

Lastly, a balance should integrate seamlessly into the laboratory. For those working with LIMS or ELN, integrating a balance can reduce potential errors associated with data transcription. Different interface ports, including USB, RS232, and Ethernet are used to integrate the balance with optional interfaces.

In some circumstances, printed data is required and a versatile system enables numerical or graphical display of results and statistics. An optional printer module offers a rapid, user-friendly option for printing. Alternatively, if a laboratory printer is available, integrating the balance to a network printer is a convenient solution.

The laboratory balance is an essential instrument in facilities worldwide. It is used for countless assays and processes, ranging from routine tasks to complex workflows. Despite this, many balances are only available in standard configurations that are well-suited for some, but not all, applications. The Sartorius Cubis® II balance is a completely modular instrument that can be configured for the specific needs of the laboratory. Thousands of potential hardware and software configurations make it possible to have your balance, your way.

Change Management

CONSULTING EXPERTS OFFER TIPS ON THE CHANGE-MANAGEMENT PROCESS

by Donna Kridelbaugh

We previously have written about the human perspective regarding how laboratory managers can lead their staff through change.[1] For this article, we want to take a deeper look into what type of organizational culture drives sustained change and explore systematic approaches that can be applied to the change-management process. To do so, we reached out to two management consultants who specialize in the healthcare and life sciences industries, Hannah Thomas (founder and CEO of New Canvas Advising, Inc.) and David Novis (president and CEO of Novis Consulting, LLC), to get their input on current trends in change management.[2,3]

Why change is necessary

Both experts agree that change is required for science organizations to continuously improve and stay adaptable in an ever-evolving technological landscape. Novis emphasizes lab directors need to keep in mind when setting business goals that technology becomes obsolete. As he remarks, "Science is fickle. Never embrace some tactic and think it's going to be the end. You need a strategy that includes a vision of change."

Thomas takes this one step further and points out that companies are, in fact, the drivers of this technological change. Additionally, she says the industry has a responsibility to move technology forward and continuously improve processes because it can have a major impact downstream on the lives of their end users (e.g., patient-health outcomes, customer profit margins). In the end, organizations need to change as necessary in order to achieve a dynamic equilibrium, be good financial stewards, and always strive for operational excellence.

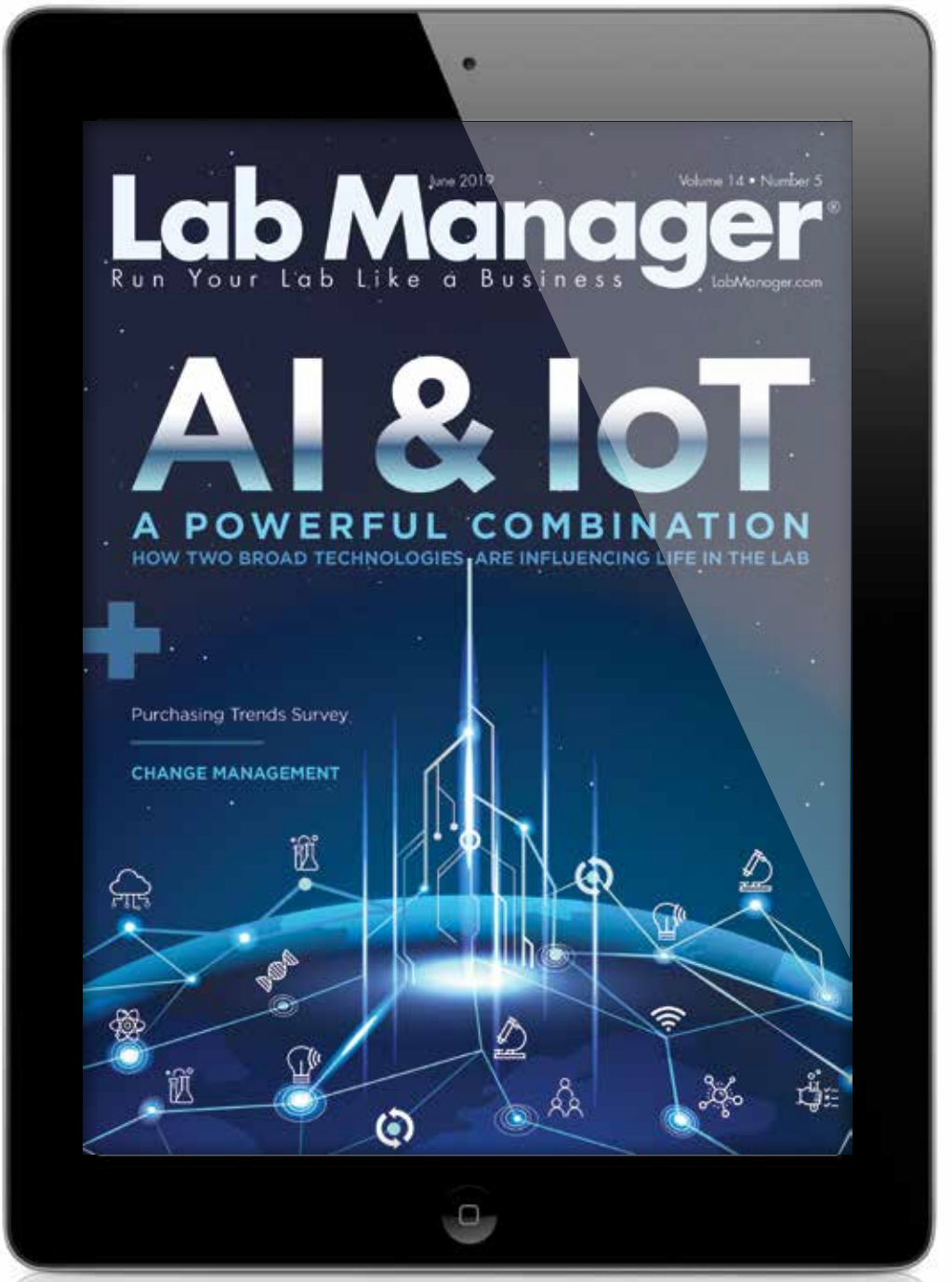
> "Change is required for science organizations to continuously improve and stay adaptable in an ever-evolving technological landscape."

Creating a culture of change

In most organizations, any sustained change will require a top-down approach that involves management action, because labs do not operate as a silo but are instead part of a complex system. Or, as Thomas explains, any changes made within the microcosm of an individual lab will impact other business units and the ecosystem as a whole. Therefore, organizations should aim for creating transformational changes and not those that are purely transactional in nature (i.e., performing triage). This requires transformational leaders and empowering staff to take ownership of the change process.

Transformational leadership style

Organizations can be prepared for change by creating a culture that is willing to embrace change and make it a priority. Thomas says this is a culture in which everyone takes ownership of their own "individual citizenship



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behavior" and all are held accountable to each other. Laboratory managers are responsible for setting this tone by modeling this behavior and adopting a transformational leadership style. In a recent blog post on the New Canvas Advising website, Thomas describes the traits of a transformational leader as including emotional intelligence, authentic and ethical leader behaviors, the ability to relate to others, and leading by example.[4]

Thomas further explains, "A model culture is not to say that there is perfection, because that's utopia and that does not exist. But there is a healthy working relationship between those who are leading and those who are called upon to execute on the deliverables." Likewise, Novis concludes it really comes down to those leaders who make you feel that you are working "with" them, not "for" them.

Empowering staff

Novis further elaborates that an organizational culture must both encourage and reward innovation among its employees and create an environment where one is not afraid to fail. He has had the most success in implementing change by presenting staff with the desired end point and then empowering them to figure out what needs to be done to get there. He advises, whenever possible, that leaders should set the strategy and leave the tactics to the employees.

During this process, Thomas says it is important to also identify change agents who can engender followership to get group buy-in and help implement the change at the microcosm scale. As Novis defines it in a *Laboratory Medicine* article, "Change agents are those bright lights who grasp the vision, become passionate about what it can accomplish, and will work hard to see it succeed."[5] These people, as he puts it, have a "spark of intellectual curiosity" and when given a platform, will excel and find the best solutions.

Thomas also cites from a LinkedIn report that the top five soft skills identified as most in-demand for 2019 include creativity, persuasion, collaboration, adaptability, and time management, all of which are essential skills for a change agent to possess.[6] Therefore, companies need to nurture this skillset in employees, during the recruiting and hiring processes, and on up to promoting these people into leadership roles.

Taking a systematic approach to change management

It is essential for leadership to acknowledge employee input and demonstrate that changes have been made if you want to perpetuate a culture of change. Unfortunately, too often there may be a disconnect between leadership and staff, and employees may not feel comfortable providing feedback for a number of reasons. To further give voice to employees, there is a value in hiring an external consultant to perform the strategic analyses required to evaluate what operational or other changes may be needed within an organization. Novis and Thomas both use various systematic approaches based on employee-centric philosophies to achieve this.

Lean production

One approach used by Novis is the lean-production methodology, as perfected by the Toyota Motor Corporation and now applied across many different industries. At the core of lean production is a focus on eliminating wastes (e.g., supplies, time) while simultaneously building quality into production processes. Novis explains in his *Laboratory Medicine* article that lean involves mapping out current workflows, identifying processes with or without value to end users, developing plans to remove any nonvalue/wasted steps, and building in ways to detect and eliminate errors early on. Ideally, a lean approach results in one continuous work flow that can increase an organization's efficiency and capacity.

In his article, Novis also details how lean can be applied to the lab setting, and ways that waste can be reduced, such as breaking down any silos that exist among operational units and simplifying the work flow during sample processing. One additional waste he identifies is unused employee creativity. As Novis writes in the article, "Failing to solicit ideas on how to improve operations from the people who are in the very best position to provide that information is, in my view, the most egregious waste in any industry."

Also, central to lean production is the concept of mistake-proofing to prevent errors (e.g., erroneous lab results) from reaching the end user. This is accomplished by using two main principles: standardization (i.e., doing things the same way) and redundancy (i.e., catching errors early on). In terms of redundancy, a variety of inspection methods (e.g., self-checks, monitors) can be put in place to detect errors. The inspection process requires management to trust employees to take ownership of finding and reporting on any errors and also giving them the authority to stop work as required to correct these errors immediately.

Overall, lean only works if laboratory managers make a commitment to their staff, who are their most important resource. As he summarizes in the article, it's all about "empowering employees, developing trust, and building a culture of continuous improvement." Further, lean production requires labs to take a look internally to start benchmarking themselves and to adopt the Toyota

mantra: "We're never as good today as we will be tomorrow."

New canvas advising methodology

Thomas emphasizes that each company has its own DNA and thus deserves its own evaluation. Her role is to critically examine both the technical and human infrastructures to determine how an organization can improve and become its best operational self. For this, Thomas uses a hybrid approach that combines the scientific (i.e., "the business of business") and Socratic (i.e., "the business of people") methods.

In the first step with the scientific method, Thomas conducts a data-driven analysis that approaches change like an experiment, with a hypothesis that is repeatable. For example, if a company is making a purchasing decision for new instrumentation with the presumption of saving money, she would do the analysis to determine what other variables (e.g., quality, safety) may come into play. All too often she sees decisions made by leadership that are based on a theory versus facts. As she explains, "People ubiquitously use the term 'theory.' The challenge with that is they have failed to ask questions, much less identify a hypothesis."

From there, Thomas can use the Socratic method to determine the human factors involved with the potential change, such as what hidden agendas may be influencing the decision or what additional value this change will provide to end users. Key to this process is collecting input from staff at all levels of the organization. She comments, "The actual information bearers are the individual contributors or middle management and so, it is my role to give them voice (and space and grace) to safely air what is on their minds." As she explains, you are not working with a widget but with people, who in the end are responsible for seeing the change through.

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Maintaining Control

GUIDELINES FOR HANDLING CONTROLLED SUBSTANCES IN RESEARCH LABS

by Vince McLeod

In the broad realm of research laboratories, some may deal with narcotics, stimulants, depressants, hallucinogens, anabolic steroids, or other chemicals used in the production of drugs. These are commonly referred to as "controlled substances" (i.e., they are strictly controlled by federal regulations). If we are using any of these materials in our research, (e.g., animal research, or practices such as veterinary services,) then we need to be very careful in how they are secured and accounted for.

> "The heart of good controlled substance management is a comprehensive written program."

Controlled substances defined

The term "controlled substances" refers to drugs and other substances listed on one of the five schedules published in the Controlled Substance Act, Title 21 Code of Federal Regulations, Parts 1308.11 through 1308.15.[1] Chemical substances are placed on the schedules based on three primary characteristics: currently accepted medical treatment use in the United States, relative abuse potential, and likelihood of causing dependence when abused. Below are simple definitions of each schedule and a few common examples of each substance.

I. Schedule I substances have no currently accepted medical use in the US, a high potential for abuse, and a lack of accepted safety for use under medical supervision. Examples include heroin, LSD (lysergic acid diethylamide), marijuana (cannabis), and ecstasy (methylenedioxymethamphetamine).
II. According to 21 CFR 1308.12, Schedule II substances are primarily narcotics or stimulants that have a high potential for abuse, which may lead to severe psychological or physical dependence. Narcotic examples include codeine, hydrocodone, morphine, opium, barbitals, and the well-known oxycodone (OxyContin, Percocet) and hydromorphone (Dilaudid). Stimulant examples include amphetamines (Dexedrine, Adderall) and methamphetamine (Desoxyn).
III. Schedule III substances have less potential for abuse than do Schedule I or II substances, and abuse may lead to moderate or low physical dependence or high psychological dependence. These include products containing not more than 90 milligrams of codeine per dosage unit (Tylenol with Codeine) and buprenorphine (Suboxone). An anabolic steroid such as Depo-Testosterone is an example of a non-narcotic Schedule III substance.
IV. Substances in this schedule have a lower potential for abuse than do substances in Schedule III. Examples include alprazolam (Xanax), carisoprodol (Soma), and diazepam (Valium).
V. Schedule V substances have a lower potential for abuse than do substances listed in Schedule IV and consist primarily of preparations containing limited quantities of certain narcotics. Examples include cough preparations containing not more than 200 milligrams of codeine per 100 milliliters or per 100 grams (Robitussin AC, Phenergan with Codeine).

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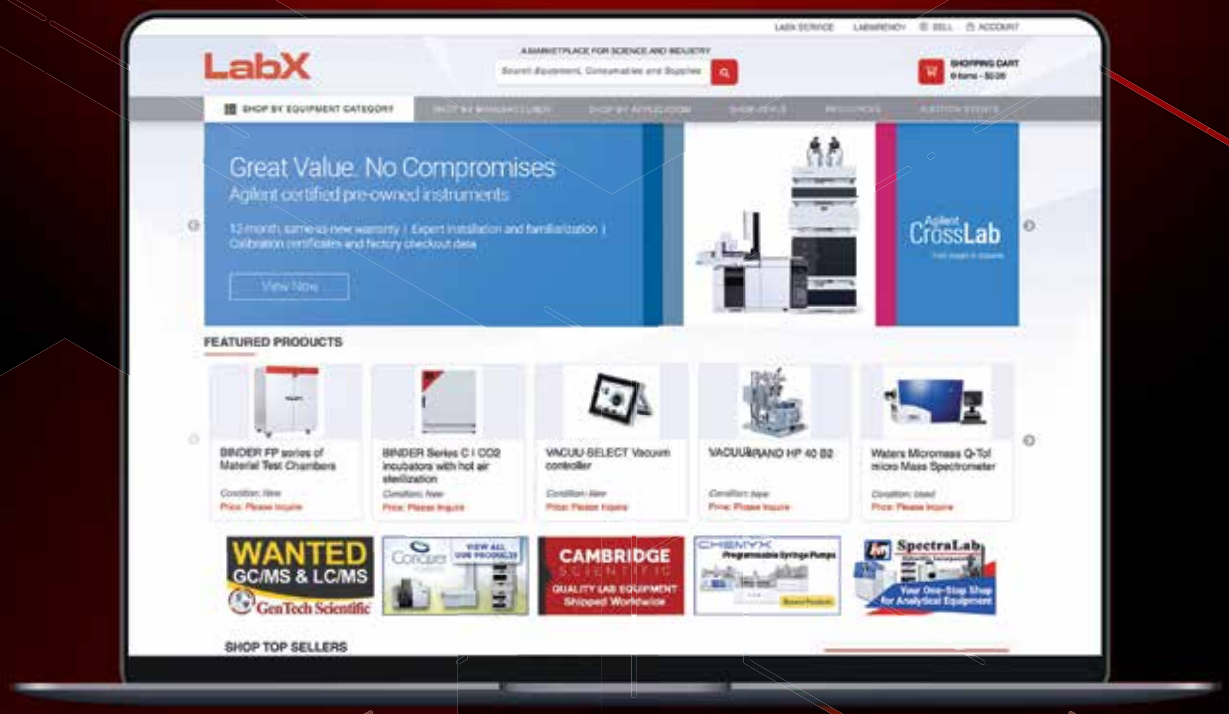

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However, we need to understand that the controlled substance schedules currently list approximately 160 specific substances, and the schedules do *not* constitute a comprehensive listing of all controlled substances. The schedules describe only basic or parent chemicals and do not list all the salts, isomers, and salts of isomers, esters, ethers, and derivatives that may be controlled substances.

For example, if a substance is an analogue and is structurally or pharmacologically substantially similar to or is represented as being similar to a Schedule I or Schedule II substance and is intended for human consumption but is not an approved medication in the US, it can be treated as a Schedule I substance for criminal prosecution.

Management plan

The main focus and important information you should take away from this article is that before you begin using any controlled substance in the lab, you should have all the appropriate licenses and registrations and have a robust program in place for managing and safeguarding these materials.

> "Licensing and registration are critical and must be secured prior to any acquisitions."

The heart of good controlled substance management is a comprehensive written program. Your certified safety management practitioner (CSMP) should address everything from acquisition to final disposal and include vigorous training, security, record keeping, and follow-up. It should clearly list the responsibilities of all stakeholders such as the CS coordinator, principal investigators, and other authorized personnel. Clearly indicate the steps for purchasing, receiving, storing, and disposal. Place extra attention on access restrictions, personnel screening, spill procedures, and handling diversion, loss, or theft.[2]

Licensing and registration are critical and must be secured prior to any acquisitions. After you obtain your state license, you need to then register with the federal Drug Enforcement Agency (DEA). Excellent step-by-step instructions with explanations are provided on the DEA registration website.[3] Pay attention to your specific research requirements for both state and federal applications. The registration is an absolute must, so make sure to apply early. State licenses usually renew every two years, whereas the DEA registrations must be renewed annually.

Set up your on-site tracking following your CSMP, beginning with receiving material through inventory listing, storage, and control during dispensing and ending with use or disposal record keeping. Do not underestimate the importance of safe, secure storage with tightly controlled access.

Finally, make sure your program has well-documented disposal procedures. You must understand that controlled substances are not considered hazardous waste, biological waste, or regulated medical waste. Therefore, they cannot be disposed of through your normal biological/medical/hazardous waste programs. Your CSMP should have requirements to return all unused or expired material to the original manufacturers or distributors or to set up reverse distributors—specialty contractors knowledgeable and approved for handling controlled substances.

Disclaimer

This article is intended to address the use of controlled substances in research, instruction, and analytical laboratories. The suggestions may be applied to medical clinical activities, medical veterinary hospitals, or pharmacies, but these are governed by federal and state accrediting and regulatory agencies and are subject to review and audit by those agencies.

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Assay Development: Vaccines

DEVELOPING SPECIALIZED ASSAYS TO ASSESS VACCINE EFFICACY, EXPOSURE, AND SAFETY

by Michelle Dotzert, PhD

Vaccine development is a long, intensive process that begins with the determination of public health needs and priorities. Several organizations have compiled priorities for research and development, including the World Health Organization/United Nations Development Program for Vaccine Development.

> "Vaccines are generally aimed at modulating or priming the immune response to a pathogen so that the body can rapidly eliminate the pathogen and minimize disease."

There are several stages of vaccine development and testing, beginning with an exploratory stage to identify natural or synthetic antigens. Next, pre-clinical work begins and cell culture and animal models are used to determine the immunogenicity and safety of a vaccine candidate. Following the approval of an Investigational New Drug application to the US Food and Drug Administration, clinical trials may begin. Specialized assays are developed in the pre-clinical and early clinical trial phases, and are validated in later clinical trial phases. Prior to lot release, assays have well-characterized parameters and criteria, although the assay development process is not without challenges. The immune system is highly complex; however, new technologies and techniques offer solutions. Eventually, a successful vaccine candidate will progress through to Phase III trials and be licensed. The entire rigorous process can take upwards of 15 years to complete.

IMMUNOGENICITY, EFFICACY, EXPOSURE, AND SAFETY

First, it is important to understand the underlying mechanism of action. "Vaccines are generally aimed at modulating or priming the immune response to a pathogen so that the body can rapidly eliminate the pathogen and minimize disease," explains Claire Richards, PhD, principal scientist, infectious disease, discovery services at Charles River Laboratories (Wilmington, MA). Pre-clinical vaccine research includes assay development, in part, for the quantification of the immune response. Rafiqul Islam, MS, executive director of bioanalytical services at Celerion Inc., echoes the importance of immunogenicity assays: "Multiple assays are required to measure immune responses to provide confidence that the candidate vaccine is at least capable of eliciting a robust immune response."

Islam provides insight into the clinical development of vaccines, which "requires a specific set of specialized assays to demonstrate the immunogenicity, efficacy, exposure, and safety. The development and validation of these assays requires integration of therapeutic insights, state-of-the-art technologies, custom reagents, and robust quality management systems."

Which assays, then, are used to assess the immune response? "A suitable assay to determine immune stimulation is usually required along with possible inhibition

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assays to show the immune response can reduce the growth of the pathogen; [for example] antigen-specific ELISAs, inhibition ELISA, neutralization assay, [and] effective concentration to give 50 percent survival (EC50)," says Dr. Richards. Table 1 outlines a summary of the assays commonly used to support vaccine development. The humoral, or antibody-mediated, immune response relies on B-cell recognition of antigens and subsequent antibody release. Ligand-binding techniques, such as ELISA (enzyme-linked immunosorbent assay), are often used to assess the humoral response. Conversely, the cell-mediated immune response relies primarily on T cells and is often assessed with ELISpot (enzyme-linked immunospot) or flow cytometry.

The immune response assays may be used to determine next steps in a pre-clinical study. According to Dr. Richards, "The immune response prior to infection may be assessed, and if a suitable response has been induced, the models can be challenged or receive a further vaccine dose."

Additionally, specific assays are required to assess vaccine efficacy, exposure, and safety (Table 1). Efficacy assays are designed to measure antigens, using "ligand-binding assays and molecular assays (e.g., qPCR)," says Islam. Both cell-based and molecular assays are used to assess infectivity, a measure of exposure and safety. The plaque-forming assay is a commonly used infectivity assay involving cell monolayers overlaid with agar to prevent the virus from spreading in the medium. As cells propagate infection, plaques begin to form. "At the end of a study, bacterial or viral load in organs may be assessed by determining the number of colony-forming units (CFUs) or plaque-forming units (PFUs)," says Dr. Richards.

ASSAY TECHNOLOGY

It is essential to select the optimal assays for vaccine development, and there are several different technologies to compare. "Assays developed to support vaccine studies should be automation friendly, as vaccine trials require analysis of a large number of samples," notes Islam. Numerous automated liquid handling and cell culture systems are available and dramatically reduce the amount of time spent performing tedious tasks as well as improving consistency.

"The most widely used technology [involves] ligand-binding assays and cell-based assays," says Islam. Ligand-binding assays such as ELISA rely on the formation of an immune complex between the antibody and antigen. Cell-based neutralization assays offer a functional antibody measurement, as they are designed to detect antibodies capable of inhibiting viral replication.

While these assays are widely used, "the trend currently is to collect and evaluate more assay parameters using a divergence of technologies," says Islam. "Technologies such as flow cytometry, ELISpot, qPCR, gene expression arrays, and multiplexing assays are gaining popularity, as each one of them provides unique insight into the safety, efficacy, immunogenicity, and biodistribution of vaccines." In the clinical realm, a T-cell ELISpot, for example, is used to quantify the number of reactive antigen-specific T cells, indicative of a patient's immune response.

Selecting the appropriate assay for vaccine development is sometimes a difficult task. According to Islam, "The choice of the most relevant assay that correlates with protection against infection or disease is challenging due to the fact that immune responses are polyclonal and multidimensional by nature." The human immune

Intended Purpose	Technology Platform	Assay Description
Immunogenicity Assessment — Humoral Antibody Response	Ligand-binding assay (e.g., ELISA, ECLIA)	Measurement of total antibody
	Cell-based assay (e.g., viral-neutralization assay, bacterial-killing assay)	Functional antibody assay measurement
Immunogenicity Assessment — Cell-mediated Immunity	ELISpot, flow cytometry	Measurement of immune cells' response upon exposure to specific antigens
Efficacy	Ligand-binding assays and molecular assays (e.g., qPCR)	Measurement of antigen
Exposure and Safety	Cell-based assays and molecular assays	Measurement of infectivity and biodistribution

▲ *Table 1. Courtesy of Celerion Inc.*

response is certainly complex. Polyclonal B-cell activation is characterized by production of numerous different antibodies against a single antigen, which may be both advantageous for the host and play a possible role in the development of autoimmune disease. Given this complexity, assay selection during vaccine development requires numerous considerations.

Scientists at Charles River outline several considerations to ensure a well-designed assay, ranging from availability of control compounds to robustness and scalability. Reagents, for example, are especially important when developing an assay for vaccine research, as they require significant time to produce. "In most cases, the generation of reagents requires immunization of animals or identification of large batches of reactive PBMCs [peripheral blood mononuclear cells], which are time-consuming," says Islam. Given the complexity of assay design, it may be useful to consult an assay-development service for expertise and guidance.

UNIQUE CHALLENGES

Vaccine development is a complex process that presents several unique challenges. From the pre-clinical perspective, Dr. Richards notes that "inducing an effective response to the vaccine, optimizing the assays to ensure sensitivity, and ensuring the disease model is appropriate and reproducible" are all challenges associated with the process.

The intricacies of the immune response pose unique challenges for assay development, notes Islam, particularly for assessing parallelism in the context of a polyclonal response. "In order for immunological assays to generate reliable immune response data, it is important that the dose response curves of the samples be parallel to the reference curve. However, in most cases, due to the varying clonal compositions of the antibody response from different subjects, parallel dose response curves cannot be expected," Islam explains. Further difficulty lies in the "demand for multi-parameter assays or multiple assays for the same analyte," says Islam. He provides an example of measuring T-cell phenotypic markers such as cell surface markers, intra-cellular markers, etc., along with functional markers such as cytokine production.

Vaccines are designed to harness the power of the immune system to identify and eliminate disease-causing pathogens, and applications have expanded from infectious disease control to include cancer and autoimmune disease. Each vaccine is developed based on the immune response to a pathogen, which is a highly complex process. As such, there are numerous challenges in the assay development and screening process for vaccines. New techniques including flow cytometry, ELISpot, qPCR, gene expression arrays, and multiplexing assays are being implemented to overcome these challenges. Further, as cell culture and liquid handling automation technology continues to improve, so to does assay efficiency. Advancements in this field have enormous potential for improving human health, beyond what we once dreamt possible.

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Khalid Shah, MS, PhD

ASK THE EXPERT

DEVELOPMENTS IN CELL ENGINEERING AND THERAPY

by Tanuja Koppal, PhD

Khalid Shah, MS, PhD, director of the Center for Stem Cell Therapies and Imaging, Harvard Medical School, and vice chair of research, Brigham and Women's Hospital, talks to contributing editor Tanuja Koppal, PhD, about recent innovations in cell engineering and editing, which has in turn led to advances in cell therapy. Dr. Shah talks about the work that he is doing in this area, while highlighting some practical considerations when it comes to translational research and technology investments.

Q: How do you define cell therapy, and what are some of the advances in cell engineering that have made cell therapy promising?

A: Cell therapy involves taking a normal cell, modifying or engineering it, and putting it into a patient to treat the disease. The type of cell therapy depends on where the cell comes from. In some cases, the patient's own cells can be extracted, modified, and delivered back into the body to generate the desired effect, which is referred to as autologous cell therapy. However, in some cases the time from disease diagnosis to starting the treatment is very short, and cell therapy, which often takes three to six months to put in place, is not an option. In such cases, cells available off the shelf from a donor that have been previously engineered are used; this is referred to as allogeneic cell therapy. Cell therapy needs to be defined in the context of the disease. For diseases that are not life-threatening, autologous cell therapy should be preferred; whereas in diseases like cancer, where time is of the essence, allogeneic approaches need to be considered for finding the right treatment option.

Cells that are commonly used for cell therapy include stem cells, lymphocytes, dendritic cells, and pancreatic islet cells, and they have been used to treat cancer and autoimmune diseases, to repair joints or a weakened immune system, and for CNS (central nervous system) disorders.

> "It is essential to understand the underlying biology behind the disease to develop mechanism-based cell therapies for that disease type."

Chimeric antigen receptor (CAR) T cell therapy uses a patient's own (autologous) immune cells (T cells) that are engineered to express a receptor that recognizes and binds to an antigen on the malignant cell. Once activated, these T cells can then destroy the malignant cell. Recently, there has been a shift from CAR T cells to natural killer (NK) cell therapy, as NK cells can be transferred from one healthy individual to a patient (allogeneic) without the risk of an immune reaction, as there is no haploidization in these cells. Another alternative is to use induced pluripotent stem cells (iPSC) from the patient to derive the T cells or NK cells and minimize the risk for immune rejection.

Q: Can you highlight some of the practical considerations for cell selection, growth, gene editing, and delivery of vectors that readers will find useful?

A: Some of the key questions that need to be answered for selecting the right cell therapy begin with identifying the disease that is being treated and finding out what's being done currently to treat this disease. Any new therapy that is introduced will have to be tailored to the current standard of care. Once those questions are answered, a correct model that mimics the disease has to be established in order to test the new therapy in a specific setting. It is essential to understand the underlying biology behind the disease in order to develop mechanism-based cell therapies for that disease type. For example, very often tumor cells are heterogenous and therefore resistant to one type of therapeutic that is released from an engineered cell. This demands changing the therapeutic or developing cells that have multiple targets on the surface of the tumor cell or tumor-associated endothelial cell.

Once the biology is well understood and the disease model is established,

the ultimate source of the cell has to be determined. Will it come from the patient (autologous) or will it come from a healthy donor (allogeneic)? How are the cells going to be grown, engineered, and delivered into the patient? Engineering the cells is a complex process, and there will be many questions related to whether we are going to transfect the cells with lentivirus or AAV (adeno-associated virus) vectors? How are we going to get the gene or the CAR T to a specific locus within the cell? For clustered regularly interspaced short palindromic (CRISPR)-based editing, questions on how to design the guide RNA (gRNA) or deliver the CRISPR-associated (Cas) protein, will need to be answered.

Q: How have you approached these questions in your lab in terms of developing new cell therapies?

A: In our experience, we have found that iPSC and mesenchymal cells are much easier to modify and edit than T cells and NK cells. We typically start out by testing the cell therapy in mouse models. We use dual imaging to image different cell populations, such as the tumor cell and stem cell, or CAR T cell homing, which uses fluorescence and bioluminescence markers. Incorporation of these imaging markers *in vivo* using genetic engineering leads to real-time information and leaves very little room for doubt when interpreting results. I recommend that real-time *in vivo* imaging markers be used from the very beginning to figure out what is happening inside the cell in real time. Are the cells still alive? Is the drug reaching its target? How are the cells responding to the therapy? These are all questions that need to be addressed, even before developing a therapeutic. Manufacturing and good manufacturing practice considerations need to be addressed further downstream.

We are focusing on three main things. First, we are developing cell-based therapies that are targeted toward certain receptors on the surface or within the cell. The fundamental questions related to how our cell surface receptor targeted therapeutic cells kill the tumor cell in a mechanism-based way or how the tumor cells develop resistance to the cell therapy always need to be answered. As the expression of a variety of cell surface receptors in different tumor types varies, we focus on developing cell-based therapies for a specific type of tumor by first understanding its mechanism of action; and once we have validated it extensively in a particular tumor type, then we can potentially use it for other tumor types, if applicable. Developing and exploring stem cell, T cell, or NK cell therapy without prior knowledge of the disease or the mechanism by which cell-based therapies work in such disease models is not going to go a long way.

"I recommend that real-time *in vivo* imaging markers be used from the very beginning to figure out what is happening inside the cell in real time."

Second, we are engineering cells to express ligands, antagonists, and antibodies or release oncolytic viruses by understanding which receptor(s) they are targeting. In general, we tend to utilize therapeutics that have the ability to target both cell proliferation and cell death pathways in tumor cells and tumor-associated cells in the microenvironment, which is also quite unique. We are creating molecules that can target cell surface receptors that are specifically expressed on tumor cells. Third, even if we have the right therapy, but it is not tested in the right disease model that can mimic what's happening to the patient in the clinic, it won't work. Hence, we are developing mouse tumor models that are key to this translation and are also utilizing imaging techniques that can be used as markers during this process.

Khalid Shah, MS, PhD, is the director of the Center for Stem Cell Therapeutics and Imaging at Harvard Medical School and the Center of Excellence in Biomedicine at Brigham and Women's Hospital (BWH). He is also the vice chair of research for the Department of Neurosurgery at BWH and a principal faculty at Harvard Stem Cell Institute in Boston. Dr. Shah and his team have pioneered major developments in the cell therapy field, successfully developing experimental models to understand basic cancer biology and therapeutic cells for cancer. Recently, Dr. Shah's laboratory has reverse engineered cancer cells using CRISPR/Cas9 technology and utilized them as therapeutics to treat cancer. He has founded two biotech companies, AMASA Therapeutics and ALIM Therapeutics, whose main objective is the clinical translation of therapeutic stem cells in cancer patients.

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NEXT-GENERATION SEQUENCING

LIBRARY PREPARATION IS A CRITICAL STEP IN THE WORKFLOW OF SEVERAL NGS PARADIGMS

by Brandoch Cook, PhD

Long ago, when interviewing as a prospective student at PhD programs across the country, a very stern and important professor at an august institution asked me to name the most significant development in molecular biology since the Watson-Crick structure of the DNA double helix. After I gave the most intelligent and elaborate version of "I don't know" I could muster, he stared me down and proclaimed, "DNA sequencing" as if that were the only possible answer. In the biomedical sciences, where lab meeting—let alone peer review—often constitutes blood sport, perhaps at least some argument was warranted; on second thought, perhaps he was right.

The technology's acknowledged pioneer, Frederick Sanger, is one of only four scientists to win two Nobel prizes, having first elucidated the amino acid sequence of insulin in the 1950s. He established the foundational idea that proteins have unique structures and properties that can be predicted, providing powerful early proof of the Central Dogma of molecular biology. At the time, there were no reliable means to examine stretches of nucleic acid sequence, and so to a large extent the Central Dogma was confirmed in reverse, with discoveries of key protein translation structures and mechanisms preceding the report of the first polynucleotide sequences in the mid-1960s. Maxam and Gilbert later devised a method of nucleotide sequencing using chemical cleavage followed by electrophoretic separation of DNA bases. Sanger improved upon this by employing primer extension and chain termination, a method that gained primacy with its decreased reliance on toxic and radioactive reagents. Applied Biosystems (Foster City, CA) provided the first automated Sanger sequencers, later incorporating innovations such as computerized data analysis and the polymerase chain reaction. Industrial-scale automation resulted in deposition of thousands of expressed sequence tags on GenBank and other databases. This provided an impetus for gene cloning and functional studies through the 1990s, and populated a lattice to be filled in by the Human Genome Project and consortia to generate complete reference sequences for important animal models.

> "The expense and expertise required to operate next-generation sequencers has largely relegated them to dedicated core facilities."

At the time, the publication of the draft sequence of the human genome might have seemed like an act of culmination; however, it was a mere prelude to the flowering of a new age of discovery, largely predicated on deep genotypic investigation of context-dependent phenotypes. The resulting pressure on the sequencing data pipeline led quickly to significant technological changes that far surpassed the Sanger method in terms of cost and efficiency by flattening the workflow. These technologies are collectively known as next-generation sequencing (NGS), and rapidly identify and record nucleotide binding to complementary strands of amplified cDNA, in massively parallel synthesis reactions with a daily throughput in the hundreds of gigabases. As a point of comparison, the sequencing of a human genome using the Sanger method in 2001 at a cost of $100 million would be reduced to $10,000 by 2014 by using NGS, with a next-day turnaround. A short list of NGS applications that have evolved since NGS inception include the ability to: 1) rapidly sequence whole genomes (genomics); 2) quantify global gene expression patterns (transcriptomics); 3) zoom in on regions of interest to deeply sequence target regions, including promoters/enhancers and micro- and non-coding RNAs (targeted and exome sequencing); 4) perform

epigenetic analyses to uncover patterns in methylation and other post-translational modifications; and 5) achieve single-cell sequencing to define and identify rare cell types important in processes such as stem and progenitor cell differentiation, and the etiology of different cancers.

Although all NGS runs on the principle of massive parallel sequencing reactions, the modes of nucleotide incorporation and fluorescence detection in the synthesis reactions differ among commercially available platforms. The most widely used are the Illumina and Roche 454 systems, which differ functionally in that Roche handles longer reads with lower throughput, but with greater cost and a tendency to miscall polybase repeats. The expense and expertise required to operate next-generation sequencers has largely relegated them to dedicated core facilities; when purchasing reagents and preparing samples, investigators must consider what systems and models are available. Because the lower limit of detection can be in the range of picograms, sample preparation must be optimized to allow the deepest coverage and the highest signal-to-noise ratio possible to ensure data validity. Regardless of the nature of the starting material—genomic DNA, mRNA, DNA-protein complexes, etc.—the precondition for generating useful NGS data sets is a broad library of nucleic acids. As in so much of molecular biology, there is always a kit for that.

A generic workflow for library preparation is as follows: 1) sample collection, fragmentation via enzymatic digestion or shear forces, 2) end-repair and phosphorylation of 5' ends, 3) polyA-tailing to allow ligation of oligo dT-based adapters, 4) and a high-fidelity PCR-based amplification step to generate a product with adapters at both ends, barcoded for identification of individual samples run as multiplex reactions in a single lane. Taking Illumina (San Diego, CA) products as an example, each library prep kit is engineered to appropriately modify and amplify the given starting material, while reducing the number of steps to avoid sample contamination. For RNA-seq studies, the TruSeq RNA kit executes a workflow of mRNA isolation, followed by fragmentation and first- and second-strand cDNA synthesis. Methyl sequencing depends on the addition of a modification, with bisulfite treatment of genomic DNA converting cytosine residues into uracil while leaving methylcytosine unmodified. The Methyl Capture Epic library

prep kit adds probe hybridization and bisulfite conversion steps in addition to fragmentation, adapter ligation, and amplification.

Finally, use of NGS technologies has become widespread, with genomic, transcriptomic, or epigenomic data sets almost a required aspect of high-impact papers. However, they provide a generalized snapshot that might not be an accurate representation of what is biologically relevant in a tissue or in a sample of mixed cell types. Single-cell sequencing is a promising development to satisfy this discrepancy, but has the biggest potential flaws in sample and library preparation. Specialized providers such as Fluidigm (South San Francisco, CA) and 10X Genomics (Pleasanton, CA) are innovating microfluidic apparatuses to handle comprehensive sample collection and library amplification protocols.

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PCR/qPCR

DECIDING ON A PCR DETECTION METHOD

by Mike May, PhD

In Fort Collins, CO, Adam Heck explores how genes control development. As a doctoral student in cell and molecular biology at Colorado State University, he works with induced pluripotent stem cells (iPSCs) using polymerase chain reaction (PCR) techniques. "I'm looking at how iPSCs control gene expression when differentiating into the various cell types," explains Heck.

Methyl readers play a role in the differentiation of iPSCs. These proteins recognize specific methylations on RNA, such as N6-methyladenosine (m6A), which is methylation of adenosine at the nitrogen-6 position. "Certain proteins recognize this on RNA and control the fate of it," Heck explains. A methyl reader could facilitate the enzymatic degradation of an RNA or promote translation. Overall, Heck notes, these processes "help stem cells control whether they stay a stem cell or differentiate into specific cell types." That's a basic, but complex step in developmental biology.

This work creates a range of challenges. Even working with the cells is tricky. Typically, scientists don't use antibiotics with iPSCs because doing so alters their development; however, this makes contamination an issue. "Plus, they are touchy cells to work with," Heck notes. "They are very ineffectively transfected with plasmids, which leaves small interfering RNA, called siRNA, for knockdown of the methyl readers." After such manipulations, Heck uses PCR to quantify the results.

PCR preferences

With qPCR (quantitative PCR), the detection method can be dye- or probe-based. Dye-based qPCR typically makes use of green fluorescence. The probes provide some advantages; for example, "Probes can help increase the specificity of the test," explains John Beeby, laboratory manager at the Cornell University College of Veterinary Medicine's Animal Health Diagnostics Center in Ithaca, NY. "We routinely use both PCR and qPCR to detect the presence of a wide range of animal pathogens in the samples we receive."

In general, qPCR detects amplification as it occurs, which explains the technology's other name—real-time PCR. Consequently, "qPCR can quantify the amount of pathogen present in the sample," Beeby explains, and "qPCR is typically much faster than conventional PCR, which helps in the rapid diagnosis and treatment of sick animals."

Going green

Heck started his work on iPSCs using qPCR but soon switched to digital PCR (dPCR). (For the history of dPCR, see an article by Alec Morley, emeritus professor at Flinders University's College of Medicine and Public Health in Adelaide, Australia.[1]) Specifically, Heck performs reverse transcription (RT) on RNA samples to make cDNA. Then, he says, that cDNA is used in RT-dPCR "with primers to specific genes in order to examine their expression."

Like other kinds of PCR, the digital form can be applied to many questions. As Heck says, "There are people on campus who use digital PCR for things like copy number variations, but the vast majority use it for analyzing changes in gene expression." In comparing quantitative and digital PCR, Heck points out that qPCR is slightly less expensive per sample. For accuracy, though, he says that "digital PCR blows qPCR out of the water."

Heck works in a lab run by Carol Wilusz, professor in the Department of Microbiology, Immunology and Pathology. In comparing dye- versus probe-based dPCR, she says, "My lab uses almost exclusively digital PCR—EvaGreen—because it's cheaper and simpler for small-scale projects." This dye can be used in various forms of PCR, including qPCR, dPCR, and droplet digital PCR (ddPCR).

In fact, Wilusz, Heck, and their colleagues used ddPCR[2] (Bio-Rad; Hercules, CA) and EvaGreen to quantify the stability of mRNA and found that "the use of dPCR allows for the detection of relatively small changes in abundance (<10 percent) that can be hard to quantify by qPCR but can reflect significant changes in half-life. However, if large changes (much greater than twofold) in half-life are anticipated, qPCR can give reliable results."

But Eva is not the only green on the PCR block. At the Iowa State University DNA Facility in Ames, assistant scientist II Kevin Cavallin describes another option. This DNA facility "provides core biotechnology laboratory services for investigators within academia, industry, and government research institutions." The facility's equipment includes two qPCR platforms: a StepOnePlus Real-Time PCR System (Thermo Fisher Scientific; Waltham, MA) and a BioMark HD (Fluidigm; South San Francisco, CA).

"The majority of our clients run SYBR Green assays," Cavallin says. "The advantage of SYBR Green verses TaqMan is cost and ease of use." Still, most pros also come with cons. "The disadvantage is that SYBR Green can generate false positives since the dye intercalates into any double-stranded DNA," Cavallin explains. "Therefore, it's essential that clients design primers that are specific to their target DNA and run a melt curve to verify that they have a single product."

Quick comparisons

At the Institute of Analytical and Bioanalytical Chemistry at Ulm University in Germany, doctoral student Manuela Gast—led by professor Boris Mizaikoff—uses qPCR[3] to quantify the amount of virus in samples, including ones in natural matrices. Although she's used both dye- and probe-based methods—that is, SYBR and TaqMan, respectively—most of her work relies on probe-based detection.

She provides a concise comparison of the two approaches. For dye-based detection, Gast points out several advantages:
- straightforward
- easy design and implementation
- easy screening of different samples
- low costs

She also notes some disadvantages:
- nonspecific binding
- requires melting-curve analysis
- longer amplicons may create a stronger signal
- not adapted to multiplex
- not suitable for qualitative qPCR

According to Gast, the advantages of probe-based detection include:
- sequence-specific detection
- broad dynamic range with low detection limit
- multiplex assays possible
- relatively robust
- high signal-to-noise ratio

On the downside, she notes that the assay design is not trivial and the cost can be high.

From animal pathogens to iPSCs and beyond, PCR is a versatile technique for many experiments. Dye- and probe-based detection methods each have unique advantages and several factors, including experimental design and cost, must be considered when selecting the best method.

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ROBOTIC WORKSTATIONS

AUTOMATION IN DRUG DISCOVERY

by Angelo DePalma, PhD

High-throughput screening (HTS) for drug discovery was conceived through the nearly simultaneous industrialization of combinatorial chemistry and the emergence of affordable laboratory automation, but its success ultimately depends on integrating factors related to chemistry, assay design, and informatics. Combichem enabled the creation of compound libraries with millions of compounds, while laboratory robots, plate handlers, liquid handlers, and supervisory information systems allowed their study.

Today, drug discovery remains a game of big numbers. John Unitt, director of bioscience at Sygnature Discovery (Nottingham, UK, and Cambridge, MA), notes that deep-pocketed companies routinely investigate libraries in the one-to-two-million-compound range, while smaller discovery organizations use much smaller libraries of only 200,000 to 400,000 molecules.

Robotics have more than kept up with the compound flow, so automation vendors now differentiate on the basis of accessibility, breadth of assay (i.e., instrument and method flexibility), and software, while library vendors focus on creating collections of original chemical scaffolds. Meanwhile, a whole separate industry works on automating and—perhaps more importantly—standardizing optical readouts, liquid handling and dispensing, and background tasks like cell culture and preparation.

For low-throughput routine automated liquid handling, Sygnature relies on the Biomek NXp Automated Workstation, a small-footprint system with two pipetting options and built-in flexibility. "We picked the Biomek system for its throughput, breadth of assay, and walk-away time," Unitt says. Sygnature uses one NXp for assay construction and another for metabolic, pK, and ADME studies.

For liquid dispensing, Sygnature uses the Labcyte Echo acoustic dispensers to prepare assay test plates using nanoliter volumes of compound solutions. "This assay automation setup conserves highly valuable compound stocks and also optimizes liquid-handling performance by using the excellent accuracy and precision of the Echo," Unitt says.

For their robotics platform, Sygnature relies on systems from HighRes Biosolutions (Boston, MA), a vendor Unitt worked with while in a previous position at a large biopharmaceutical company. The ACell benchtop automation system provides entry-level, deploy-anywhere automation and easy integration with HighRes plate storage units. "A typical drug discovery laboratory will also want to invest in the storage unit and maybe cell culture as well, plus informatics to communicate and capture all data generated during screening," Unitt says. "With the ACell system modular, you can grow and expand in terms of assay readouts, end points, and capacity."

Despite still relying on huge molecule collections, HTS is no longer merely about compound library size. The emphasis, Unitt notes, is on quality versus quantity. "For our projects, senior medicinal chemists assess all structures for chemical diversity and lead-like structures while emphasizing synthetically novel scaffolds."

Quality has become a priority for library developers because, in the past, compound collections included entries with significant side products and impurities. False positives and negatives resulting from unanticipated, unknowable interactions between impurities and targets can thwart the potential for mining a collection of hits for structure-activity relationships, which discovery scientists use to generate lead molecules and eventually drug candidates.

What would a manager in a drug discovery lab like to see in future automation products? "We're always looking for ways to do things faster," Unitt says. "Accuracy and precision of existing automated systems are already very good, so the emphasis should be on customer support to minimize downtime."

One key to the success of HTS is the application of assays that ask the right questions of the right compound library. "If an identifiable bottleneck exists, it is adapting a standard laboratory test—immunoassay, enzyme inhibition, etc.—to microplate formats and successfully marrying that assay to the robotic workstation," Unitt explains. Assay developers have made great strides in this area, "but over the years, HTS has overcome problems like these as more and more screening platforms have been adapted to it."

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SHAKERS

A PRIMER ON DIGITAL SHAKERS

by Brandoch Cook, PhD

When you Google "digital shakers," one of the most popular page results is the digital archive of the Shaker society and its history. The article you are reading now is not, however, about a utopian society whose own demise was implicit in its charter. Rather, this article is intended to give some information on the laboratory machines used to agitate liquids. For the purposes of this article, there are two types of shakers: 1) the big, slow orbital shakers used to culture bacteria; and 2) the high-speed microplate shakers designed to emulsify buffers or lyse cells as uniformly as possible. In both cases, it is beneficial to go digital for a number of reasons. The only advantage to purchasing analog shakers is the initial cost savings, especially if they are part of the start-up of a new lab or central core with an intensive focus on microbiology or high throughput screening, where many machines are required. Even with the initial savings, however, analog shakers often require maintenance and parts replacement at least yearly. Digital shakers usually come maintenance-free and offer a greater range of speeds compared with their analog counterparts; digitization allows the ability to program multistep shaking protocols and, often, to analyze speed, time, and temperature data in compatible software.

Big and slow

There is a huge variety of floor, stackable, and benchtop models designed to mix culture samples at low speed, and there are three key considerations that will drive decision making when it comes to selecting a model:

1) What types, sizes, and numbers of vessels will be shaken? Floor models typically allow shaking of several 2- or 3-liter flasks up to about 500 rpm, while benchtop models usually accommodate smaller volumes and lower total weight limits on their orbital platforms.
2) What is the optimal shaker footprint for your lab space? A larger laboratory may initially have ample space for floor-model shakers, especially if there is a significant amount of bacterial culture planned. As more equipment accumulates, you may find floor shakers migrating to inconvenient corners. Therefore, smaller benchtop models might be more suitable in the long run.
3) What temperature range is necessary? For a price premium, there are stackable benchtop systems with refrigeration available, such as Eppendorf's New Brunswick Innova series; or massive, console models such as ThermoFisher's MaxQ HP shakers. Typical floor-model shakers, on the other hand, can generally operate at temperatures from slightly below ambient up to 50 or 60 degrees Celsius. A cost-saving solution if refrigeration is necessary is to move shakers to a cold room.

Small and fast

One confounding variable in the high-throughput screening pipeline is the tendency for nonuniformity of conditions in multi-well plates. This often comes in the form of lysis, temperature changes, or reagent mixing, proceeding unevenly at the edges of plates compared with the wells toward the center. Dedicated, high-speed microplate shakers can mitigate eventual discrepancies in data collection by providing platforms for consistent, vigorous, and simultaneous agitation of multiple plates. Troemner (Thorofare, NJ) offers NIST-calibrated microplate shakers that operate up to 2500 rpm, accommodate up to 48 microplates, and have a heft and suction-enforced base to minimize any tendency to walk along the bench when operated at high speeds. These machines take up only a couple of square feet of bench space, but can seriously improve the workflow of screening and other applications that require mixing.

Shakers are ubiquitous items in biomedical laboratories and, therefore, a crucial purchase to consider, even though their features, costs, and varieties are often an afterthought. On the large scale, a wide array of options for bacterial shakers can suit many different laboratory needs. In miniature, digital microplate shakers can improve consistency in high-throughput applications.

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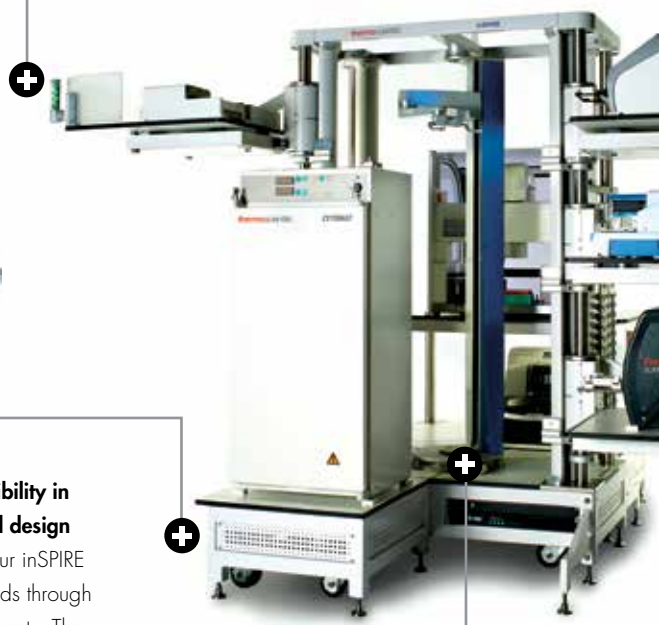

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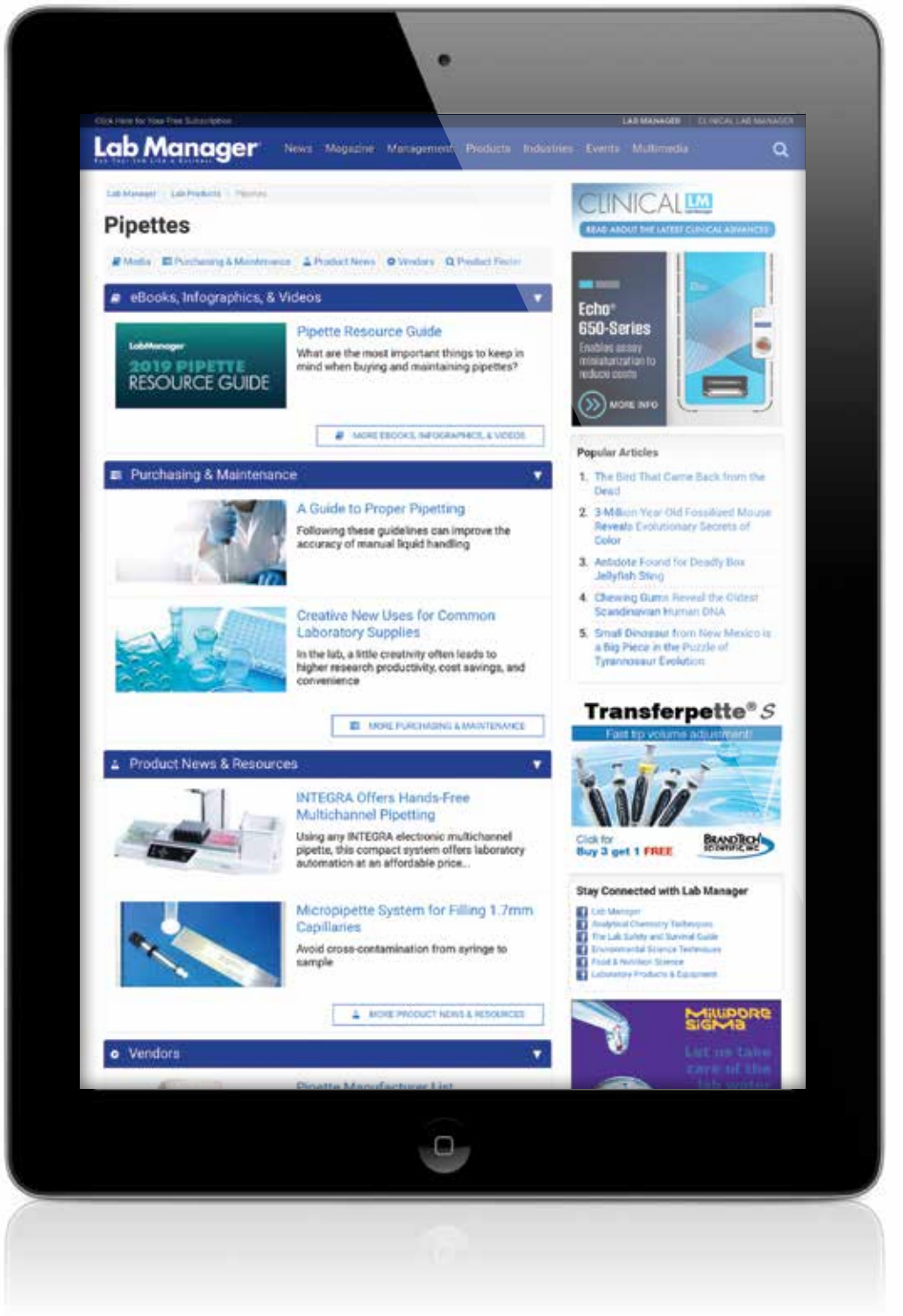

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- Incorporates a stainless-steel chamber with mechanically refrigerated walls
- Runs with minimal operator attention and requires as little as 26.7 x 52.1 x 27.9 cm lab space

SP Scientific www.spscientific.com

Centrifuge

BI-XDC

- Measures the size of particles according to the time the particle takes to sediment in the detector according to Stokes law
- Proven to give error-free quantitative measurements across a broad range of samples including nanoparticles, minerals, clays, ceramics, and metal oxides
- Features a reproducible digitally controlled disk speed to ensure high performance and accuracy

Testa Analytical www.testa-analytical.com

Biological Safety Cabinets

Herasafe, Maxisafe 2030i

- Two new units developed to optimize contamination prevention, information protection and management, and user convenience
- Offer a "smart" self-monitoring safety capability to automatically maintain appropriate air flow and monitor critical conditions in real time
- Connect to the secure Thermo Scientific Cloud for simplified, remote sharing and monitoring of key operational and performance data

Thermo Fisher Scientific www.thermofisher.com/bsc

Cleanroom Cabinet

CAB100

- Integrates world-class instruments for monitoring parameters into a simple, pre-configured enclosure
- Ideal for data collection specifically in cleanrooms, and in other demanding industrial environments
- Configurable according to application requirements, with various options for measurement inputs and safety barriers to instrumentation used in hazardous areas

Vaisala www.vaisala.com

Titrators

TitroLine®

- Designed with innovative features that make the instruments simple to use without sacrificing accuracy
- Series includes instruments for automatic, manual, or multitasking titration
- TitriSoft® software supports daily workflow during sample preparation
- Wide range of electrodes, sensors, conductivity cells, solutions, and buffers are also available

YSI www.ysi.com

INFORMATICS

Document Management Module

- Developed for the company's lab information management system, CloudLIMS
- Useful for food and beverage, cannabis, water, and soil testing laboratories
- Enables labs to meet ISO/IEC 17025:2017 accreditation
- Helps manage and track documented processes as part of ISO 17025, and provide access to these documents to laboratory personnel

CloudLIMS www.cloudlims.com

Thermal Imaging Software

FLIR Research Studio

- Designed for use across multiple platforms and in 22 languages to allow R&D and engineering teams to collaborate on thermal data collection, analysis, and sharing
- Provides powerful tools for analyzing complex live and recorded thermal data and collecting meaningful results
- Rich with features such as custom workspaces

FLIR Systems www.flir.com

Universal Temperature Transmitter

IPAQ C/R330

- Developed for maximum flexibility, accuracy, and reliability
- Compatible with RTD and thermocouple sensors, Ω, and mV inputs
- Offers high vibration resistance and noise immunity, guaranteeing reliable and accurate operation under the most demanding conditions
- Universal input enables simple, on-demand configuration and sensor selection

INOR Process AB www.inor.com

Electronic Batch Record Platform

MODA™ ES

- Offers a flexible and user-friendly solution for consolidating and managing batch and quality data generated by non-automated manufacturing processes
- Facilitates paperless execution across manufacturing and QC processes
- Modular design allowing individual modules to be created, validated, and used across different processes

Lonza www.lonza.com

Flowmeter Software

- Gives customers the option to move the measurement window to ensure users always measure at the optimal point of signal
- Functionality is available for the company's Atrato and MetraFlow ultrasonic flowmeters
- Overcomes challenges associated with measuring fluids that transmit ultrasonic sound waves within a band (e.g. +/- 30%) around the speed of sound in water at 20°C

Titan Enterprises www.flowmeters.co.uk

KITS

ELISA Kit

EndonucleaseGTP™

- Useful for the detection and quantitation of residual endonuclease impurities in recombinant vaccines and viral vectors used for gene therapy
- Boasts a detection limit of ~ 0.06 ng/ml, and is three times more sensitive than other commercially available options
- Contains all the necessary ready-to-use reagents for 96 analyses in microplate format

Cygnus Technologies www.cygnustechnologies.com

ChIP-seq Kit

Chromatrap® 2.0

- Developed to perform chromatin immunoprecipitation (ChIP) with unparalleled sensitivity
- Uses proprietary bead-free technology in parallel with high throughput sequencing to streamline workflows
- Allows users to perform up to 24 ChIP assays from cell collection through to immunoprecipitation, including up to 10 chromatin sample preparations

www.chromatrap.com/chip-kits

Single-Tube Lyophilized Reagent

Qscript lyo 1-step

- Optimized for highly sensitive and reproducible RT-qPCR RNA applications
- Facilitates easy reaction setup and prevents potential cross-contamination
- Contains a hot-start thermostable polymerase, a genetically engineered reverse transcriptase, as well as other components to ensure higher performance detection

Quantabio www.quantabio.com

DNA/RNA Isolation Kit

MagMAX

- Automation-ready for scalable recovery of RNA and DNA from difficult to lyse microorganisms
- Includes a proprietary enzyme mix that allows lysis and nucleic acid recovery from the toughest pathogens
- Uses magnetic-bead technology to ensure reproducible recovery of high-quality nucleic acids compatible with a broad range of applications

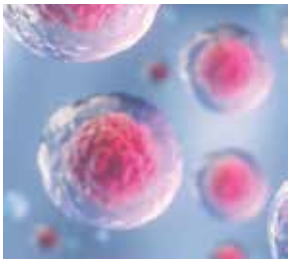
Thermo Fisher Scientific www.thermofisher.com

LIFE SCIENCE

Cell Culture

XerumFree™

- Allows researchers to culture cells without the use of serum
- Takes into account what is missing in traditional basal cell culture media to sustain growth of all cell types
- Contains no animal or human derived material, as well as no hormones, cytokines, or unknown serum compounds



AMSBIO www.amsbio.com

Isotype-Specific Secondary Antibodies

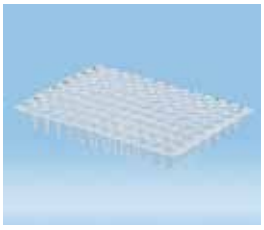
- Directed against the three main mouse isotypes: IgG1, IgG2a, and IgG2b
- Offer improved signal detection and specificity in imaging, ELISA, flow cytometry, and western blotting
- Generated using a proprietary method of phage display with guided selection methods to obtain highly targeted reagents

Bio-Rad Laboratories, Inc. www.bio-rad-antibodies.com

PCR Plates

Multiply®

- Available in transparent and white, and have a maximum well volume of 100 µl
- Compatible with commonly used thermocyclers with a 0.1 ml block format and can be sealed with a variety of adhesive films
- Certified to be free of human DNA, bacterial DNA, DNase, RNase, and PCR inhibitors



Sarstedt www.sarstedt.com

Tube Selector

Mohawk

- Designed to allow easy cherry-picking of desired tubes from SBS racks
- Sets a new standard for frozen or thawed sample tube picking from 96-position racks
- Can run a pre-selected "picking list" generated from Ziath Samples™ software, a LIMS, or an Excel worksheet

Ziath www.ziath.com

MICROSCOPY

SEM Microscopes

SU3800, SU3900

- Feature the ability to accommodate large, heavy specimens
- Offer advanced functionalities for automated measurement and wide-angle camera navigation

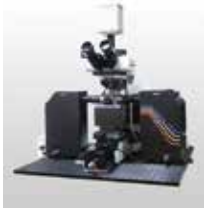
- Enable high-throughput, and are easy to use for both new and experienced operators
- SU3900 can accommodate a 300-mm sample diameter and loading capacity of up to 5 kg

Hitachi High-Technologies www.hitachi-hightech.com/us

Confocal Microscope

Alpha^3

- Product is the result of a partnership with PhaseView, an advanced 3D microscopy and scientific imaging company based out of Paris
- Combines Olympus' BX43 upright frame and optics with PhaseView's advanced multiview selective plane illumination technology
- Provides high temporal and spatial resolution of both fixed and live biological samples for 3D imaging



Olympus www.olympus-lifescience.com

X-Ray Microscopes

Xradia 600-series

- Two new models—Xradia 610 and 620 excel through faster non-destructive imaging of intact samples without sacrificing resolution and contrast
- Provide insights into the morphology of energy materials and their behavior under operating conditions
- Offer the most accurate 3D nanoscale support for digital rock simulations in the raw materials industry

ZEISS www.zeiss.com

ASK LINDA
AUTOMATED LAB INSTRUMENTS

QUESTION:

Dear Linda,

It seems like every day I read about a new automation technology being introduced into the lab. I would like to implement more automated instruments into my lab, but the initial expense is high, and I am uncertain of how this new equipment may affect my staff and our workflow. Many of my employees have been working here for a long time and have developed a comfortable routine. Do you have any advice on ensuring a smooth transition toward automation?

Thanks,

Betty

ANSWER:

Dear Betty,

From automated sample preparation to cloud computing, automation and robotics are changing the way labs operate. Implementing automated instruments and software can free up your staff for more complex and meaningful tasks, which will boost overall productivity and morale. Re-structuring your staff for other tasks will also likely help you gain a return on investment, easing the burden of initial expense when purchasing automated equipment.

But despite the speed of technological advancements, introducing new systems and processes in a laboratory can take time. Identify one or two staff members who have the skillset to educate others on the automated instruments you'll be introducing, and your lab will be running efficiently in no time.

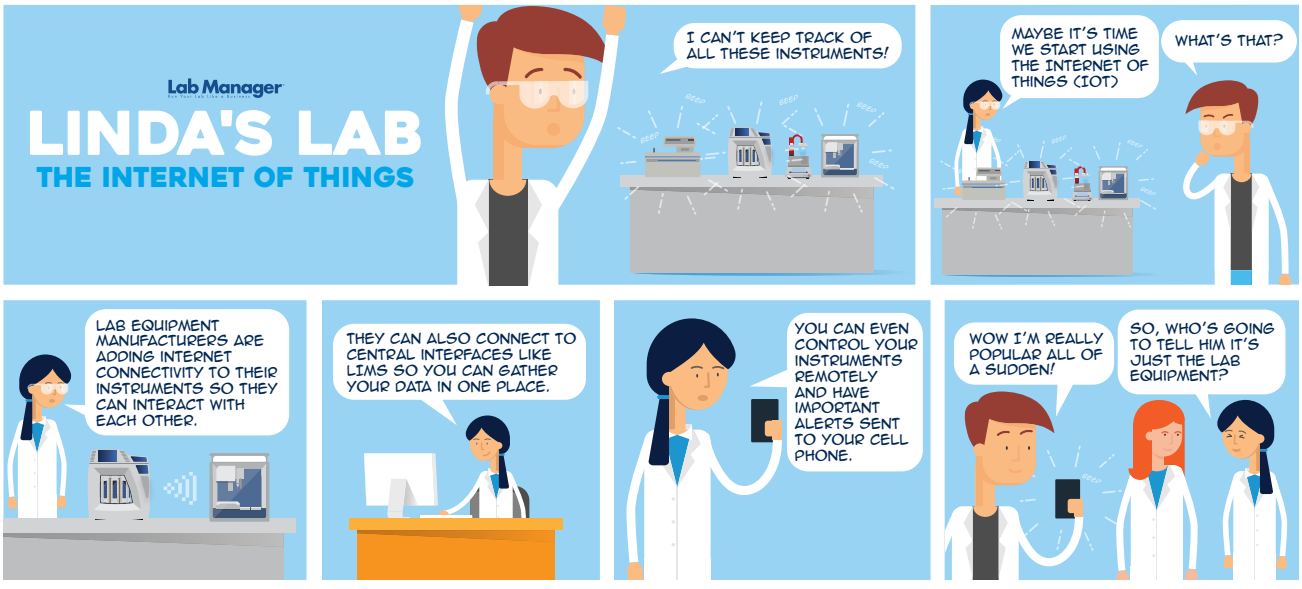
Good luck.

Cheers,

Linda

FOR MORE INFO: LABMANAGER.COM/AUTOMATION-GUIDE

HAVE A QUESTION FOR LINDA?
EMAIL HER AT: *LINDA@labmanager.com*



ADVERTISER INDEX

Company	URL	Page
Analytik Jena	www.analytik-jena.com	5
Audit® MicroControls	www.auditmicro.com	2
CARVER	www.carverpress.com	35
Clippard	www.clippard.com	17
Eppendorf	www.eppendorf.com	26-27
Huber USA Inc.	www.cglifesciences.com	9
INTEGRA	www.integra-biosciences.com	29
Labconco	www.labconco.com	3, 63
LabX	www.labx.com	37, 61
Metrohm USA, Inc.	www.metrohm.com	11
MilliporeSigma	www.sigma-aldrich.com	64
PLAS-LABS, Inc.	www.plas-labs.com	25
PolyScience	www.polyscience.com	41
Promega Corporation	www.promega.com	7
Salesmaker Carts	www.foldingcarts.com	61
Sartorius	www.sartorius.com	30-31
Stirling Ultracold	www.nocompressors.com	19
Thermo Fisher Scientific Inc.	www.thermofisher.com	52, 53

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LAB MANAGER ONLINE

We look back at our web content since the May issue and look forward to what's in store for the upcoming July 2019 issue.

1 Essentials to Consider When Starting a New Lab

Starting your own lab is both an enormous accomplishment and an ambitious undertaking. Investing time at the outset to plan and organize your "business" helps keep your lab running smoothly so you can answer your most important research questions. Download our free infographic to learn about all the considerations.

Read more at **LabManager.com/lab-startup**

2 Trending on Social Media: Moving Up the Ladder

As of May 17, *Lab Manager*'s top May issue article posted to social media was our Ask Linda column on "Moving Up the Ladder." While technical ability is essential to becoming a successful laboratory manager, it is not sufficient. Many outstanding scientists or engineers have failed as lab managers because they lacked the right attitude. Linda the lab manager outlines 10 attitudes you will need in order to be successful.

Read more at **LabManager.com/Linda-management**

3 Most Popular Webinar

Our most recent top webinar on LabManager.com with 226 registrants was "Innovations in Mass Spectrometry." This TechTrends webinar discussed the latest in mass spectrometry applications and examined the next generation of technologies. The speakers also offered tips on how to troubleshoot common problems and optimize your workflow. Though it ran on April 25, you can still register to watch on-demand.

Read more at **LabManager.com/mass-spec-innovations**

LabManager.com

NEXT ISSUE ➡ Lab Automation Trends

Automated labs can increase throughput and free up scientists from mundane tasks to allow them to focus on more complex projects. However, as with any new technology, there is a learning curve to consider. Our July cover story will discuss the history of automation both inside and outside the lab, how lab managers are implementing automated equipment, and some of the concerns of introducing this technology.

Evaporation Solutions for All Types of Labs: RapidVap Dry Evaporators

Your samples are valuable, just like the equipment you use. This is why Labconco RapidVap Dry Evaporators were designed to protect both. The chamber and sample block are PTFE-coated while all mechanical components are isolated from chemical fumes. This resilience to strong chemicals, along with repeatable methods and programmability, gives you the confidence you need to run your samples unattended without issue. With four models of RapidVap Dry Evaporators to choose from, the evaporation process can be optimized to meet the needs of any application.

Efficiency

RapidVap Dry Evaporators are made to quickly reduce multiple samples to complete dryness or to an end point volume using direct heat, a vortex motion and either a vacuum or nitrogen stream. The vortex motion used by the RapidVap Vacuum, N2, and N2/48 Evaporators produces remarkable evaporation rates by dramatically increasing the surface area of your samples, saving you precious time. The constant washing of solvent down the sidewalls of the glassware also increases the recovery rate of the analytes being tested.

With the RapidVap Vertex, evaporation occurs using a combination of nitrogen blowdown and heat. Nitrogen blowdown reduces the partial pressure directly over the liquid, using a slight vortex motion within the sample to speed evaporation, creating a gentler way to evaporate. The dry block supplying heat in the Vertex is angled to increase the surface area of your samples for faster evaporation.

All RapidVap Dry Evaporators feature a dry block heater that supplies a controlled amount of heat to the samples. Unlike water baths, the dry block heater also eliminates the potential for condensation accumulating on the lid and causing cross contamination. Additionally, the block heaters require no additional maintenance.

Versatility

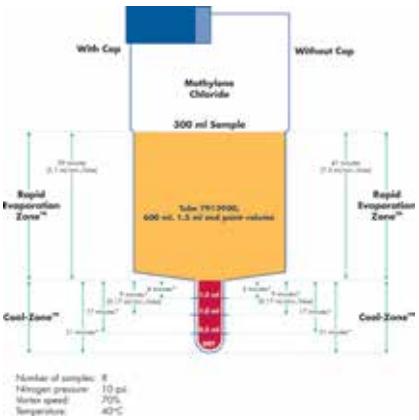
Sample processing and methods can be fluid as your research changes over the years. That is why the RapidVap is designed to accommodate your needs with interchangeable sample blocks.

- The RapidVap Vertex can process sample volumes up to 60mL
- The RapidVap Vacuum, N2 and N2/48 Systems can process volumes up to 450mL

End Point Detection

For certain types of research, it is important the samples do not evaporate to complete dryness. The RapidVap Vacuum, N2 and N2/48 Evaporators offer unique ways to ensure your samples are protected, allowing you to work on other things instead of watching your samples dry.

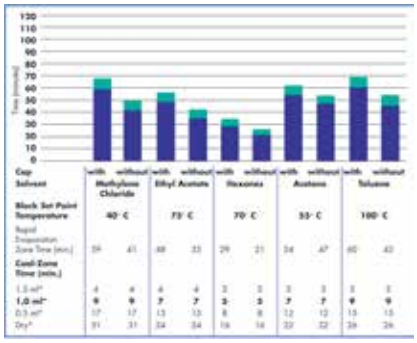
- The Cool-Zone™ insulates samples in a glassware stem for end point, dramatically slowing down the evaporation process for the last few milliliters of sample. Glassware with stems are offered in a variety of end-point volumes.

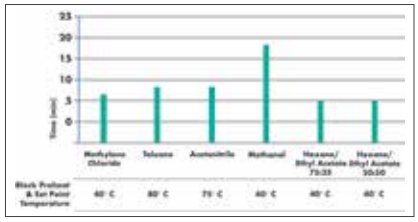


- As a backup to the Cool-Zone, the RapidVap monitors the system temperature in the block and in the heater. During operation, evaporative cooling of the solvent creates a differential between the block and heater temperatures. Once evaporation is nearly complete, the two temperatures equalize indicating end point is near. The alarm sounds and the PREHEAT/END ALARM indicator light flashes.
- The operator can always set the end point time and when set time has expired an audible alarm sounds and the RapidVap automatically turns off all functions.

Environmental Protection

As we continue to find new ways to help protect our environment, recovering solvents during evaporation has become increasingly important. The RapidVap Vacuum Evaporator can be used with a cold trap, in addition to the RapidVap Trapping Valve, to collect large volumes of volatile solvents. This lengthens the vapor dwell time within the cold trap, dramatically increasing trapping efficiency.





LABCONCO

RapidVap Dry Evaporators are an efficient, versatile solution to evaporation for a broad range of sample preparation applications. To learn more about dry evaporators, please visit **Labconco.com/DryEvaporators.**

MilliporeSigma

We'll focus on the water, so you can focus on the next big thing.

Whether you're rewriting the textbooks, striving for analytical perfection or discovering innovative new treatments, your work should be your focus not your lab water.

That's why the Milli-Q® portfolio supplies best-in-class water solutions for every kind of water purity, because we cater for every kind of laboratory. And with the right expert support it means we can save you precious time and physical space, helping you keep your focus on the bigger picture.

To find out more, visit:
SigmaAldrich.com/EmpoweringFocus

The Life Science Business of Merck KGaA, Darmstadt, Germany operates as MilliporeSigma in the US and Canada.

Milli-Q®
Lab Water Solutions