

Lab Manager[®] MAGAZINE

Run Your Lab Like a Business

May 2011

Volume 6 • Number 4

Laboratory Etiquette

How lapses in etiquette can devastate a lab's morale, productivity and business success

EMPOWERING YOUR STAFF: TRAINING, MENTORING AND OTHER TECHNIQUES

The Lab Manager's Role in Developing
New Revenue Streams

Cell Culture Contamination: Understanding
the Causes, Managing the Risks



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Laboratory Etiquette

Etiquette is the generic component that keeps all the pieces of the lab working together — whether it is in the form of written or unwritten rules. “Without proper etiquette, entire systems can go adrift, which can be a tremendous time waster in the end.”

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Wally Thompson, along with his five-person team, process thousands of samples a year for Gambro (Daytona Beach, FL), providing microbial analysis for the products — medical device and pharmaceutical solutions for renal intensive care — manufactured at that facility.

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John K. Borchardt



SCIENCE APPS FOR APPLE SMARTPHONES AND GOOGLE ANDROIDS. HYPE OR USEFUL?

According to some sources, smartphones have become ubiquitous in laboratories as increasing numbers of apps are now targeted to scientists. Examples include: Solutions, an app that helps you prepare your buffers before you start an experiment; chemical databases PubChem and Chebi; The Elements, dubbed “the periodic table on steroids;” and MyCalculator, designed for those dealing with 2D and 3D math that lets you plot your function and find those points of interest on your iPhone. Some vendors are also releasing laboratory apps for biological research. Obviously, this technology will only become more important to lab professionals. Because of that, we will be closely tracking its growing acceptance and adoption among our readers. Are you on board? If so, what have you found most useful? Do you see opportunities for new applications? Beyond science, are there apps you use to manage your lab? Please take a minute to send an email (pam@labmanager.com) and let me know. [WE NEED YOUR INPUT.](#)



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Lab Manager Magazine® (ISSN: 1931-3810) is published 10 times per year; monthly with combined issues in February/March and July/August, by LabX, P.O. Box 216, 478 Bay Street, Midland, ON Canada L4R 1K9. USPS 024-188 Periodical Postage Paid at Fulton, MO 65251 and at an additional mailing office. A requester publication, *Lab Manager*, is distributed to qualified subscribers. Non-qualified subscription rates in the U.S. and Canada: \$120 per year. All other countries: \$180 per year, payable in U.S. funds. Back issues may be purchased at a cost of \$15 each in the U.S. and \$20 elsewhere. While every attempt is made to ensure the accuracy of the information contained herein, the publisher and its employees cannot accept responsibility for the correctness of information supplied, advertisements or opinions expressed. POSTMASTER: Send address changes to *Lab Manager Magazine*®, Hallmark Data Systems, 7300 N. Linder Ave. Skokie, IL 60077. ©2009 *Lab Manager Magazine*® by Geocalm Inc. All rights reserved. No part of this publication may be reproduced without permission from the publisher.

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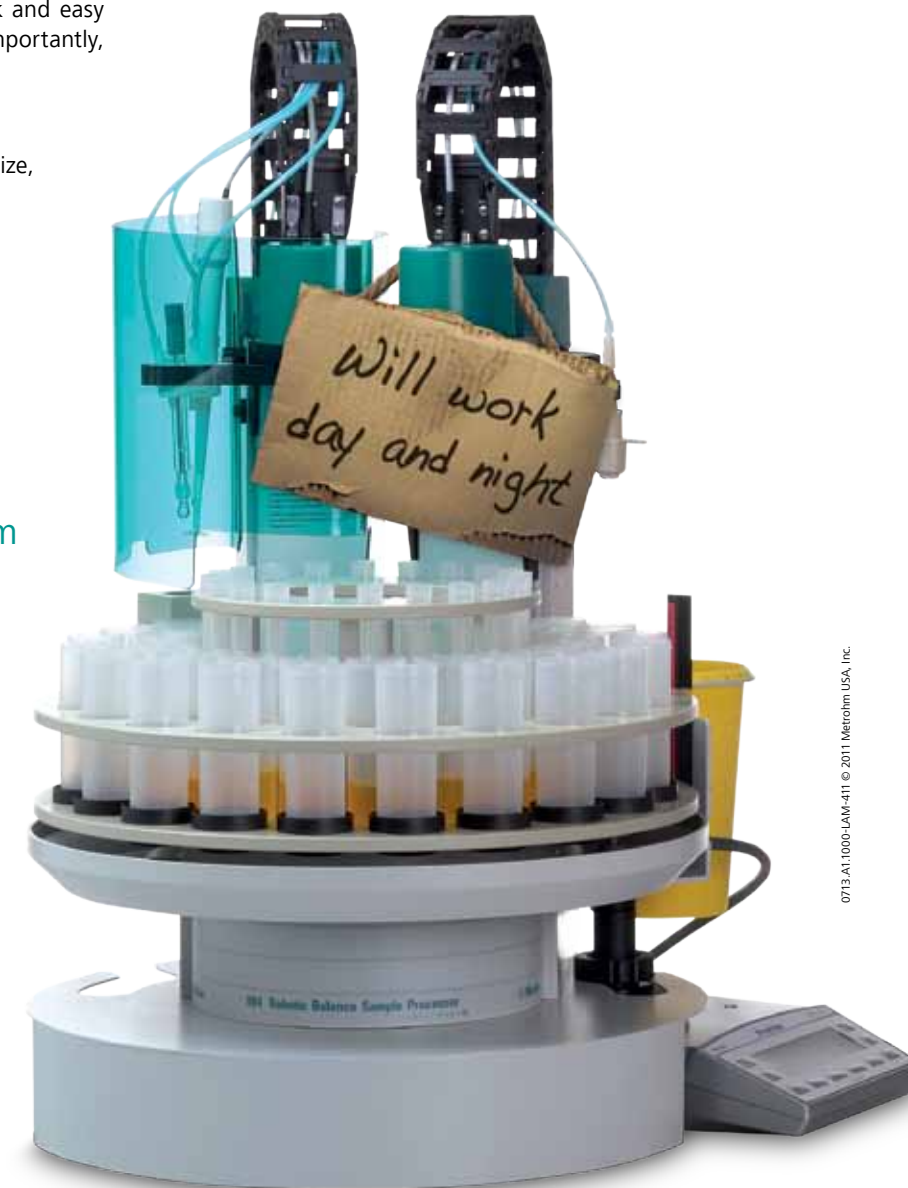
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Etiquette rules

Unlike the recent British nuptials, where strict social etiquette dictated every nod, handshake and curtsy at the ceremony, rules of behavior in today's laboratories are slightly more relaxed. But whether strict or subtle, good manners and proper social conduct are keenly important to lab professionals—judging by the 1,160 of you who registered for our recent Lab Manager Academy webcast: "Lab Etiquette - Maintaining High Professional Standards in the Lab."*

Based on feedback to a survey on the same topic, issues of concern included not cleaning up after oneself, taking the last supply and not re-ordering, using lab computers for things other than lab work, overuse of cell phones, bad attitudes and outright rudeness.

If you're among those who wonder what ever happened to common courtesy in the workplace, turn to page 10 to learn what lab managers can do to reverse this trend and perhaps increase a sense of teamwork and professionalism in the lab.

But manners alone do not a great laboratorian make. Lab professionals also need regular training to keep their skills and knowledge from languishing, skills that are not limited to research and scientific techniques, but include management. According to a 2006 study, 42 percent of a scientist's time is consumed by administrative matters. This month's Leadership & Staffing article, "Empowering Your Staff," shares techniques for improving your staff's skill set across multiple areas in order to enhance your lab's research culture and decrease the managerial burden.

In keeping with our tag line, "Running Your Lab Like a Business," this month's Business Management article addresses the very important and bottom line-improving matter of creating new sources of revenue for your organization. As author John Borchardt points out, "Recently, big pharmaceutical companies have cited the failure to develop new products and develop new revenue streams as the rationale for R&D cutbacks and even the closure of large research centers. Preventing this sort of situation from occurring at your company is a major responsibility for lab managers at all levels of the organization." Turn to page 68 to learn some proactive techniques to help your lab become aware of new science and business developments and how to take advantage of them.

This month we introduce the first in a three-part series of articles on cell culture contamination. "Since the sources of culture contamination are ubiquitous as well as difficult to identify and eliminate, no cell culture laboratory remains unaffected by this concern." If this is true for your lab, turn to page 28 to learn the causes of and possible techniques for managing this problem.

And if you're in the market for a biological safety cabinet, but overwhelmed by the myriad of choices, turn to page 16 where panelists from our February "Product Showcase" webinar on this same topic will help guide your decision-making process.

Lastly, in preparation for an article we're working on for the July/August issue, I am soliciting your opinion concerning the use of iPhone and iPad apps in the lab. Are you an early adopter or a skeptic? We will be sending out a survey soon on this topic, but if you have anything to share on that now, I'd like very much to hear from you.

Here's hoping all those April showers deliver an abundance of May flowers. Happy Spring!

Pam Ahlberg

Pamela Ahlberg
Editor-in-Chief

*If you missed this event, go to www.labmanager.com/etiquette to view the archived webcast.

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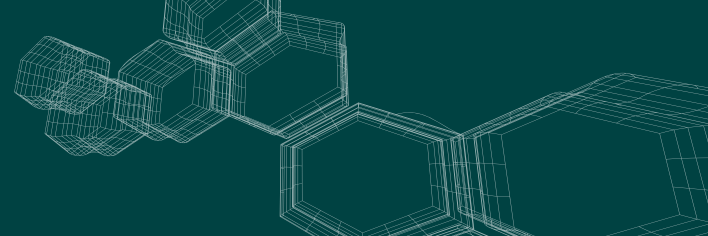
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Laboratory Etiquette

HOW LAPSES IN ETIQUETTE CAN DEVASTATE A LAB'S MORALE, PRODUCTIVITY AND BUSINESS SUCCESS by Bernard Tuls

Many lab managers still remember them from their student days—a handful of hastily stapled printouts sternly titled “Laboratory etiquette—Acceptable standards of conduct.” Those were rules to live by, and the smallest violation landed a budding laboratory scientist in front of the ticked-off chief instructor. Many years later, for most lab managers, these rules are alive and well, and perhaps a bit more appreciated. They essentially lay out the guidelines for how things are done in labs in every industry—and they are growing in complexity and sophistication.

At its most generic, laboratory etiquette describes the preferred if not required conduct in the laboratory. In reality, however, its relevance could reach way beyond such strictly pedestrian concerns. According to Alaina Levine, an internationally known career development consultant for scientists and engineers, while skills and capabilities are essential, etiquette and manners are important, too. Levine, who is also a noted science writer, states that proper etiquette projects commendable qualities such as professionalism, intelligence, respectability, industriousness and talent.

Today, lab etiquette occupies rapidly evolving territory. The United States attracts scientists from all around the world and, as a result, technologists with different training and practice norms and from disparate cultures work side by side in laboratories across the country. Workforces in most labs now encompass a broad spectrum of ages and have solid gender representation. The labs themselves are changing into more open, multidisciplinary operations, with greater emphasis on mobility

and modularity. A relentless onslaught of new technologies has dramatically changed work-related communications. On top of that, the invasion of personal communications and entertainment devices has been embraced enthusiastically by some lab staffers, while others view them as monumental annoyances.

A cursory literature search, discussions with lab directors and consultants, and a webinar/discussion conducted by *Lab Manager Magazine* unearthed a variety of opinions and positions about etiquette in the laboratory. They range from everyday rudeness and inconsiderate

behavior to profound questions that may merit adjustments in overall lab policies. Most labs—from those in colleges to others situated in clinical and industrial settings—have rules

that essentially forbid food, drink and inappropriate cell phone use and, of course, practices such as smoking on the premises. These rules of etiquette are guided by the need for laboratory personnel to conduct themselves in a businesslike manner. Christina Mastromatteo, Ph.D., senior analytical chemist with The Lubrizol Corporation, sees etiquette in the laboratory as “a means of getting the job done professionally, following the rules of professional conduct yourself, and not hindering the work of others—in effect, being professional for the benefit of all.”

Laboratories have clear rules on the labeling and handling of chemicals and reagents and on the maintenance of clean work areas. Clinical lab settings have detailed rules and instructions about the disposal of materials, such as used surgical gloves, needles and biological tissue. In some cases the penalties for noncompliance, including

“Etiquette is often interpreted as overlapping with ethics.”

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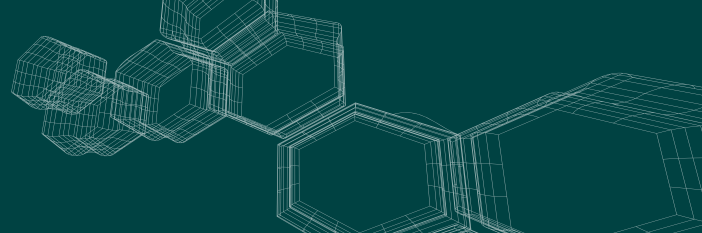
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hefty fines, are clearly indicated. “With the exception of the gloves, all those are included in our lab rules,” says Maryann McDermott-Jones, Ph.D., undergraduate laboratory supervisor, Department of Chemistry and Biochemistry, University of Maryland. “To be practical about it, large numbers of students view their introductory lab course as a hoop they have to jump through. That seems shortsighted to me, but it is a practical reality,”

“Defining and strictly enforcing safety regulations are high priorities for us. One of the first things we do at the start of each semester is let students know what safety criteria they will be responsible for—and we test them on those,” says McDermott-Jones. “We teach students to be honest in how they deal with the results of experiments. We stress that this process is heavily reliant on professional ethics and behavior and academic and intellectual integrity,” she adds, demonstrating that etiquette is often interpreted as overlapping with ethics.

Overall, there seems to be a solid propensity to link etiquette to safety, efficiency, productivity and, of course, ethics. Etiquette is generally viewed as a key component in the ability to work well with others, and in the maintenance of harmonious professional relationships in the lab. Acutely aware of this, educators try to inculcate the im-

portance of proper etiquette at the earliest opportunity. She says that with the advent of Lean Six Sigma, there is a lot more cross training in the laboratory workspace, which creates a friendlier environment but increases the workload for each individual. This has almost become the norm for a number of laboratories as they grapple with finding ways to deal with this tough economic period. “Lean systems have reduced the number of people in analytical labs, and there is more sharing of tools and systems, which makes proper etiquette all the more important,” she says.

A number of lab managers engaged in the rigor of their technical tasks opted not to discuss the question of etiquette with us. Part of the reason is that for many professional managers, good etiquette is a given—people simply internalize the rules and over time they conduct themselves well naturally. Rules of etiquette are nice to have but, at the end of the day, the good workers follow them reflexively, they believe. Many labs are fortunate; they attract high-quality professional staff and do not need to spend much time on niceties like etiquette.

Lapses in etiquette, however, can be devastating to morale and may have other profound implications. They may translate into workers not receiving due recognition for their work—such as not being named as an author of

record on a poster presentation or peer-reviewed publication, despite substantial contributions to the research effort. This has the effect of denying well-deserved credit or accolades because someone, such

as a team leader, opted not to extend the usual courtesy (etiquette) to another contributor. This kind of conduct could lead to financial consequences as well, and even legal action—for example, when an etiquette-challenged research leader decides not to include the name of a key technical contributor on a patent.

Dr. Henry Nowicki, president at PACS Testing, Consulting and Training, deals with a large number of laboratory managers and their staff in a number of capacities. In his training activities, which include courses in chromatography, mass spectroscopy and related areas, he interacts directly with laboratory personnel of all stripes. To him, “Etiquette represents a state in which individuals need to be conscientious. They need to think and present themselves in a manner that enables them to get their assigned tasks done and advance their career.”

For Nowicki, this translates first into some basics: “They should leave work areas a bit cleaner than when

“Etiquette seems to be a generic component that keeps all the other pieces working together.”

portance of proper etiquette at the earliest opportunity.

Consideration for others ranks high in the lab etiquette book. When engaged in laboratory activities, punctuality is very important and plays a key role in ensuring that common areas that must be scheduled and shared are used efficiently and smoothly. In addition, proper usage and respect for all equipment, user rosters and maintenance schedules are critical. It is considered an egregious error to interfere with ongoing experiments set up by fellow lab workers. Included in the discussion on laboratory etiquette is appropriate behavior in the performance of an experiment. Rules of etiquette also address the key issues involved in recording the outcome of an investigation.

“Etiquette seems to be a generic component that keeps all the other pieces working together—whether it is in the form of written or unwritten rules. Without proper etiquette, entire systems can go adrift, which can be a tremendous time waster in the end,” says Dr. Mastromatteo.

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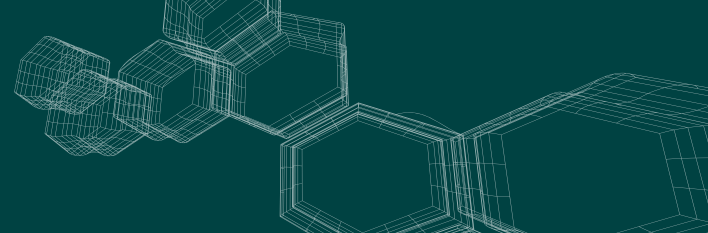
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they started. They need to be conscientious—reorder or bring to the appropriate person's attention that certain supplies are running low and should be replenished. There is a tremendous need to be courteous and tactful because this makes for smoother, safer operations and a cooperative, well-functioning environment."

Nowicki unhesitatingly states that in an environment with good etiquette, efficiency and productivity will increase. "When everyone knows that everything has its place, that they need to return tools and reagents to their proper storage areas, and that they must ensure that all instruments are properly calibrated and functioning at top form, and they engage in courteous and effective communications, productivity will increase for the whole group."

"Etiquette benefits from each person setting a good example. A key part of this entails informing others tactfully and courteously about their shortcomings. If these weaknesses are not pointed out to them, they may

continue to be unaware of the problem. Managers and others in leadership positions should take care to show a suboptimal producer that there are attractive potential benefits associated with improving, and help that person work through a plan of corrective action," says Nowicki.

Turning to the question of why there seems to be heightened interest in etiquette today, Nowicki says, "We are operating at a faster pace now and with greater stress. A lot of our communications have migrated to the email format, and we are expected to answer them by the next day, or at least within 24 hours.

"Headcounts have been reduced in many laboratories, and workers are expected to do more and different kinds of work compared to years ago. This creates stress, and in stressful situations it is easy to ignore proper etiquette and good manners and slide into a harsh work environment."

To ensure harmony in an environment that consciously tries to maintain proper etiquette, Nowicki believes that it is important to apologize for impolite conduct to other workers as well as to provide positive feedback and acknowledgement of good performance. If managers do not convey client satisfaction to their subordinates, the workers will not know that their work has been commended. In today's economic environment, where it is harder for companies to offer greater monetary rewards, such compliments are all the more

"In stressful situations it is easy to ignore proper etiquette and good manners and slide into a harsh work environment."

necessary, according to Nowicki.

On the role of generational differences on etiquette, Nowicki says there has been an age-long tendency for older generations to view the younger ones as lacking in commitment and as less industrious. "This is quite natural, but I do see differences in today's young lab workers. They are not as willing to do overtime or work on weekends. They want their free time, and seem to have stronger social connections to certain community activities, because of their more recent involvement with them than the older generation.

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"Of course, they always seem plugged into their electronic gear. This is to be expected because our technology is different, expectations are different, and society is much faster-paced now. There is some concern, however, because they spend a relatively large amount of money on electronics compared to their earnings—and the electronics they carry around could interfere with their productivity."

"Management can play a key role in the fostering of proper etiquette."

Cultural differences are real, and cultural diversity is increasing in our labs compared to the past. According to Nowicki, the answer is greater tolerance and the belief that it is desirable for people from all cultures to learn

more about each other.

Management can play a key role in the fostering of proper etiquette writ broadly, according to Nowicki. He says that in his experience, managers fit into two categories—those who assign tasks and leave workers alone with very little structure, and those who micro-manage. "What is needed is something in between. Managers need to figure out which worker needs what kind of supervision. This will generate better feedback and lead to overall harmony and greater productivity."

"We need to do everything we can to improve productivity as a nation. Good etiquette leads to self-improvement and opens up the possibility to make us better and more productive on a regular basis."

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

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In February 2011, *Lab Manager Magazine* hosted a “Product Showcase” webinar, focused on the different features and uses of biological safety (or biosafety) cabinets (BSCs). The webinar featured a panel of six experts representing the American Biological Safety Association (ABSA) and some of the leading vendors in the field, who provided their perspectives on what users should consider when deciding which BSC is right for their labs and applications. This online event attracted a large international audience, with members from diverse industries, looking for an opportunity to interact with the panelists in real time and get their advice on the key factors they should consider when making their buying decisions. Each panelist gave a brief presentation to outline the features and uses of BSCs and to help the users decide which one is right for them.

Below are answers to attendees’ follow-up questions, provided by the panelists. Webinar participants included:

- Karen Byers, *President, American Biological Safety Association*
- Brian Garrett, *Product Specialist, Labconco Corporation*
- David Phillips, *Applications Specialist, Thermo Fisher Scientific*
- Scott Christensen, *Vice President North American Sales, NuAire*
- Mike Martin, *General Manager, ESCO Technologies*
- Cybelle Guerrero, *National Sales Manager, The Baker Company*
- **Moderator:** Tanuja Koppal, Ph.D.

Q: How do you determine which biosafety cabinet is right for you?

Byers: Laboratory managers should work with their safety professionals to identify the appropriate biosafety

cabinet for the proposed work. This process should have been part of the risk assessment and risk management process that reviews the hazards associated with the proposed work and identifies the controls to minimize risk of exposure to biohazards.

Consideration should be given to the primary function of the biosafety cabinet. Was the biosafety cabinet selected for sterility, biosafety or a combination? What is the risk group of the proposed biohazard that will be handled in the biosafety cabinet? Will other laboratory hazards, such as volatile hazardous chemicals or radioactive materials be utilized? These are just some of the questions that should be asked to determine which biosafety cabinet is right for your lab. Refer to Appendix A: Primary Containment for Biohazards, Selection, Installation, and Use of Biological Safety Cabinets in the CDC-NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL), available online at www.cdc.gov/biosafety/publications/bmbl5/.

Garrett: A BSC should first and foremost offer total safety. You should also consider reliability, productivity, energy savings and user comfort. Price is also important, but not as most of us think of it. The upfront cost of a unit may be attractive, but attention must be given to the operating costs of the unit.

Q: What are the most important factors to be considered when buying or upgrading a biosafety cabinet?

Garrett: The most important factors will be different depending on the customer’s conditions—it may be the size or the price of the unit (operating costs are of extreme importance). Factors could also include ergonomics, product/customer support, and materials of construction. Primary considerations should involve safety and preservation of samples. Secondary thoughts should focus on price and cost of the unit. Once narrowed down, focus on ergonomics, usability, customization and options.

Phillips: When replacing a cabinet, improve. Modern Class II BSCs have more stringent design requirements, so you will probably be safer. Look for a cabinet that compensates for the normal filter loading and alarms if the airflows change too much. If you were using external exhaust as in a canopy connected Type A2, B1 or B2, really

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review your need. External exhaust is expensive and can result in a cabinet that is more complex to operate safely. Look at energy efficiency and the total cost of ownership.

Q: What are some of the things a user needs to look into for routine maintenance and proper use of biosafety cabinets?

Byers: Certification is essential to ensure that the Class II cabinet is performing according to NSF/ANSI Standard #49-2009 and protecting both the worker and the sterility of the work. The certification testing should be conducted by well-qualified professionals when the biosafety cabinet is installed, annually, and whenever the biosafety cabinet is moved.

Phillips: The best resource is “Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th Edition” by the CDC and NIH. The BSC operating manual will help make you aware of special features on your cabinet. For routine maintenance, the most important thing is to get the Class II BSC field certified at least annually.

Christensen: Many users rely on ultra-violet (UV) light to provide disinfection of the cabinet work area. Others may simply close the window of the cabinet, and put the cabinet into standby mode where the motor continues to run at a slower velocity to maintain the cleanliness of the work area. While these may be useful back up methods, the primary method of disinfecting a biosafety cabinet should be through a spray and wipe down of the cabinet interior with an isopropyl alcohol/water mix or another suitable disinfectant. The cabinet's HEPA filters and air flows should be checked by an experienced independent certifier on a regular basis to ensure the integrity and safety of the cabinet.

Q: Any advice or recommendations for using disinfectants and burners in the biosafety cabinet?

Byers: The disinfectants used must have demonstrated effectiveness against the microorganisms that may be present in the samples manipulated, and must be used

according to the directions on the label. Consult your safety professional to ensure that you have selected the appropriate disinfectant for the potential biohazards in your laboratory. Two common choices are 70% ethanol and 1:100 bleach solution. Appendix B: Decontamination and Disinfection, of the 5th Edition of the CDC/NIH BMBL provides excellent background information on this topic and should be consulted.

Garrett: Open flames are generally not recommended in BSCs, especially Class II units. The heat from the flame can cause turbulence in the laminar down flow, causing cross contamination, while the flame itself can cause physical damage to the cabinet and its filters.

Christensen: The use of Bunsen burners is generally not recommended, as the flame may disrupt the air flow in the work area. If a burner is used inside a cabinet, then a “demand type” burner would be the choice. This is a burner that is activated by a motion sensor or foot switch.

Q: How amenable are these cabinets to customization? Any requirements for more specialized applications and when working with animals inside the cabinet?

Christensen: Every BSC should be configured to meet the specific needs of the laboratory where it is to be used. The number and location of service valves, right or left hand side, use of a cord pass-thru for tubing and power cords, not to mention the appropriate type of cabinet control system are just a few of the basic considerations to keep in mind. If a Class II BSC is to be used for animal research, then an entirely different set of criteria need to be considered. The access opening needs to be set at 12” (30 cm) to facilitate the movement of cages in and out of the work area. The air barrier also needs to be maintained at 105 FPM to ensure Class II type product and personnel protection.

Guerrero: There is a wide variety of customization available with BSCs. However, anything that affects the airflow through the sash opening such as changing the height of the opening can void the NSF listing. Introducing various types of instrumentation is a

trend these days for BSCs. The manufacturer should do its own microbiological testing to prove that the modification does not alter the protection classification of the unit. The basic modifications for animal research work are adding a pre-filter in the work area to capture gross hair and dander and preserve the life of the HEPA filter. Larger sash openings to accommodate larger rodent cages are also typical.

Q: Are there any differences that should be considered when a biosafety cabinet is used in a clinical versus a non-clinical setting?

Garrett: Most clinical labs' BSCs are recommended or required to undergo certification every six months opposed to annual certification in non-clinical labs. Historically, when BSCs are in use, their airflows change with the loading of HEPA filters. In clinical settings, where patient samples are being processed, there is always a risk of human disease contamination, so there was added emphasis on making sure the BSC was always operating safely. Current BSC technology has allowed for precise airflow control that automatically maintains safe working conditions no matter the load condition of the HEPA filters.

Q: What are some of the improvisations that users are demanding and that companies are now working on?

Byers: Ergonomic features (due to the long periods of time BSCs may be used) are frequently requested by users. The ability to house larger pieces of equipment, such as cell sorters, within biosafety cabinets is also increasing in demand. Finally, customization of BSCs for use in high-risk animal research experiments is another increasingly common request among end-users.

Garrett: Laboratories are energy hogs; many new facilities are trying to find ways to lower operational costs. BSCs are becoming more energy efficient and more suitable for modern scientific needs.

Guerrero: Reduced sound levels, reduced vibration for imaging, improvement on operational costs, and improvements that provide increased productivity are some of the types of improvements that users are demanding.

Q: How can users keep up with new safety requirements and regulations for biosafety cabinets?

Byers: Biosafety cabinet certifiers are an excellent resource for updates of ANSI NSF49 certification requirements. More information regarding the NSF/ANSI Standard #49-2009 may be found at the following website: www.nsf.org/business/biosafety_accreditation/standards.asp?program=BiosafetyCabCert

Christensen: Users can keep up with new safety requirements and regulations by visiting the CDC and NIH websites, to download a copy of the current BMBL or websites for organizations such as the WHO (World Health Organization), ABSA, and CETA. A recognized biosafety professional is also a good source of information. Useful information is also available on the websites of biosafety cabinet manufacturers.

TO READ THE FULL Q&A WITH THE PRESENTERS, PLEASE VISIT WWW.LABMANAGER.COM/BSC-PANELISTS

To view the archived webinar, please visit www.labmanager.com/biosafety-cabinets. The website also hosts a number of biosafety cabinet-related articles, application notes and information on upcoming events and webinars.

ANYONE USING A BIOSAFETY CABINET SHOULD BE TRAINED IN AT LEAST THE FOLLOWING:

- The rationale for why the biosafety cabinet has been selected (sterility, biosafety, or a combination). This would include the risk assessment process that led to its selection for use.
- Aseptic technique and good microbiological work practices.
- Personal protective equipment (PPE) required for the proposed use of the biosafety cabinet, including how PPE should be donned and doffed.
- How the biosafety cabinet operates and what are the potential interferences of successful operation.
- How to use the biosafety cabinet, from turning it on, preparation for work, carrying out work, and how to terminate work and decontaminate the biosafety cabinet to prepare it for its next use.
- Maintenance of the biosafety cabinet.
- How to determine if the biosafety cabinet is operating adequately (checks of pressure gauges, odd noises, emanation of odors, etc.) and to whom they should be reported for investigation.

(Source: Karen Byers, President, American Biological Safety Association)

A LIST OF USEFUL LINKS RELATED TO BIOSAFETY CABINETS

- www.cdc.gov/od/ohs
- www.absa-canada.org
- www.who.int
- www.hse.gov.uk
- www.absa.org
- www.inspection.gc.ca
- www.biosafety.be
- www.nsf.org

(Source: Scott Christensen, Vice President North American Sales, NuAire, Inc.)

EMPOWERING YOUR STAFF

TRAINING, MENTORING AND OTHER TECHNIQUES FOR RAISING MANAGEMENT SKILL LEVELS IN THE LAB

by F. Key Kidder

In 2002, the Howard Hughes Medical Institute (HHMI) and the Burroughs Wellcome Fund (BWF) embarked on an educational project to leave no young manager behind. HHMI and BWF, both in the business of career development, sought to lighten the load of novice investigators running labs without the benefit of formal management training. They convened grantees and distilled their observations into *Making the Right Moves*, a reference manual on lab management. Published in 2004, it was a runaway success in the scientific community. A second edition, beefed up by input from a luminous cadre of PIs and managers on human resource issues and other hot topics, was soon in the works—and in demand, as nearly 496,000 downloads in 2009-10 attest.

This managerial “how-to” clearly struck a chord and, while *Making the Right Moves* targeted lab-based academic institutions, its success reflects a broader-based need common among scholars who transition to industry or government labs and become leaders—formal managerial training and supervisory prowess, the lack of which is often made manifest in mediocre staff skill levels.

In a 2003 Sigma Xi survey, fully half of America's post-docs admitted to receiving no management skills training, while the remainder settled for “ad hoc” training. Just four percent had the benefit of a workshop or formal coursework.

This reality, which per-

petuates itself as staff ascend the leadership ladder, leaves something to be desired when propagating best practices, says John Boothroyd, former senior associate dean for

“In a 2003 Sigma Xi survey, fully half of America's post-docs admitted to receiving no management skills training.”

research and training at Stanford University's School of Medicine, who heads up a microbiology/immunology lab on campus. Boothroyd envisions a scenario wherein lab skills are transmitted to generations of scientists by “people trained on the fly by someone else trained on the fly, who was also trained on the fly.”

Critics of the current state of lab skills, while acknowledging the general technical proficiency of scientists, perceive that labs come up short when the discussion turns to the “soft skills” required to practice science within a social context—the laboratory setting, with its increased emphasis on complex collaborative endeavors and “big science” teams.

Are there any role models? The surge in team science and external collaborations notwithstanding, success in science is often measured by hitting individual marks, like numbers of publications and citations. Lab practitioners are traditionally rewarded for narrowly focused contributions to a particular lab or product.

“The word is hubris,” says Alice Sapienza, professor, industry consultant and author of “Managing Scientists: Leadership Strategies in Science.” They think, “If you're good enough to get an MD or PhD, you're good enough and smart enough to lead people in a laboratory ... but you wouldn't turn me loose to operate very complex equipment unless I was trained, yet we turn untrained scientists loose on even more complex human beings.”

An empowered staff enhances the laboratory research culture and potentially decreases the managerial burden; according to a 2006 study, 42 percent of a scientist's time

is consumed by administrative matters. Other benefits of improved staff skills can include decreased costs of mismanagement, misconduct and research inefficiencies—a general lowering of institutional risk.

Given the paucity of leadership training, many managers arrive, ready or not, with an incomplete education and the expectation that their continuing education in the managerial arts will only proceed on the basis of their future experiences—the very situation that HHMI and BWF sought to address.

Making the Right Moves added welcome muscle to the chapter of the scientific management oeuvre dealing with training the trainers. Notable print companions include *At the Helm: A Laboratory Navigator*, by Kathy Barker; *Academic Scientists at Work*, by Boss and Eckert; and Karyn Hede's *Managing Scientists*. Customized career development courses and conferences—where supervisors exchange ideas, partake in peer review and hone leadership skills—are another option. Prominent venues include the Marine Biology Lab in Woods Hole, Mass.; The Jackson Laboratory in Bar Harbor, Maine; Cold Springs Harbor Lab in New York; and the European Molecular Biology Organization in Germany.

HHMI/BWF's endeavor cast a wide net, with input from a multitude of universities and professional societies that agreed to use the manual as a basis for future leadership training courses. The disinclination of leaders to deal with soft skills issues was palpable, said Maryrose Franko, HHMI senior program officer, who coordinated the project.

“If you mentioned human resources, everybody shut down,” said Franko. “They became dismissive. There was this preconceived notion that you don't really know what it's like to be a scientist and live under the ‘publish or perish’ knife.” Franko said they subsequently “sheepishly acknowledged that scientists have workforce challenges similar to others They knew they needed help.”

A study published in March 2011 (Edwards, Tramontin, Simon, Dhanekar & Sheikh) points to a substantial payoff for managers attuned to the care and feeding of staff. While top-down approaches to improving productivity (new technology and reorganization) deliver “variable success ... managers should focus equally on ‘bottoms-up’ approaches” to improve the skills of bench researchers.

“People-oriented behaviors,” concludes the study, “have the largest impact on performance.”

“We turn untrained scientists loose on even more complex human beings.”

Common techniques to improve staff skills include mentoring, training/coaching, conferences, classes and seminars, e-learning, and bringing in outside experts. But the extent to which managers use these techniques is neither readily discernable nor uniform, and is often subject to variables beyond their control, including institutional and corporate resources and

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After arriving at a core set of behaviors found at both academic and industry labs—encompassing talent, collaboration, strategy/role, portfolio/project management and problem solving—the authors surveyed more than 4,300 researchers in 247 labs to determine productivity drivers.

Talent wins out, although it's "not simply about attracting the right people, but also actively managing their careers." The best labs,

says the study, have personal development plans for all researchers, reviewed annually, and "structured mentoring" and apprenticeships. Survey results

showed 36 percent of labs apprenticed newcomers, but just 23 percent offered longer-term mentoring. Overall, just 27 percent of the respondents said their labs were fully in sync with best practices.

Industry, says Sapienza, at least "has the notion they have to pay attention to training" staff, and typically

brings greater resources to bear on career development, often cloaked in confidentiality. Mentoring has long been the lead dog pulling the academic skill set. Tom Sakmar, former acting president of Rockefeller University who now runs a molecular biochemistry lab there, sees more industry mentoring as biotech-academic partnerships proliferate and "big pharma reaches out to universities" for new ideas—the bottoms-up approach.

Gael McGill, CEO of Digizyme, sees a similar spillover of academic-based mentoring into the life sciences. McGill mentors by "projecting in my actions the behaviors I

expect." Industry consultant Susan Morris says organizations that identify and train mentors achieve more productive outcomes. Virginia Commonwealth University's School of Medicine thinks its newly created Academy of Mentors, a voluntary program for faculty and students, will do just that, says Dean Jerome F. Strauss. The

process can ordain a long-term emotional investment; for Sakmar, "how to be a good mentor is a very personal thing."

So is the business of building staff skills, at least among the PIs and lab leaders who collaborated with HHMI/BWF in 2005 and were "regarded as model laboratory leaders by their peers, students or post-docs," according to HHMI/BWF literature. Instead of adhering to any formalized skill-building program, these leaders are often inclined to script their own methods.

"PIs in my field," says developmental biologist Karen Bennett of the Missouri School of Medicine, "do it 'by the seat of their pants,' without any training, classes, e-learning or outside help." Bennett, who organizes boot camps for new faculty and re-boot camps for mid-career faculty through funding from the Society of Developmental Biology, availed herself of the Briggs-Myers personality test to sharpen her management skills. "Research is an all-encompassing passion for most of us, and many of us are very strong INTJs! [A personality characterized by intuition, introversion, thinking and judgment.] We

"According to a 2006 study, 42 percent of a scientist's time is consumed by administrative matters."




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don't realize the need until we realize what a bad job we're doing as leaders of our groups."

"Mentoring," said HHMI investigator Elaine Fuchs, "is an active process. You have to be mentoring someone on how to mentor. You can't read a book." MentorNet thinks you can do it on-line; the California-based service targets women and minorities in science and engineering fields and is partnered with 150 campuses, corporations, and professional societies and organizations, according to CEO David Porush, who says MentorNet has matched up more than 28,000 mentors and mentees. Absent face-to-face communication, the company uses logarithms to determine compatibility.

Although academic training "has traditionally been imparted in one-on-one conversations, it's increasingly understood that it's not very efficient," said Boothroyd, who portends a greater shift toward group classes; Fuchs uses group presentations to drive development of critical thinking skills. Coaching is also labor intensive for managers, but in Fuchs' lab, the best training can occur when actions are not taken. She doesn't micromanage or "spoon feed" staff because "they won't develop as scientists. That was uncomfortable for me at first, because individual projects would go faster if we were looking over their shoulders to catch their mistakes. But in the long run, their productivity is much greater."

Staff skill development can require managers to maintain an arsenal of techniques, said Morris. "You may have visual learners, auditory learners or kinesthetic learners. Some need to see a skill demonstrated, or read about it, or be tested on it, or see it in a formal class. Some need a variety of approaches, or one technique in combination with another." Retaining outside expertise is an option for equipment training and delicate interactive skills such as conflict resolution, although Sapienza is wary of "bringing in someone with an agenda."

The March study, which notes that the best labs involve staff in the recruitment process, found that 22 percent give staff a say in selecting newcomers. Fuchs gives staff "the authority to choose the colleagues they bring into the lab through a vote, but they're then obligated to support that person" and provide training as needed. "I made all those decisions when I started out and nearly created WWII."

The impact of technology on staff skills is intensifying. McGill predicts that Digizyme's graphic visualizations and animations will become a skill-building workhorse in the life sciences, assuming major roles in communications and research. E-learning "is fantastic for things that are cut and dried," said Boothroyd. "Open

head, pour in information, close the head. But it's not so great for the more nuanced dimensions of management that must be practiced." Morris touts e-learning's availability on demand. Sakmar wonders if IT might "decrease the importance of international scientific conferences sponsored by professional organizations or eliminate the need for face-to-face meetings."

Managers unequivocally praise the skill development capability of conferences and seminars. NIH investigator Susan Gottesman values the "informal trading of advice and methods." Staff who don't avail themselves of such events "are probably the most in need of going," said Morris. Conferences combat lab myopia and develop critical collaboration and communication skills. "Science," said Sakmar, "is all about communicating."

F. Key Kidder left journalism to pursue a career in government relations, politics and PR, but he still likes to keep one hand in writing. He can be reached at k2@keykidder.com or 410-828-6529.

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INVEST IN SKILL BUILDING AND WATCH POTENTIAL GROW

Know where the safety equipment is. Don't eat or drink on the job. Wear the right clothes. And please don't casually pour chemicals down the drain.

Such precautions may sound elementary, but these important and fundamental lab safety practices must be mastered or quality down the line could suffer. Call them the "basics" of running a lab—the kinds of things that have to be taken care of before the real work can begin.

But once you've done that, it may be time to consider some other "basics" of running your lab. One of the most important basics—knowing how to effectively raise the skill level of your staff—may not seem as critical as making sure people know how to handle chemicals with care. Your employees' success in this area, though, as well as your ability to foster it, is every bit as critical to the future success and viability of your lab.

Consider the reality first when it comes to running any type of business in today's extremely competitive and constantly evolving work environment. More and more, the success of a company is tied to its capacity to identify and respond to changes quickly, with minimal disruption to operations or profit. Cycle time across nearly all aspects of business

has been reduced by sophisticated technology, making speed and agility more critical to market success.

The scenario is no different in the business of running today's modern laboratories, and having a tangible plan for growing the skill level of employees is the key to building versatility and being able to face these business situations head-on.

"Having a tangible plan for growing the skill level of employees is the key to building versatility..."

The "basics" of skill building are also important because of the specific challenges facing labs and the science industry as a whole. The basics include more project-based work that requires multiple skill sets for longer—or shorter—terms. Economic fluctuations can often drive inconsistent funding and customer demand that require either quick thinking or a totally new course of action. And there are constant innovations in scientific technology and research and development that require employees to continually develop new skill sets.

In fact, "versatility," defined as the ability to be versatile, can apply to an employee, to a specific job function, or to any organization or business. Organizations are adapting to change, and for many, the concept of "versatility" is increasingly relevant to their strategic implementation of effective workforce solutions.

Developing a plan for facilitating the growth of skills among employees requires managers to first make sure they know all the challenges facing their particular labs. Do you know what's happening in your unique marketplace? Are you aware of the business trends of the customers the lab serves? Are you operating in a way that allows you to be fully responsive to all the trends affecting how the lab executes its core competencies and its work for customers' specialized needs? And are you confident that you can optimize the output of new technologies? Being able to optimize all the technologies available through specialized skill sets is particularly critical, since doing so will enable the lab to take advantage of new revenue streams.

The answers to these questions will identify the most critical skills your employees need to retain and keep up to date, as well as the ones they might still need to learn or improve.

They will also identify your own path toward helping your employees take advantage of their skills and continually build new ones.

Though a one-size-fits-all plan won't work for every lab, more than likely your plan will include some sort of ongoing training system that will consistently engage your employees and allow them to take control of their skill sets and careers. This approach is gaining momentum, especially in the science world where contingent labor is on the rise and potential employees are increasingly realizing that they've got to be able to arrive at a job ready to go.

After identifying the most relevant skills needed in your own lab, take advantage of the Internet to feed that

knowledge to your employees. Technology-oriented online communities are a great way to figure out what employees want to learn as well, and you can use this tool to push them to other resources online that can help them build their skills in those areas. Or create a news feed that is sent to employees on a regular basis that will keep them interested in always pursuing a higher skill set.

Companies that provide contingent labor are already doing these things and more, realizing that the employees they provide must already possess the skills to get the job done in the wake of dwindling resources and cutbacks on in-house training. Labs that are able to integrate contingent labor into their overall workforce

gain both the value of these built-in programs and highly qualified professionals who can add to the organization's "versatility."

Make investing in your employees' skills a priority, and watch your lab's overall quality, output and revenue grow.

Alan Edwards is senior director and product leader of the Kelly Services® Americas Products Group—Science. Kelly Services, Inc., a leader in providing workforce solutions, is headquartered in Troy, Michigan. For more information, visit www.kellyservices.com. You can also follow Alan on LinkedIn (www.linkedin.com).

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THE COST OF DISORGANIZATION...

CAN YOU AFFORD IT? by Patty Kreamer

For most, being organized means “a place for everything and everything in its place,” but the true definition of being organized is being able to find things when you need them, not three weeks later.

If you ask me, being organized means saving BIG money. Simply put, time is money. If you waste time all day long looking for things, you are wasting money.

If you spend an average of just five minutes of every hour of an eight-hour day looking for things, that adds up to over four weeks per year (166+ hours). This adds up quickly when you take each employee’s hourly rate of pay and multiply it by 166 hours per year. Yet we often spend hours looking for things.

So what can be done to eliminate most of this wasted time?

READY...

For starters, if you aren’t as organized as you’d like to be, you have to *look inside yourself* and explore WHY you are not organized. By understanding your nature, you can learn to work WITH your habits instead of AGAINST them. Here are a few examples of these habits:

- You might need it someday!

- If you can’t see it, you forget it.
- You have too much stuff!

SET...

Next, you have to take the time to look at your space and map out what you want the space to look like when you are done BEFORE you touch the first piece of clutter. Here are some things you’ll need to do in this step:

- Define the activity for the room.
- Have a realistic time schedule.
- Have the URGE TO PURGE.

GO!

Finally, you get to declutter by sorting and putting away in a methodical fashion. In order to make the paper clutter go away, a **simple process** is necessary. When it comes to papers and office clutter, I recommend the **E.A.S.Y.** system. There are only four things you can do with a piece of paper:

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Most skip the READY and SET steps and just start to tear into the clutter, but they don’t develop any long-lasting systems. This Band-Aid® will only last a short while before clutter begins to creep back into your life.

The bad news is that getting organized takes time and commitment. It has to be on your list of priorities for it to really become achievable.

The good news is that getting organized is simple if done methodically. An additional bit of good news is that it pays off. Organization provides a less stressful work environment, boosts morale, increases productivity and positively affects the bottom line.

Can you afford to be disorganized? Schedule the time to declutter, and soon you’ll be inspired to continue because you’ll feel like a huge weight has been lifted off your shoulders!

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If you missed Patty Kreamer’s Lab Manager Academy webinar “But I Might Need it Someday – How to be Organized in the Lab,” originally broadcast Wednesday, May 4th, visit www.labmanager.com/organization to watch the archived video.

CELL CULTURE CONTAMINATION

UNDERSTANDING THE CAUSES AND MANAGING THE RISKS

by Mary Kay Bates and Douglas Wernerspach

This is the first in a three-part series on CO₂ incubation.

Biological contamination is the dread of every person working with cell culture. When cultures become infected with microorganisms, or cross-contaminated by foreign cells, these cultures usually must be destroyed. Since the sources of culture contamination are ubiquitous as well as difficult to identify and eliminate, no cell culture laboratory remains unaffected by this concern.

With the continuing increase in the use of cell culture for biological research, vaccine production, and production of therapeutic proteins for personalized medicine and emerging regenerative medicine applications, culture contamination remains a highly important issue.

Introduction

Cell culture is continuing a 60-year trend of increasing use and importance in academic research, therapeutic medicine, and drug discovery, accompanied by an amplified economic impact.^{1,2} New therapies, vaccines, and drugs, as well as regenerated and synthetic organs, will increasingly come from cultured mammalian cells. With greater usage and proficiency of cell culture techniques comes a better understanding of the perils and problems associated with cell culture contamination. In the 21st century, there are better testing methods and preventive tools, and an awareness of the risk and effects of contamination requires that cell culturists remain vigilant; undetected contamination can have widespread downstream effects.

Biological contamination: a common companion

The chance discovery of penicillin back in 1928 was one of those rare occurrences that most researchers can only dream about. After returning from a summer vacation during which he carelessly left a set of Petri dishes

stacked up in a corner of his lab, Alexander Fleming discovered one of the 20th century's most powerful drugs. Fleming noticed that one of his bacterial cultures was contaminated with a fungus, but the colonies of *Staphylococci* immediately surrounding the fungus had been destroyed. The fungus was, of course, *Penicillium notatum*, and Fleming went on to discover antibiotics. This is, however, a very rare example of contamination actu-

ally advancing the path of scientific research. For the most part, the contamination of cultures remains every scientist's worst nightmare. Carolyn Kay Lincoln and Michael Gabridge summed up the problem in 1998: "Cell culture contamination continues to be a major problem at the basic research bench as well as for bioproduct manufacturers.

Contamination is what truly endangers the use of cell cultures as reliable reagents and tools."³

The biological contamination of mammalian cell cultures is more common than you might think. Statistics reported in the mid-1990s show that between 11 percent and 15 percent of cultures in U.S. laboratories were infected with *Mycoplasma* species.⁴ Even with better recognition of the problem and more stringent testing of commercially prepared reagents and media, the incidence of *mycoplasma* growth in research laboratory cul-

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tures was 23 percent in one recent study,⁵ and in 2010 an astonishing 8.45 percent of cultures commercially tested from biopharmaceutical sources were contaminated with fungi and bacteria, including *mycoplasma*.⁶

In the research laboratory, contamination is not just an occasional irritation, but it can cost valuable resources including time and money. Ultimately, contamination can affect the credibility of a research group or particular scientist; publications sometimes must be withdrawn due to fears about retrospective sample contamination or reported results that turn out to be artifacts. In biopharmaceutical manufacturing, contamination can

have an even more dramatic effect when entire production runs must be discarded. It is extremely important, therefore, to understand how sample contamination can occur and what methods are available to limit and, ultimately, prevent it.

What causes biological contamination?

Biological contaminants can be divided into two subgroups depending on the ease of detecting them in cultures, with the easiest being most bacteria and fungi. Those that are more difficult to detect, and thus present potentially more seri-

ous problems, include *Mycoplasmas*, viruses, and cross-contamination by other mammalian cells.

Bacteria and fungi

Bacteria and fungi, including molds and yeasts, are ubiquitous in the environment and are able to quickly colonize and flourish in the rich cell culture milieu. Their small size and fast growth rates make these microbes the most commonly encountered cell culture contaminants. In the absence of antibiotics,



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bacteria can usually be detected in a culture within a few days of contamination, either by microscopic observation or by their direct effects on the culture (pH shifts, turbidity, and cell death). Yeasts generally cause the

growth medium to become very cloudy or turbid, whereas molds will produce branched mycelium, which eventually appear as furry clumps floating in the medium.

Mycoplasmas

Mycoplasmas are certainly the most serious and widespread of all the biological contaminants, due to their low detection rates and their effect on mammalian cells. Although *mycoplasmas* are technically bacteria, they possess certain characteristics that make them unique. They are much smaller than most bacteria (0.15 to 0.3 μm), so they

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can grow to very high densities without any visible signs. They also lack a cell wall, and that, combined with their small size, means that they can sometimes slip through the pores of filter membranes used in sterilization. Since the most common antibiotics target bacterial cell walls, *mycoplasmas* are resistant.

Mycoplasmas are extremely detrimental to any cell culture: they affect the host cells' metabolism and morphology, cause chromosomal aberrations and damage, and can provoke cytopathic responses, rendering any data from contaminated cultures unreliable. In Europe, *mycoplasma* contamination levels have been found to be extremely high—between 25 percent and 40 percent—and reported rates in Japan have been as high as 80 percent.⁴ The discrepancy between the U.S. and the rest of the world is likely due to the use of testing programs. Statistics show that laboratories that routinely test for *mycoplasma* contamination have much lower incidence; once detected, contamination can be contained and eliminated. Testing for *mycoplasma* should be performed at least once per month, and there is a wide range of commercially available kits. The only way to ensure detection of species is to use at least two different testing methods, such as DAPI staining and PCR.⁵

Viruses

Like *mycoplasmas*, viruses do not provide visual cues to their presence; they do not change the pH of the culture medium or result in turbidity. Since viruses use their host for replication, drugs used to block viruses can also be highly toxic for the cells being cultured. Viruses that cause damage to the host cell do, however, tend to be self-limiting, so the major concern for viral contamination is their potential for infecting laboratory personnel. Those working with human or other primate cells must use extra safety precautions.

Other mammalian cell types

Cross-contamination of a cell culture with other cell types is a serious problem that has only recently been

considered alarming.^{7,8} An estimated 15 percent to 20 percent of cell lines currently in use are misidentified^{9,10}, a problem that began with the first human cell line, HeLa, an unusually aggressive cervical adenocarcinoma isolated from Henrietta Lacks in 1952. HeLa cells are so aggressive that, once accidentally introduced into a culture, they quickly overgrow the original cells. But the problem is not limited to HeLa; there are many examples of cell lines that are characterized as endothelial cells or prostate cancer cells but are actually bladder cancer cells, and characterized as breast cancer cells but are in fact ovarian cancer cells. In these cases, the problem occurs when the foreign cell type is better adapted to the culture conditions, and thus replaces the original cells in the culture. Such contamination clearly poses a problem for the quality of research produced, and the use of cultures containing the wrong cell types can lead to retraction of published results.

Sources of biological contaminants in the lab

In order to reduce the frequency of biological contamination, it is important to understand how biological contaminants can enter culture dishes. In most laboratories, the greatest sources of microbes are those that accompany laboratory personnel. These are circulated as airborne particles and aerosols during normal lab work. Talking, sneezing, and coughing can generate significant amounts of aerosols. Clothing can also harbor and transport a range of microor-

ganisms from outside the lab, so it is crucial to wear lab coats when working in the cell culture lab. Even simply moving around the lab can create air movement, so the room must be cleaned often to reduce dust particles.

Certain laboratory equipment, such as pipetting devices, vortexers, or centrifuges without biocontainment vessels, can generate large amounts of microbial-laden particulates and aerosols. Frequently used laboratory equipment, including water baths, refrigerators, microscopes, and cold storage rooms, are also reservoirs for microbes and fungi. Improperly cleaned and maintained

incubators can serve as an acceptable home for fungi and bacteria. Overcrowding of materials in the autoclave during sterilization can also result in incomplete elimination of microbes.

Culture media, bovine sera, reagents, and plasticware can also be major sources of biological contaminants. While commercial testing methods are much improved over those of earlier decades, it is paramount to use materials that are certified for cell culture use. Cross-contamination can occur when working with multiple cell lines at the same time. Each cell type should have its own solutions and supplies and should be manipulated separately from other cells. Unintentional use of nonsterile supplies, media, or solutions during routine cell culture procedures is the major source of microbial spread.

Conclusion

Contamination is a prevalent issue in the culturing of cells, and it is essential that any risks are managed effectively so that experiment integrity is maintained. Antibiotics can be used for a few weeks to ensure resolution of a known microbial contamination; however, routine use should be avoided. Regular inclusion of antibiotics not only selects for resistant organisms, but also masks any low-level infection and habitual mistakes in aseptic technique.

The best approach to fighting contamination is for each person to keep records of all cell culture work including each passage, general cell appearance, and manipulations including feeding, splitting, and counting of cells. If contamination does occur, make a note of the characteristics and the time and date. In this way, any contamination can be pinpointed at the time it occurs and improvements can be made to aseptic techniques or lab protocols. In the next article of this series, we explore in more detail effective measures for contamination prevention, in particular the key role of the CO₂ incubator.

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EVOLUTION OF CHROMATOGRAPHY COLUMNS

BY JOHN BUIE

The history of chromatography begins during the mid-19th century when a rudimentary version of the technique was used for the separation of plant pigments such as chlorophyll. The first chromatography column was developed by the Russian botanist Mikhail Tsvet who, in 1901, washed an organic solution of plant pigments through a vertical glass column packed with an adsorptive material. He discovered that the pigments separated into a series of discrete colored bands on the column, divided by regions entirely free of color.

Column chromatography was popularized during the 1930s when the chemists Richard Kuhn and Edgar Lederer successfully used the technique to separate a number of biologically important materials. Since that time, the technique has advanced rapidly and column chromatography is now used widely in many different forms. The column itself has also been refined over the years, according to the type of chromatography, but fulfils the same essential separating function in all forms of column chromatography. Key milestones in the development of the chromatography column are presented below.

In **1938**, Harold C. Urey and T. I. Taylor developed the first ion exchange chromatography column based on a zeolite stationary phase. This technique allowed for the first time the separation of particles based on their charge.

In **1941**, the concept of using water as a stationary liquid supported on inert silica in conjunction with a mobile chloroform phase was developed by two British chemists, Archer Martin and Richard Syngé. Their design enabled the solute molecules to be partitioned between the stationary liquid and the mobile liquid phases, improving separation. Martin and Syngé were instrumental in the development of increasingly sophisticated chromatographic techniques during the 1940s and 1950s.

Later in **1957**, nylon capillary columns were shown to yield effective separations. However, although nylon was readily available, it was found not to be suitable for general use due to a limited operating temperature.

In **1958**, the British scientist James Lovelock first proposed the use of supercritical fluids (gases at temperatures above their critical temperature) as mobile phases for column chromatography at high pressure.

In **1968**, Pedro Cuatrecasas and colleagues developed the technique now known as affinity chromatography, in which a biomolecule, such as an enzyme, binds to a substrate attached to the solid phase while other components are eluted. The retained molecule is subsequently eluted by changing the chemical conditions of the separation. This technique is able to achieve exceptional separation.

In the early **1970s**, a transition from large porous particles to small porous particles in HPLC columns began. Microparticulate silica gel began to be used at this time, although microparticulate packing materials were still irregularly shaped.

In **1986**, a patent was granted for an adapted chromatography column that allowed the accommodation of a pre-column. The use of pre-columns allows the substances that are to be chromatographed to be preconcentrated before entering the main column for greater efficiency.

In the first GC columns, the carrier flow rate was controlled indirectly by controlling the column head pressure. However, during the **1990s**, headed columns were developed that allowed carrier pressures and flow rates to be adjusted during the run, creating pressure/flow programs similar to temperature programs.

In **2000**, Merck KGaA launched Chromolith Performance and Chromolith SpeedROD, new monolithic columns developed for HPLC. Chromolith columns were light, slim, and up to 10 cm in length. These columns were capable of separating the most complex mixtures into their components rapidly and accurately, reportedly separating 33 different pesticides in less than 15 minutes. Chromolith Performance columns were also able to be joined together to create a combined length of up to 1 m, further improving separating performance.

In **2000**, further improvements in HPLC packing materials were realized when Stellar Phases filed a patent for a high-performance line of spherical, high-purity, silica-based HPLC packings, which were to be sold under the trademark AstroSil®. The spherical, fully porous particles of AstroSil could be packed to high efficiency, and repacked repeatedly under high pressure.

In **2004**, Waters Corporation reached a landmark in column chromatography when it introduced its Acquity Ultra Performance LC (UPLC) system. At the heart of the Acquity UPLC system was the column, which incorporated second-generation, pressure-tolerant reversed-phase silica/organosiloxane hybrid particles of extremely narrow size distribution. This allowed uniaxial separation. Many laboratories subsequently replaced HPLC technology with Acquity UPLC as their gold standard for liquid chromatography separations.

Finally, in **2006**, Phenomenex researchers achieved a breakthrough in gas chromatography, an industry segment that had become regarded as fairly mature. They managed to solve the problem of the restricted upper temperature limit possible in gas chromatography with the Zebron Inferno™ GC column. This new column was able to sustain scorching temperatures up to 430 °C (806 °F). A polyimide coating protected the column from extreme temperatures, allowing it to be used in measuring contaminants in a host of biodiesel, pharmaceutical, life sciences, and food and beverage products. It also yields greater accuracy in workplace drug testing and the use of banned substances in athletics.

In **2008**, Shimadzu launched its new Ultra Fast Liquid Chromatography System that doubled separation performance and reduced analysis time to one fourth that of conventional systems. This system relied on the Shim-pack XR-ODS II series columns, which incorporated optimized particle pore diameters, longer column lengths, increased system pressure resistance and minimized flow path dead volume. These attributes effectively doubled separation performance, while preserving ultra-fast analysis times.

Also in **2008**, a method of avoiding pre-filtration prior to column chromatography became available when Upfront Chromatography launched the world's first expanded bed adsorption (EBA)-based disposable chromatography column. These pre-packed, pre-sanitized antibody purification columns also offered the added benefits of cost-effectiveness and flexibility associated with disposable chromatography columns.

In **2009**, Chiral Technologies, Inc., a subsidiary of Daicel Chemical Industries of Japan (the first company to manufacture chiral chromatography columns during the 1980s), succeeded in developing 3-µm versions of their standard 5-µm chiral columns. The new, smaller columns offered high-speed and high-efficiency separation with the same stability and selectivity as the earlier larger columns. Also in this year, Chiral Technologies Inc. extended its line of 5-µm chiral columns by introducing columns packed with new stationary proprietary coated polysaccharide-based chiral stationary phases for improved separation.

Prior to **2010**, characterization of synthetic RNA and DNA by LC/MS was time consuming and often showed poor sensitivity. This issue was resolved with the Clarity® Oligo-MS™ column from Phenomenex, which offered rapid and efficient LC/MS characterization and quality control of synthetic RNA and DNA. Based on the company's core-shell particle technology, the high resolving power of Clarity Oligo-MS allowed impurities in complex synthetic mixtures to be separated from the peak of interest in less than 10 minutes.

In **2010**, Thermo Scientific launched its Syncronis range of HPLC columns, engineered to deliver exceptional reproducibility by providing highly pure, high surface-area silica, dense bonding and double end-capping.



An HPLC column from YMC America.

In **2010**, YMC launched its Triart C18 hybrid HPLC column, developed utilizing YMC experience in microaction chemistry. The techniques developed gave highly uniform particles that contributed to the chromatographic performance of the finished product. This column was able to give excellent peak shapes due to a multi-reagent, multi-step, end-capping process.

Also in **2010**, innovations in HPLC particles continued to advance with the new 160-angstrom Fused-Core™ particle design devised by Supelco, a division of Sigma-Aldrich, and used in the Ascentis Express Peptide ES-C18. This column design exhibited very high column efficiency, providing a stable, reversed phase packing with a pore structure and pore size that was optimized for reversed-phase HPLC separations of peptides and polypeptides.

1940

1950

1960

1970

1980

1990

2000

2010

In **1942**, ion-exchange column chromatography was used to great effect during the Manhattan Project to separate elements such as uranium fission products produced by thermonuclear explosions.

In **1944**, Erika Cremer devised a system of gas chromatography using a solid stationary phase.



Marcel Golay with an early glass capillary column.

In **1957**, a consultant for the PerkinElmer Corporation, Marcel Golay, calculated that using a very long gas chromatographic column (greater than 90 m in length) of narrow diameter (around 0.25 mm) lined with a thin film of liquid would significantly improve the separation of different molecules. The resulting capillary, or Golay, column revolutionized chromatography techniques, ultimately allowing the separation of hundreds of components within a single run.

In **1961**, John Moore, working at Dow Chemical in Freeport, TX, invented an instrumental method of analyzing polymers using gel columns. Waters Associates recognized the significance of this invention and successfully negotiated for an exclusive license to Moore's patent, allowing the company to begin developing its own systems.

In **1962**, Ernst Klesper working at Johns Hopkins University reported the first use of supercritical fluids in column chromatography, using the technique for the separation of closely-related porphyrins.

In **1963**, Waters Associates launched its first gel permeation chromatographic instrument, the GPC 100. This instrument, which was larger than a refrigerator, was enormous by modern standards and extremely heavy.

In **1964**, the American chemist J. Calvin Giddings refined liquid chromatography to achieve separations comparable with those achieved with gas chromatography. This was the origin of the technique now known as high-performance liquid chromatography (HPLC), and relied on very small particles with a thin film of stationary phase in small-diameter columns.

In **1978**, Dr. W. Clark, still working at Columbia University, pioneered the technique of flash column chromatography—a rapid form of preparative column chromatography in which the mobile phase is accelerated through the column by use of a positive pressure.

Before **1979**, the process for separating chiral molecules relied on purely chemical methods and was time consuming and often unreliable. Then, in 1979, Yoshio Okamoto, a former chemistry professor at Nagoya University in Nagoya, Japan, synthesized for the first time a helical polymer of triphenylmethyl methacrylate in a single-handed form that was stable at room temperature. He later showed the same synthetic principles could be applied to chiral chromatography, and developed the first chiral chromatography columns. This breakthrough was commercialized in partnership with Daicel, now a leading Japanese manufacturer of chiral chromatography media.

During the **1980s**, new perfusion packings were commercialized by PerSeptive Biosystems to provide improved chromatographic performance, particularly for larger molecules.

In the early **1990s**, Type B silica gradually became the standard packing material in most commercial-based analytical HPLC applications because of the low levels of trace metal content and improved levels of purity.

In **1994**, in an attempt to improve on the reproducibility of HPLC columns, Waters Corporation developed a process for the manufacture of packing materials using high purity raw materials as well as improved column packing procedures. This technology was first used in Waters' Symmetry HPLC columns launched that year.

In **1999**, Waters Corporation was responsible for an exciting development that allowed improvements in HPLC technology in terms of speed, peak shape and operating pH range. The XTerra HPLC column had a major role in accelerating the analytical and purification processes for lead generation and optimization in the field of drug discovery.

Until **1999**, underivatized amino acids could only be separated using an ion exchange column, which caused difficulties because many of the buffers required in these methods are not LC/MS compatible. Therefore, amino acids tended to be derivatized prior to separation by HPLC in a costly and time-consuming procedure. In 1999, Restek solved this problem with the Allure Acidix column that allowed amino acids to be analyzed by liquid LC/MS for the first time.

In **2005**, still pursuing the goal of improved HPLC particles, Waters Corporation released the XBridge HPLC column family, a major expansion of Waters' 2nd generation Ethylene-Bridged Hybrid particle line (BEH Technology™). These breakthrough hybrid particles combined the efficiencies of silica-based materials with the pH resistance more common to polymer packing materials.



Kinetex HPLC columns from Phenomenex.

Until **2006**, protein analysis by column chromatography was problematic. In this year, Wyatt Technology Corporation launched its first size exclusion chromatography (SEC) columns for protein analysis by multi-angle light scattering. These SEC columns were designed to achieve the best resolution and reproducibility as well as the maximum detection sensitivity for protein characterization.

Also in **2006**, Agilent Technologies tried to capture some of the success of the Waters Acquity UPLC system by launching its 1200 Series LC system, a high-resolution, high-speed system designed specifically to compete with Waters' model. The Agilent 1200 Series system was based on a second-generation ZORBAX Rapid Resolution HT 1.8-µm column that provided 60% higher resolution than HPLC columns of the same dimension.

In **2009**, a new method for achieving UHPLC results on any LC instrument platform was devised by Phenomenex, allowing researchers to attain performance comparable to sub-2 micron columns without investing in UHPLC systems. The Kinetex columns, based on the company's new core-shell silica technology, delivered significant improvements in speed and separation efficiency over traditional 3- and 5-micron columns.

In **2009**, Analtech began a partnership with Separation Methods Technologies to offer the columns developed by Dr. David Fatunmbi that utilized proprietary bonding technologies, resulting in bonded phase coverage that approaches 100%.

Also in **2010**, capillary-column technology advanced even further with Thermo Scientific's TraceGOLD GC capillary columns. These ultra-low bleed columns provided outstanding run-to-run, as well as column-to-column reproducibility for consistent, reliable data, as well as extended column life. In addition, the columns were extremely inert, ensuring that the best peak shapes were obtained, even for highly active or difficult compounds that often cause peak tailing.



A TraceGOLD GC column from Thermo Scientific.

FUTURE OF COLUMN CHROMATOGRAPHY

Column chromatography is one of the most widely used techniques for both preparative and analytical purposes. The technique has come a long way since the first experiments with chlorophyll, and continues to adapt with many advances in the design of columns and the creation of better-performing resins. Although many new materials have emerged, silica-based packings retain their dominance in most laboratories and will be used for a long time. For simple sample mixtures encountered, the trend towards the use of smaller porous particles (now down to 1.5 µm) packed into columns will continue allowing shorter columns to achieve the same separation.

Future developments are likely to involve hydrophilic interaction chromatography (HILIC), which is rapidly gaining interest as a method for analyzing biomolecules and drug metabolites that are poorly resolved by reverse-phase liquid chromatography. The rational design of more efficient affinity ligands is another area of interest, along with the rise of disposable membrane chromatography and monoliths as a viable alternative to traditional packed-bed columns.

« EXPERT: Daniel Zimmerli

ASK THE EXPERT

KEEPING UP WITH HPLC AND UHPLC ADVANCES

by Tanuja Koppal, Ph.D.

Daniel Zimmerli, associate scientist and lead of the Separation Science Point group, discusses how his team uses high-performance liquid chromatography (HPLC) and ultra-high performance (or pressure) LC (UHPLC) technologies for analytical and preparative work in the Chemistry Technologies and Innovation department at F. Hoffmann-La Roche. He shares his perspectives on the changes taking place in liquid chromatography-based separations, both with the instrumentation hardware and data analysis software. He advises chromatographers and lab managers to keep their eyes and ears open for new instruments being released in the marketplace, and to look six to 12 months into the future on the types of applications they will be working on when making their buying decisions.

Q: In which types of applications do you use chromatography?

A: I work in the Discovery Chemistry group at La Roche, and we do a lot of separation and purification to support early discovery work. We have two dedicated laboratories with a lot of chromatography instrumentation. We have 12 different HPLC instruments and one UHPLC for high-throughput work. We use HPLC for chiral separation and preparative work,

and for separating biological samples we use UHPLC. On average, we run about 800 to 1,000 samples per instrument per day. For the preparative work, which involves around 1g to 10 g of sample, we average 3,000 samples per year using traditional HPLC.

“Maybe in the next 10 to 20 years everyone will upgrade to UHPLC.”

Q: What types of changes have you seen in the chromatography market over the years?

A: I have worked for 12 years in this lab, and in the past few years I have seen traditional HPLC moving more to UHPLC. We have seen new machines and new columns in the market that have made separations faster and more high-throughput. We have seen sample run times go down from 30 minutes to one or two minutes, and we are much faster now than we were 10 years ago. We now have different column chemistries, and the particle size and dimensions of the columns have also changed. Previously, we worked at pressures of around 200 bar, but now we can go up to 1,500 bar with the new column

packing. With faster run times we save a lot on solvents, too. One year ago when the cost of acetonitrile—our main solvent for reverse-phase chromatography—went up nearly five times, we saved a lot of money and solvent with our fast columns.

Q: How is the transition from HPLC to UHPLC?

A: The cost of UHPLC is about 20 to 25 percent higher than traditional HPLC, but in about three to six months you break even. You have to invest more to begin with, but depending on the number of samples you run, you can break even very quickly. Our lab works seven days a week, and we average about 2,000 samples on each machine per week.

Q: How often do you upgrade your instruments and technology?

A: We are always looking for machines that are fast, that we can easily adapt to our columns, and that are robust. Every year, we buy at least two or three new HPLC instruments. We either move the older HPLCs to other labs within La Roche or donate them to universities. Our department is Chemistry Technologies and Innovation, and we need to constantly upgrade to use the newest technology and use the best that's out there on the market. We test a lot of machines during the year, keep our eyes

Daniel Zimmerli is an associate scientist and the lead of Separation Science Point, a subgroup of the Chemistry Technologies and Innovation department in the Discovery Chemistry group at F. Hoffmann-La Roche Ltd., in Basel, Switzerland. He has worked at La Roche for more than 25 years, the first half of which he spent in a synthesis laboratory working with small molecules. He then started working with preparative chiral HPLC, performing around 100 separations a year. In 2010, the group performed more than 2,200 preparative chiral separations. The group supports nearly 70 research synthesis labs at La Roche on all kinds of separations. He has a bachelor's degree in informatics and a master's degree in chemistry from the University of Zurich.

open for what's new on the market, and attend conferences to keep up with new releases. In our group, we are not expected to buy only from a certain vendor. In some other departments where they are controlled or under regulatory restrictions, they have to work with only one vendor and they change their machines only every five to seven years.

Q: What are your experiences with using the instrument software?

A: Now, there are some really good machines and columns coming in for the UHPLC market. But in most cases, in the beginning, they all have problems with their software. It takes nearly six months to a year before the software bugs can be worked out. Sometimes we are the first users on a new machine, and we have to give feedback to the company, and then updates are made. We have service contracts with every company, and most companies provide two-day user training. But we are very familiar with a lot of different instruments and software, so in our group we usually don't need any special training. Most companies have good customer service, and they all have good technical support and are open to discussion.

Q: What are some of the limitations with using chromatography?

A: There has been no change in the preparative market in the past five to 10 years. Everything is for the analytical market; this is possibly because not many people work in the preparative market. We are hoping that we will be able to apply UHPLC technology to the preparative work. For the separation of some chiral molecules and peptides, we need hours to separate the compounds and we need a lot of solvent. For chiral molecules that take 10 minutes to separate in the analytical scale, it may take up to an hour in the preparative scale. Hopefully, companies will come out with new instruments in the preparative market in the next couple of years, and preparative work will get better, faster and cleaner with the use of supercritical fluid chromatography (SFC).

Q: What do you see happening in this field going forward?

A: I think the traditional HPLC market will stay but the percentage of use will go down every year. Maybe in the next 10 to 20 years everyone will upgrade to UHPLC. In most companies, there are labs that work in a controlled environment and have protocols

validated for regulatory use with traditional HPLC instruments. For those labs it will take time, about three to five years, and money to adapt their protocols and transfer everything to UHPLC. Some departments at La Roche have 20 traditional HPLC instruments and they are changing three instruments every year to UHPLC analysis.

Q: What is your advice for lab managers looking to invest in HPLC or UHPLC?

A: When you are looking to buy a new instrument, you should know what you want to separate and how much resolution is needed. Look a little into the future, about six to 12 months ahead, to figure out exactly what you need. For a smaller lab with lower throughput, cheaper machines working at low pressure may suffice, depending on the application. All vendors offer a range of different machines, and there are instruments that are in the range between HPLC and UHPLC that are sometimes 20 percent cheaper. So keep your eyes open and speak to different people.

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A BIG CHALLENGE FOR SUPERVISOR WALLY THOMPSON IS NAVIGATING NON-U.S. REGULATORY AGENCIES

by Sara Goudarzi



▲ View of lab with Joanne McPherson emptying her tested bags.

▲ Joanne McPherson after completing particulate testing.

Wally Thompson is the Microbiology Supervisor at Gambro in Daytona Beach, Florida. Gambro is a global medical technology company, with manufacturing facilities in countries all over the world including Italy, Sweden, Germany, France, Korea, and China, that develops and manufactures products and therapies related to kidney diseases.



"We provide our solutions to hospitals and trauma centers for use in intensive care situations," Thompson says.

monitoring of clean rooms, and other projects associated with the facility," he says.

"With proper control measures, endotoxin doesn't make it to the final product."

Thompson's lab is one of Gambro's many facilities around the world. His lab provides microbial analysis for the products—medical device and pharmaceutical solutions for renal intensive care—manufactured at that facility.

"We are also responsible for the analysis of the water used for product manufacture, environmental

◀ *Wally Thompson, Microbiology Supervisor at Gambro.*

Gambro Daytona manufactures solutions that are used in renal intensive care. Part of the product monitoring includes pre-sterilization testing to monitor potential organisms and their amount before a product undergoes sterilization.

"We test the product after sterilization to make sure it's sterile," Thompson explains. "We also test for liquid particulates where the particles could be living organisms or other foreign matter that you can't

see with the eye but are large enough that they could cause a problem for our patients. There are standards that we follow such as [The United States Pharmacopeia] USP, [The U.S. Food and Drug Administration] FDA guidelines, and that sort of thing."

One such problem could be the presence of endotoxins—a type of toxin that's found in the cell walls of some bacteria—in the final product. When certain bacteria die, they release spores, which are basically resistant to the steam sterilization and are near impossible to get rid of. If such impurities end up in pharmaceutical products over a certain amount, they could cause fever in patients. But with proper control measures, endotoxin doesn't make it to the final product.

Thompson's team also monitors the

environmental condition of the clean rooms—rooms with little particulate matter such as dust and bacteria, used for manufacturing sterile products—through air-viable, surface-viable, and air-particulate testing.

"Together, the team processes thousands of samples a year."

"We manufacture our products in clean rooms—they are ISO Class 8, which is a fairly clean environment, and we check the rooms and the operators for contamination to make sure that they limit the amount of contamination that could possibly contaminate our product," Thompson

says. "Even though our product is not exposed in most of the rooms, we try to maintain that contamination-free environment just in case."

Lab structure

The production area in Daytona Beach, Florida, which includes the quality control labs, is almost 100,000 square feet. The microbiology lab takes up approximately 1,500 square feet of this space.

"Our manufacturing plant operates seven days a week," Thompson says. "We have personnel working in the lab seven days a week. Technically we don't need to be working on the weekends, but it actually works with a couple of my employees' schedules better if they can work on the weekend and have a day off during the week."

Thompson and his five-person team run the laboratory. Thompson reports to a quality manager who reports to the Vice President of Quality for the America's group and then on up the chain to the President of Quality for the company.

There are other microbiology labs within the company as well, Thompson explains. "There's a lab in Alabama, a lab in Germany, one in Italy, and a few more."

To run the operation, Thompson has put together a team of biologists and chemists.

"To ensure that the microbiology lab is well stocked, everyone takes part in routine inventory."

"My employees have diverse backgrounds; [we have] a chemist, two biologists, and two working on degrees," he says. "I am a biologist by degree and have worked in the chemistry lab as well as the micro lab."

Together, the team processes thousands of samples a year. For example, last year Thompson and his five employees went through more than 17,000 just for the environmental monitoring that they conduct on a weekly and monthly basis.

"My lab coordinator, Adria, does a terrific job keeping the day-to-day activities in the lab organized and running smoothly," he says. "[Also], communication is the key to making sure all testing is performed correctly. It is especially important

when working with the other labs and production on special projects."

Inventory, maintenance, and hiring

To ensure that the microbiology lab is well stocked, everyone takes part in routine inventory. When a team member notes that a material is running low, he or she reports it to the lab coordinator—one of the five lab staff designated to handle such matters.

"My coordinator handles the ordering and makes sure that inventory of materials stays at a level where we always have enough to perform our testing," Thompson says.

Maintenance of lab equipment is also handled by lab personnel. The lab staff utilize a variety of instruments. However, the top five most used instruments are the Rion KL-04 Liquid Particle counter, Cambrex WINKQCL endotoxin software with ELIX reader for endotoxin testing, Biomerieux Air Ideal impact air sampler, Metone Hand Held Particle Counter-6, and Binder BD400 Incubator

"If there are other issues outside of equipment or if there is a problem that cannot be handled, our maintenance staff will investigate and repair or make sure the proper vendor is contacted to repair," Thompson says.

Thanks to smooth protocols and organized scheduling, the small and competent staff team handles all these tasks without a hiccup.

Having people you can trust who are dedicated to what they are doing and possess good skill sets and knowledge to back it up is very important to running a successful lab, Thompson says.

At times, when a team member has to leave his or her position or a new position opens, Thompson takes great care to ensure that a person with a good fit joins the group.

"I'll bring the need for new personnel up to my boss and she'll request an additional person to work in the lab," Thompson explains. "Once the approval comes from corporate then we start bringing in potential employees." Depending on the position being filled, interviews are conducted by department, HR, and associated managers.

"A lot of times we'll go through a scientific temp agency, bring the person in and I and maybe my manager will interview them," he says. "Then from a number of interviews that we have, we will determine who seems the most qualified and hire that person through the temp agency. If that works out then we usually make that person permanent."

Incentives

To keep employee morale high and the staff productive, both the company and Thompson work hard to reward those who are doing excellent work.

The company has an employee of the month for the facility, who receives the Top Dog award. Additionally we have employee lunches, holiday and health fairs where the company provides free health screenings and exams, and we serve a healthy lunch to our employees," Thompson explains.

"As far as what I do, every once in a while I'll bring in breakfast for my employees to say thanks for doing a great job."

Challenges

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pharmaceutical manufacturing is probably being in compliance with all the applicable regulations. The lab supervisor typically handles the largest burden of the task.

“Thompson takes great care to ensure that a person with a good fit joins the group.”

“It is difficult to keep up with standards and guidelines since they are constantly being updated,” Thompson says. “It is also a challenge to ensure that we are following

the regulations from the different countries that we are selling our products or will be selling our products to.”

Being a global company, Gambro is expanding into markets outside the United States, such as Mexico. Most recently, the company is working on approval to sell its products in Brazil,

which has regulatory agencies that function much like the FDA.

“They have their requirements just like the FDA does, a lot of similar things, but some things are different and so they inspected our facility to make sure that we meet their regulatory requirements for manufacturing our product and selling it in their country,” Thompson explains.

Although challenging, such expansions are new and stimulating for Thompson.

“It’s exciting working on getting the requirements that meet the expectations of other regulatory

agencies, whether it’s Brazil, Europe, Canada or Mexico,” he says. That’s exciting as well as challenging because they all vary a little bit. Another country might have a slightly new requirement that we’re not used to seeing and it’s my responsibility to stay on top of that to make sure that we can meet those requirements.”

Additionally, the company is continually developing new formulations of its product in order to provide solutions that will encompass a wide range of needs from the patients, Thompson explains.

“Each time we work on these projects, it is an exciting time because of the new ideas, methodologies, and all other aspects that go into the project.”

Thompson spends most of his day overseeing details related to these projects, revising documents, preparing project protocols and final reports, and keeping an eye on the events in the lab. But to him, it’s all in a day’s work.

His advice to other lab managers

“Look at the big picture and don’t get drawn into spending all of your time and focus on one or two details,” Thompson says. “This may cause you to miss an important element or requirement and leave you scrambling to come up with a solution. Listen to your employees and allow them to have input on the tasks performed in the lab. They know what works best and you need to make sure that everyone is on the same page.”

Thompson attributes his success in the lab to his supportive family, a competent staff, and the overall importance of the work.

“I know the importance of what I do in the grand scheme of saving and improving the lives of the patients who receive our product,” he says.

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

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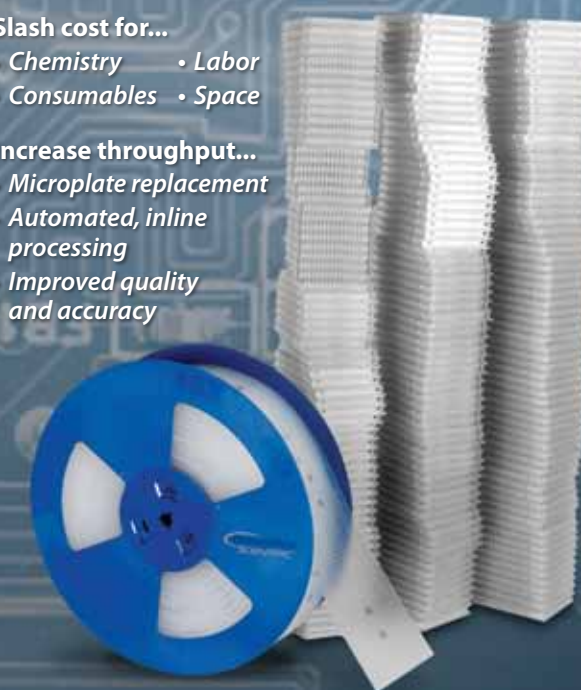
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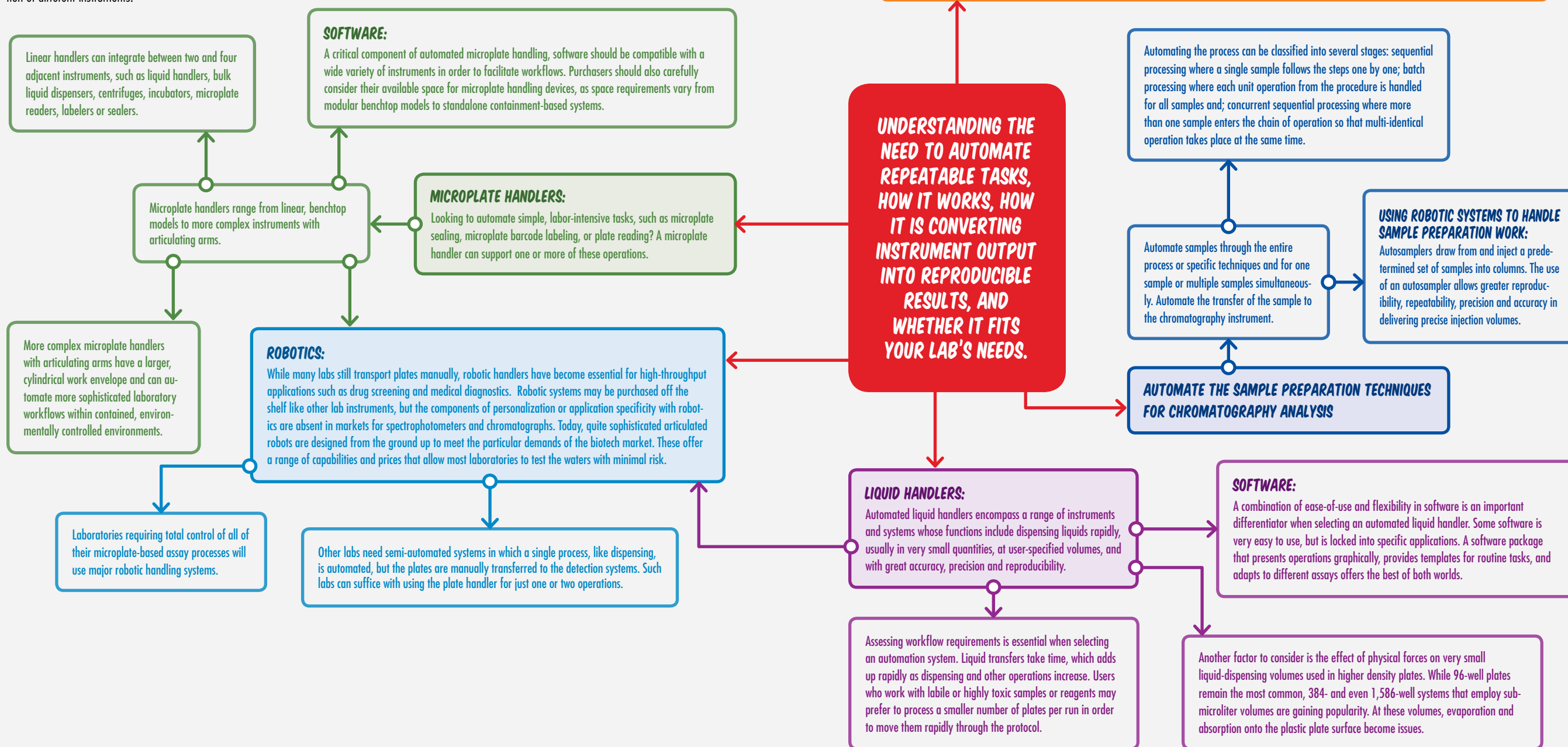
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MINDMAP: INCREASE MY LAB'S PRODUCTIVITY THROUGH AUTOMATION

By John Buie

Driven by the pressure to control costs while generating better quality data, automated, unattended, and reliable operation is what lab professionals are looking for from their instruments. Compact and scalable lab automation modules provide the flexibility labs require to quickly adapt to changing research needs. Such modules range from compact, benchtop workstations to sophisticated containment-based systems featuring environmental control. As research needs change, most modules can be easily repurposed. Today's investment in laboratory automation modules provides more utility, reliability and benefits than ever before. However, creating an effective lab automation system requires more than the simple purchase of an 'off the shelf' package. There are many factors to consider when trying to improve productivity through lab automation, and no single solution will suit all laboratories.

This MindMap presents some of the issues to be considered and taken into account when trying to improve productivity through lab automation, including the integration of different instruments.





SURVEY SAYS: ARE YOU IN THE MARKET FOR AN INCUBATOR?

Laboratory incubators have evolved steadily over the latter part of the twentieth century, and have remained an important piece of laboratory equipment. Experts believe that in the future, the incubator market will derive most of its growth from the biotechnology industry. As medical knowledge and technology improves, and researchers become increasingly exacting, it is believed that growth chamber-type incubators will be required that have an even greater sensitivity in the control of temperature and relative humidity.

Another potential area of growth for incubators is within the field of genetic engineering, in which scientists manipulate the genetic materials in explants, sometimes combining DNA from discrete sources to create new organisms. Although genetic engineering is a controversial subject for many, this technology has already delivered tangible benefits, including the manufacture of insulin and other biologically essential proteins. Genetic engineering has also been shown to improve the nutritional content of fruits and vegetables and to increase the resistance of certain crops to disease. Genetic engineering relies heavily on the use of well-controlled and adjustable incubation, and it is within the field of biotechnology that some experts believe the greatest potential of the incubator can be found.

Cell culture incubators, also known as carbon dioxide (CO₂) incubators, are by far the largest group in terms of sales and applications. CO₂ incubators support cell culture work in basic research and in the biotechnology industry where CO₂ is used to control the pH of cell culture media and to provide a more lifelike environment in which cells can grow. Diagnostics and pharmaceutical firms also use these incubators to grow test cells. Some manufacturers line the insides of incubators with copper to reduce bacterial growth; others employ HEPA filtration to prevent contaminants from entering. Incubators are usually kept free of contaminating bacteria through a combination of HEPA filtration and manual cleaning.

Respondents who are currently using a CO₂ incubator are using the following types:

Water jacketed	17%
Air jacketed	17%
Thermistor-controlled CO ₂	15%
HEPA filtered	14%
Passively humidified	11%
Infrared-controlled CO ₂	7%
Actively humidified	5%
Auto-decontaminating	4%
Copper-lined	3%
O ₂ control	3%
Refrigeration option	2%
Data logging	1%
Other	1%

Incubators are heated, controlled-climate chambers used mainly to grow cells or microorganisms. Together with the culture medium, conditions inside incubators are meant to mimic a cell's natural physiological conditions. Incubators come in two basic sizes. Benchtop models tend to be small (6 to 7 cubic feet in volume) and stackable. Anywhere from one to half a dozen lab workers might use a single unit. Reach-in floor-model incubators are larger (up to about 30 cubic feet) and might hold samples for up to several dozen workers or an entire department. Floor models are popular in hospitals, which require high-volume incubators to meet demand for patient testing and sample segregation. Pharmaceutical and biotech companies also use large incubators to support cell line development, clone selection and cell culture seeding for biomanufacturing, or to create cultures of test cells.

Benchtop incubators outsell reach-ins by about 20:1. Laboratory incubators are mainly used in the following industries: pharmaceutical, biotechnology, health care, and food and related products.

Respondents' fields of work:

Biochemistry and biology	19%
Pharmaceutical	15%
Microbiology	13%
Environment	12%
Clinical and blood banking	12%
Chemical	8%
Food and related products	5%
Other	16%

Drying out is a serious issue that destroys cell cultures. Some units today employ steam generators to replenish humidity to close to 100 percent within the incubator. Steam pans—containers filled with water—are more common.

Thirteen percent of the respondents do not have high enough humidity without condensation and 25 percent don't know.

Yes	61%
No	13%
Don't know	25%

Contamination is the single most devastating occurrence in cultured cells. Contamination can delay critical diagnoses in hospitals, destroy tissues in fertility clinics, ruin basic research work on cells that may have taken months to develop, or delay a cell-based manufacturing project by months. Contamination arises from the lab environment, the researcher, or the medium being used.

Fourteen percent of the respondents have problems with contamination in their unit and 12 percent don't know.

Yes	14%
No	74%
Don't know	12%

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

\$0 to \$1,000	37%
\$1,000 to \$2,500	14%
\$2,500 to \$5,000	18%
\$5,000 +	9%
Don't know	22%

Each of the following components meet the application needs of the lab to ensure maximum performance from the incubator.

High-temperature disinfection	23%
Data logging	18%
Cooling options	14%
O ₂ control	13%
Infrared O ₂ control	13%
RH control	11%
Other	8%

A majority of the respondents expect to spend \$5,000 - \$10,000 for their next incubator purchase.

Less than \$5,000	25%
\$5,000 to \$10,000	37%
\$10,000 to \$15,000	22%
\$15,000 to \$20,000	10%
\$20,000 to \$30,000	2%
\$30,000 +	5%

Many manufacturers are working toward addressing some of the common challenges associated with culturing cells, the most important of which is reducing aerial contamination. A number of incubators now offer a high-temperature decontamination cycle that works much like a self-cleaning oven—at the push of a button, users can heat-sterilize the incubator and get rid of any decontaminants or hazardous spills.

There are also continuous contamination prevention units that work all the time and do not have to be initiated manually. One technology uses HEPA filtration to continuously cycle the air and remove airborne particulates and contaminants. The other technology that is gaining a lot of interest is the use of incubators that have interiors made of solid copper components.

At the end of the day what customers really care about is having a reliable unit in which to grow their cells. Hence, the lab environment, the application and the customer's comfort level with the technology is what plays a big role in the selection of the equipment. Ultimately, lab professionals want an incubator that best meets their requirements.

Factors/features important in the buying decision making process	
Reliability of results/durability of product	98%
Service and support	97%
Ease of use	95%
Low maintenance/operating costs	95%
Price	94%
Safety and health features	92%
Warranties	92%
Audible and visible temperature alarms	91%
Availability of supplies and accessories	89%
Minimal temperature control	89%
Fast recovery times	86%
Stable O ₂ control	81%
Small footprint	73%
Computer interface to log data	46%



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SURVEY SAYS: ARE YOU IN THE MARKET FOR A FUME HOOD?

One of the primary safety devices in laboratories where chemicals are used is the laboratory fume hood. A well-designed fume hood, when properly installed and maintained, can provide a substantial degree of protection for the researcher, provided its proper use and limitations are understood.

Laboratory fume hoods are designed to protect workers by containing and exhausting harmful or toxic fumes, gases, or vapors emitted by chemicals used in the hood. A typical fume hood has an exhaust blower mounted so that air from the room is pulled into and through the hood, creating directional airflow. The “pull” at the hood opening is termed “face velocity” and is usually measured in feet per minute (fpm).

Proper face velocity of the hood is critical to the protection of the worker. Too little flow allows currents or disturbances in the laboratory air to overpower the hood and draw contaminants into the room. Too much flow can result in turbulence and eddies that also can lead to contaminants escaping the hood. Baffles and other aerodynamically designed components determine how air moves into and through the hood. Contaminants inside the hood are diluted with room air and exhausted to the outside via the hood’s duct system, where they are dispersed.

The volume of air exhausted by the hood depends on a number of factors, the most important of which are hood size and design. With the average chemical fume hood exhausting around 750 to 1,000 cubic feet per minute of conditioned air, you can see how hoods put a large load on the laboratory’s heating, ventilating and air-conditioning (HVAC) system, thus impacting operational costs.

Chemical fume hoods are inspected annually by the Office of Environmental Health and Safety. Labels that indicate the sash height for adequate containment are affixed to the fume hood. All fume hoods are equipped with a manometric gauge or other continuous monitoring device to monitor the flow of air. Proper readings of the monitoring device can also be found on the inspection label.

What is the frequency of the inspections of your fume hood?

Monthly	12%
Quarterly	12%
Every 6 months	13%
Annually	52%
Every two years or more	5%
Not applicable	1%
Don’t know	5%

It would be difficult to imagine a chemistry laboratory without at least one fume hood. Eighty-nine percent of respondents have a fume hood in their lab.

Yes	89%
No, but planning to purchase	5%
No, and no plans to purchase	6%

Fume hoods are notorious for consuming expensive resources, particularly electricity and conditioned air that is vented to the environment along with volatile chemicals and other toxins.

A decade ago, low-flow hoods revolutionized the industry by reducing air throughput and related energy costs by 40 percent. More recently, ductless hoods changed the equation in favor of greater energy efficiency and cost savings.

Ductless fume hoods use activated carbon filters to remove toxins from the airstream. Unlike traditional hoods, which vent tens of thousands of cubic feet of heated or conditioned workspace air per day, ductless fume hoods return conditioned air to the lab. This translates to a significant drop in energy use and operating costs while protecting the environment. A ductless fume hood requires no ductwork, arrives fully assembled, and may be installed in locations where, barring a significant and expensive renovation process, a traditional fume hood could not.

Conventional ducted fume hood	60%
Benchtop ductless fume hood	10%
Canopy ducted fume hood	10%
Variable air volume ducted fume hood	8%
Down flow workstation	6%
Portable ductless fume hood	5%

A great deal of innovation has occurred in fume hoods during the last decade. Fume hood manufacturers have incorporated interesting innovations. Today’s hoods have expanded viewing areas and improved counterbalance systems that assist in raising and lowering the glass window. Fume hood vendors have also addressed ergonomics, an important consideration, since many organic chemists practically “live” inside their hoods. Hood entrances are now slanted back, rather than outward, which makes them easier to work in for long periods. Sash designs have also improved, and some units now feature horizontal sliding panels.

Another interesting development is the “intelligent sash,” which closes when a motion sensor detects no movement in front of the hood for a specified time period, for example, when the operator walks away. This feature alone can reduce energy consumption by 70 percent.

Hood baffle designs have also undergone significant improvements. Baffles are cleverly angled, and even perforated, to allow for best airflow navigation to the exit point; that is, to reduce airflow residence time in the hood as much as possible. Today’s baffles are also easily removed for cleaning, which prolongs the service lifetime of the hood.

Most new fume hood purchases are for new laboratories, according to Environmental Health and Safety.

Setting up a new lab/developing a brand new method	38%
Replacement of aging fume hood	32%
Addition to existing systems; increase capacity	22%
Changing from the current type of fume hood	4%
Other	4%

Fume hoods are installed in laboratories to protect workers from hazardous vapors generated by laboratory experiments. However, simply conducting these experiments in the fume hood does not guarantee adequate protection. What labs are doing when it comes to their fume hood specification and maintenance programs:

	Agree	Disagree
All fume hoods have been tested within the past year (see the next question for frequency of tests).	90%	10%
Test labels are properly affixed to the fume hoods tested.	86%	14%

Storage in fume hoods is kept to a minimum and care is taken to not impede proper airflow (According to EH&S - Minimize the number of objects stored in the hood – keep at least 50% of the working surface clear, if possible).

To maximize hood effectiveness and minimize personal exposure to toxic vapors or gases, our lab uses fume hoods in accordance with the operational guidelines (According to EH&S - The efficiency of a fume hood is very dependent on its functional status and on how it is used. Users must ensure proper operation of fume hoods by performing the proper maintenance checks before each use).	97%	3%
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Users should be aware of problems that may arise during fume hood specification and installation. Traditionally, laboratory furniture suppliers provide fume hoods as well. Although a few manufacture hoods that are standards-compliant, many still construct fume hoods as though they were simple boxes. Fume hood prices are often bundled with furniture prices, and that makes it difficult for the end user to make informed decisions.

Environmental Health and Safety provides the following wish list for potential fume hood buyers:

- Local installation and support for ducting, controller and exhaust blower
- Appropriate safety certifications
- Construction materials for specific application: for example, polymer inner liners for corrosive acids, ceramic work tops for high temperatures
- Local references for the supplier/installer
- Aesthetics and cost

Factors/features important to lab research respondents in their decision-making processes:

Durability of product	98%
Low maintenance/easy to clean	98%
Performance of product	97%
Safety and health features	96%
Ease of use: ergonomic operation	95%
Low operating costs	90%
Total cost of ownership	86%
Value for price paid	85%
Warranties	85%
Service and support	79%
Availability of supplies and accessories	74%
Vendor reputation	68%
Past experience with product	41%
Currently using vendor’s product	21%



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CONNECTING INSTRUMENTS TO THE DATA BACKBONE

by Angelo DePalma, Ph.D.

Laboratory information management systems (LIMSs) are software packages that connect instruments, other software and sample management to human operators and other data systems, including electronic laboratory notebooks (ELNs).

Despite their independent developments for different tasks, distinctions between ELNs and LIMSs are not obvious, notes John McCarthy, VP for product marketing and strategy at Accelrys (San Diego, CA). ELNs occupy a supervisory position—a larger lab data management platform—that accesses the activities of LIMSs.

LIMSs tend to be application- or workflow-specific, which results in different products for chemistry, biology, quality assurance, and related protocols. Notebooks handle a wider range of data, and present them in forms that enable collaboration.

Bruce Pharr, VP for products and marketing at GenoLogics (Victoria, BC), explains the crucial difference. Laboratories are built around two key assets: workers and instruments. “The ELN is for the scientist; the LIMS is for the instrument,” he explains. The control panel for instrumentation serves as the LIMS user interface,

whereas the ELN can be viewed as the control panel for the entire laboratory. The LIMS works around a structured data set, tracking samples from the time they enter a lab through the numerical results. ELNs, as replacements for paper notebooks, handle unstructured data as well, such as photographs, spectra and written notes.

“If you’re in a lab notebook, you don’t want to have to switch to a LIMS to obtain a sample ID.”

“In terms of that hierarchy, a lab might use a LIMS for a pK study, to manage samples and crunch data, but would use an electronic notebook to share these analyses across a number of experiments, among groups that might have different LIMSs,” Mr. McCarthy explains. “Notebooks handle data originating from different labs.” They allow, for example, a medicinal chemistry lab to access analytical or biology functions that have their own LIMS. “Electronic notebooks cut across these workplace silos.”

Coalescing around standards

Nevertheless, the two products are

coalescing or converging for some operations such as sample preparation and identification. “If you’re in a lab notebook, you don’t want to have to switch to a LIMS to obtain a sample ID,” Mr. McCarthy says.

Data standards have become a huge focus area for LIMS developers. Standards are needed so that data reposi-

ries can communicate, for example, so a LIMS designed for one task can read data from a different LIMS.

Accelrys is working with three large pharmaceutical companies on standard LIMS interfaces based on BatchML (batch markup language) and B2MML (business-to-manufacturing markup language), extensions of XML (extensible markup language). XML is a way to encode documents for machine readability. These capabilities will allow new LIMS deployments to read data directly from legacy LIMSs, without the need to rekey data or transfer it to a word processing document.

In the past, LIMS purchase decisions

were made at the laboratory level. Increasingly, companies select these products on an organization-wide basis. “There’s a pricing benefit, no doubt, but standardization—not having to rekey data—is the driver,” Mr. McCarthy tells *Lab Manager Magazine*. LIMS interoperability may also be achieved through the ELN’s supervisory role, as mentioned, by applying an appropriate markup language.

Who uses them?

LIMSs were originally developed for analytical labs, which is where most are still used. According to *Labs on LIMS 2009: A Worldwide Survey of LIMS Users*, a study by Strategic Decisions International, the LIMS market is valued at \$400 million per year. Main purchasers include materials analysis and testing (43% of users), the environmental industry (26%), life sciences (17%), “general focus” (10%), and clinical research and diagnostics (3%). Among these, chemicals, oil and gas and food/bever-

age are significant purchasers. Three-fourths of usage occurs in regulated industries.

LIMSs fit well with workflows that involve automation and require high reproducibility. GenoLogics’ spe-

“A lab might use a LIMS... to manage samples and crunch data, but would use an [ELN] to share these analyses.”

cialty, for example, is LIMSs for next-generation genomics sequencing. This market is driven by the adoption of next-generation sequencers, which numbered 200 in 2007. Today more than 1,900 such instruments have been deployed around the world.

GenoLogics has been receiving requests from labs requesting products that work out of the box and do not need to be specially configured. “These users don’t want custom im-

plementations,” says Mr. Pharr.

Toward this end, the company has been working since 2007 with Illumina (San Diego, CA), which designs and markets gene sequencing equipment, on LIMSs for next-generation genomics. These LIMSs are preconfigured around sample preparation and sequencing, which are vital operations for Illumina’s instrument platform.

Despite this trend, a LIMS may not make sense for many “low event” labs, many of which are comfortable inputting data manually. “Their state of the art might be Excel spreadsheets, open-source software, or home-brewed applications,” Mr. Pharr explains.

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SURVEY SAYS:

ARE YOU IN THE MARKET FOR A LIMS?

A Laboratory Information Management System (LIMS) serves as the interface to a laboratory's data, instruments, analyses and reports. For many analytical laboratories, a LIMS is an important investment that assists management in evaluating the efficiency of the laboratory's operations and reducing costs. LIMS products vary from processor workflow-oriented software for small laboratories to systems for enterprise-class distribution, where large implementations can cost millions of dollars and encompass licensing, training, validation and all the other services required. As with other software products, there are many ways to implement and purchase a LIMS, from boxed software to commercial licenses for COTS (Commercial Off-the-Shelf) to open source to SaaS (Software as a Service). Possibilities vary greatly regarding the choices appropriate and available for the specific type of laboratory where the LIMS will be implemented. It is important to note that a LIMS and an ELN (Electronic Laboratory Notebook) are not the same thing. An ELN is a literal replacement for your paper laboratory notebook. As such, it is a place to enter and keep your laboratory notes and get signoff; you use it just as you would use a paper notebook.

The confusion between LIMS and ELN occurs partly because there is some overlap between them. Additional confusion arises now that some LIMS include ELN features, some ELNs contain LIMS features, and some products combine LIMS and ELN. Beyond the LIMS/ELN question, there are yet other products that sound like they might be a LIMS but have different names.

A LIMS is used primarily in industrial labs that process and analyze samples where reliably tracking samples throughout the scientific process is difficult yet absolutely necessary. Transcription errors, wrong versions of files or other mistakes are all too common and can lead to delayed product rollouts—or may even result in a product never making it to market. Hence, for labs having hundreds, thousands or even tens of thousands of samples stored in a variety of containers in numerous locations, LIMS is found to be the best method for sample management.

Sample management	48%
User reporting	15%
Workflow automation	9%
Instrument connection	8%
QA/QC	7%
Regulatory management	5%
All of the above	2%
Other	4%

Until about a decade ago, most LIMS were offered as software packages that resided within the individual user's computers. "Thick client" and "thin client" products followed where software packages resided on the organization client-server.

One of the most significant developments in LIMS has been the emergence of Web-based LIMS developed on the "software as a service" model. These systems resemble common office and e-mail applications offered online. Web-based LIMS are targeted toward small to mid-sized companies for which LIMS are essential, but which cannot afford the high costs associated with a full-blown deployment.

LIMS installed on customer computers and Web-based products have their strengths and weaknesses. The former are faster, provide connectivity to instruments and printers, may be more secure, and work when Internet connections don't. Their major drawbacks are high upfront and upgrade costs, ongoing maintenance expenses and limited connectivity to the outside world.

Web-based LIMS are subscription-based products that limit capital investment while providing a nearly complete LIMS experience within a familiar browser environment. IT requirements are minimal and data may be shared with any computer connected to the Internet. The limitations are dependence on an Internet connection and lack of instrument connectivity. Close to 80 percent of the labs surveyed have an internal information technology (IT) department that supports laboratory systems.

Types of LIMS installation selected by respondents.

Client/server	46%
Web-based	29%
Standalone	17%
Thin client/server	7%
Other	1%

More than 60 percent of the labs surveyed have 1 to 10 instruments integrated with the LIMS.

1 to 10	64%
11 to 25	16%
26 to 50	12%
51 to 100	2%
100+	6%

Number of users having access to the LIMS.

1 to 10	27%
11 to 25	23%
26 to 50	16%
50+	35%

Nearly half of the labs surveyed have a LIMS in their labs and another 17 percent are planning a purchase and implementation of LIMS. Fifty-five percent of the labs reported that this will be a first-time LIMS purchase.

Yes	48%
No, but planning to purchase	17%
No, and no plans to purchase	35%

Respondents' primary reasons for purchasing a LIMS for the lab:

Upgrading existing LIMS	25%
Sample management	21%
QA/QC	11%
Setting up a new lab	9%
Regulatory management	7%
User reporting	7%
Workflow automation	7%
Addition to existing systems; increase capacity	4%
Web-based access	4%
Other	4%

Selecting and buying a LIMS takes effort and time in advance of the actual purchase for several reasons. First you have to make clear what it is that you need; LIMS products often include features that do not fall into this simple model, but that seem to be natural extensions of the work being done.

A LIMS is usually not implemented for just one laboratory, but spread within and across different departments. So you have to find out about the workflow within and between departments. This user requirement specification has to be written down in a clear and structured way so that potential vendors can read and understand it. The vendors can then demonstrate how their system best fits your needs.

The biggest challenge for respondents in installing a new LIMS is staff adoption and training, since all respondents agree (100%) that service and support from the vendor is the most important factor in making their decision, followed closely by price, ease of use and versatility.

Another challenge identified by respondents was system selection—the types of LIMS available are somewhat overwhelming. There are environmental LIMS, general-purpose LIMS, Web-only LIMS, PC-only LIMS, R&D-focused LIMS, QC-focused LIMS and forensic LIMS, to name just a few. Products have been developed for specific industries, company sizes and specific technical solutions as well.

What all this means is more choices for labs to consider. But even though more choices may make the selection process lengthier, the best solution for your laboratory is out there and readily available.

Most important factors in the decision-making process

Service and support	100%
Price	99%
Ease of use	99%
Versatility	99%
Privacy/security	96%
Uptime	95%
Customization	95%
Ease of installation	94%
Scalability	93%
Upgrade pricing	91%
Web-based access	91%
Multi-platform	86%
Remote access	83%

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THE GRAVITY OF IT ALL

by Angelo DePalma, Ph.D.

Centrifuges separate particles and structures suspended in liquid by applying thousands of gravitational force equivalents to the sample through spinning. Laboratories use centrifuges to clarify suspensions, separate liquids, isolate suspended particles, perform density measurements and for many other applications.

Many users, and some manufacturers, specify centrifuges and centrifugation in terms of rotor revolutions per minute (rpm), but as Dr. Lars Borrermann, group marketing manager at Eppendorf (Hauppauge, NY), notes, rpm is a vague term that says nothing about separation power.

"Customers still ask about rpm, but that only tells you what the motor can do and nothing about the force being applied."

The operative term these days is RCF, relative centrifugal force, which is a function of rotor radius and the square of the rotational speed. Two centrifuges with the same RCF provide comparable resolving power. Transferring methods between centrifuges is difficult without knowing the instruments' RCF values.

Ergonomics and usability

Dr. Borrermann places centrifuges into two basic categories: inexpensive in-

struments that provide basic speed and capacity, and units designed to ergonomic and "eco-friendly" specifications.

Labs tend to be noisy places, with numerous devices contributing to the din. A loud centrifuge can tip the noise balance into the intolerable range. "You don't want a screaming loud instrument right next to where you're working," Dr. Borrermann tells *Lab Manager Magazine*.

"Centrifuges should be fun to work with."

Accessibility is another often-overlooked ergonomic issue. Larger benchtop units may require operators to stand on a step stool to access samples. Coupled with poorly designed lids whose operation requires extreme force, these units are recipes for injury. Dr. Borrermann therefore advises potential purchasers to consider units with a low profile and easy-open-and-close lids.

The final ergonomic consideration is ease of operation. Eppendorf, for example, engages the services of a German institute that specializes in human-machine interaction to provide "a highly satisfactory experience with our centrifuges, beyond speed and capacity," according to Dr. Borrermann. "Centrifuges should be fun to work with."

Materials lead the way

For Maurizio Merli, senior product manager for benchtop centrifuges at Thermo Fisher Scientific (Milford, MA), improved materials of construction have been the most significant trend in centrifugation. New materials and designs provide levels of biological and workplace safety that did not exist 15 years ago.

"Centrifuges generate a lot of energy," Mr. Merli notes. When a centrifuge spinning at tens of thousands of rpm crashes, the device becomes a kind of centrifugal fragment bomb that can destroy a lab and cripple or kill anyone nearby. Most units today employ high-quality covers and paneling to keep flying metal inside.

Manufacturers have paid special attention to rotor design to minimize the effects of a crash, particularly for high-speed units. Aluminum alloys and lightweight metal amalgams provide mechanical integrity and high performance. Composite rotor materials, which Thermo has pioneered, do an even better job by providing the highest strength-to-weight ratings ever.

in real time (DART) directly ionizes samples, with no preparation, at atmospheric pressure and under gentle conditions. DART is suitable for the direct analysis of pharmaceuticals, chemicals, and even samples of dried blood, with no sample prep.

Diab Elmashni, senior marketing manager for LC and LC/MS at Thermo Fisher Scientific (San Jose, CA), also notes

that the "big trend" in MS these days is more routine analysis.

Instruments have become easier to use in response. A great deal of usability resulted in instrument design, innovations in ionization and detection, and the general miniaturization of instrumentation components. Specialists accustomed to room-size spectrometers of twenty years ago would marvel at how MS is now employed as a detector for liquid and gas chromatography. A related capability

is the rapid expansion of MS targets from smallish organic molecules to macromolecules.

The greatest strides in usability, says Mr. Elmashni, have been in software design. Software opens up a mass spectrometer's full range of features

"DART ionizes samples, with no preparation, at atmospheric pressure and under gentle conditions."

to expert users while simplifying protocols for routine users through various levels of permissions. These allow the lab director or high-end operator to tweak the instrument as needed, or to write methods, while simplifying the interface for technicians through a nonalterable interface.

Similarly, software templates have simplified the process of running samples and analyzing data by taking over routine tasks such as data entry and report generation. "A lot of cus-

tomers want simply to walk up to an instrument, introduce the samples, and come back in fifteen minutes to read the report," Mr. Elmashni tells *Lab Manager Magazine*.

Angelo DePalma holds a Ph.D. in organic chemistry and has worked in the pharmaceutical industry. You can reach him at angelo@adepalma.com.

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UNDER-RECOGNIZED “UTILITY” ESSENTIAL FOR LABORATORY OPERATIONS

by Angelo DePalma, Ph.D.

Like the late comedian Rodney Dangerfield, laboratory water purification systems get no respect. Lab workers use them every day, but few realize—beyond opening the spigot—how they operate.

“The level of knowledge in the average lab about lab water is not very high,” says Julie Akana, Ph.D., product manager for water purification products at Thermo Fisher Scientific (Ashville, NC).

Pure water is classified, in order of decreasing purity, as Type 1, Type 2, and Type 3. Culture media, clinical laboratory analyzers, and buffer preparation get by nicely with Type 2 water, which also serves as feedstock for Type 1 purification systems. Labs use Type 3 “pure” water for labware washing and rinsing and for heating and cooling devices in which mineral deposits from circulating water are a problem.

More than one method

Common techniques for water purification include distillation, filtration, deionization, electrodeionization, re-

verse osmosis, adsorption, and ultraviolet oxidation. Distillation is the oldest method and the broadest in terms of impurity removal, but even the best stills produce “only” Type 2 water, and reverse osmosis systems, Type 3. Stills (including double- and triple-stills) are still quite common because of their simplicity and the fact that they require no consumables.

Nick Papp, president of Aqua Solutions (Jasper, GA), describes distillation as “dead but refusing to get buried.” Negatives of distillation include high energy costs and maintenance and rapid degradation of the product.

Most single purification methods excel at one type of removal, e.g., ions, organics, or particles, and individually produce water intermediate between Type 1 and high-end Type 2. Ultrapure water systems combine several of these techniques.

For example, in a high-end ultrapure water system, tap water feeds through

a reverse osmosis membrane, then into deionization cartridges, an ultraviolet cell to destroy bacteria and oxidize organics, an activated carbon cartridge to remove organic by-products of the UV step, and finally an ultrafiltration membrane to remove pyrogens and nucleases. Customers can usually mix and match techniques according to their needs.

Most of Thermo Fisher’s water system customers use Type 1 or Type 2 water and tend to think in terms of their application rather than the official water designation that supports it. Dr. Akana admits that when she worked in the lab

“we just looked for the magical 18.2 megohms on the display, and once we got it, we used it for everything.” Later she would go on to write Thermo’s definitive primer on water purification.

Because of budget cuts, institutions are moving away from centralized, shared-resource water purification systems. The paradox is that such systems are probably the most cost-effective, albeit capital-intensive. As a

result, business is booming for smaller units suitable for a single lab or group.

Nothing lasts forever

“Trends in pure water systems are driven by the capability of analytical instrumentation to detect lower and lower levels of contaminants,” observes Nick Papp. “We’ve essentially gone from part-per-million detection to part-per-billion, so more people are demanding purer water.”

Users, he says, should pay special attention to what they’re using the water for and what species might interfere with their analyses. For example, ion analysis requires water that is as ion-free as possible; if your lab tests for pyrogens in drug samples, water purification should focus on removing those contaminants.

Estelle Riche, Ph.D., an applications scientist at EMD Millipore (Billerica, MA) warns about “emerging contaminants” in tap water, and their potential impact on ultra-pure water used in laboratories. Emerging contaminants

include common prescription and over-the-counter pharmaceuticals, caffeine, herbicides, pesticides, flame retardants, and components of personal-care products.

These compounds have been flushed down drains, both intact and in human waste, for decades. Given the sensitivity of modern analytical instrumentation, Dr. Riche wonders, “Are these contaminants making their way from the tap into the high purity water used in the laboratory?”

Many such contaminants, such as endocrine-disrupting chemicals (EDCs), are highly biologically active. Dr. Riche argues that if these are present in low-quality purified water, say type 2 or type 3, they could easily disrupt delicate bioassays involving live cells or enzymes, or DNA microarrays.

For the truly concerned, it is conceivable for EDCs and other unknown or emerging contaminants to leach from water systems themselves, particularly plastic components and holding vessels.

The take-home lesson here is to monitor water, even ultrapure water, for as many contaminants as is practical, and not take conductivity readings as the final arbiter of purity.

Given modern technology, reaching the “magic 18 megohm” reading has become relatively easy. The more ion exchange resin used, the more cycles, the purer the feed water becomes. But maintaining that level of purity is problematic. As soon as ultrapure water is dispensed, it begins to interact with its environment, picking up gases from the atmosphere and impurities from its container.

“Ultrapure water is the world’s best solvent,” says Nick Papp. “It begins degrading as soon as you stop circulating and purifying it, and as soon as you generate it, it tries to dissolve its surroundings.”

Angelo DePalma holds a Ph.D. in organic chemistry and has worked in the pharmaceutical industry. You can reach him at angelo@adepalma.com.

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DIAMONDS

NOTHING SAYS WE CARE MORE by Vince McLeod



We all know how diamonds are formed. You take a lump of carbon and subject it to intense pressure and high temperatures, and magically those carbon atoms are pressed into a diamond. The diamonds we are discussing in this article are formed much more easily.

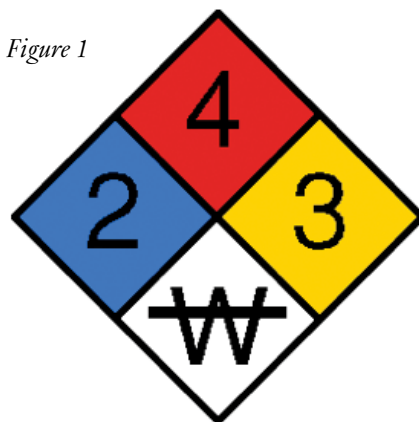
This month's safety column is another in our series on safe laboratory chemical management. Loyal readers of our safety column might recall previous articles dealing with laboratory waste handling, chemical storage tips, safe flammable materials storage and, most recently, material safety data sheets (MSDSs). That last article was an in-depth review of all the information contained in a typical MSDS and a tutorial on understanding material safety data sheets. This article will discuss the National Fire Protection Association (NFPA) hazard diamond, sometimes referred to as the fire diamond, and how to decipher the information it contains.

Classes and the NFPA Hazard Diamond

Experienced laboratory managers know that there are four basic categories of chemicals: toxic, corrosive, flammable and reactive. However, in our chemical world there are many additional categories and subsets of these main four. We should also keep in mind that many chemicals exhibit a combination of properties and would fall into more than a single class or category. These four properties are the foundation of the NFPA hazard diamond. Coincidentally, these four categories are the main criteria used to define wastes as hazardous

under the federal Resource Conservation and Recovery Act (RCRA). The hazard diamond has gained wide acceptance, and most manufacturers include it on their labels when appropriate. Figure 1 shows the layout of the different sections; our discussion will start at the top and work clockwise around the diamond.

Figure 1



"... many chemicals exhibit a combination of properties and would fall into more than a single class or category."

ethyl ether, acetylene and cyclohexane.

Flammability may be the single most hazardous characteristic, causing more injuries and damage than any of the other properties in the diamond. If there is anything other than a zero in this part of the diamond, make sure to use this material with adequate ventilation, clean up spills immediately, and above all, keep heat and flame well away from the area of use.

Flammability

The top of the diamond indicates the flammability hazard. The chemical is rated from zero to 4. A zero means the material will not burn under most common circumstances. Examples include hydrogen peroxide and sodium hydroxide. A rating of 1 indicates the material will ignite and burn at temperatures greater than 200°F. Materials that fall into this category are glycerin and propylene glycol. A 2 indicates substances that will burn at temperatures less than 200°F, such as naphthalene, octyl alcohol and nitrobenzene. A rating of 3 denotes materials with flashpoints below 100°F, such as xylene, amyl acetate and butyl alcohol. Finally, a 4 indicates extremely flammable substances. These include acetone,

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Reactivity

Moving clockwise, as promised, the next part of the hazard diamond designates the potential reactivity of the material, which is also rated from zero to 4. Zero indicates a stable chemical under nearly all conditions, even fire. Substances that are normally stable but can become unstable when heated, or may react with water, but not violently, are rated a 1. Chemicals that are rated a 2 are normally unstable and readily undergo violent decomposition. They may also react violently with water. Materials with a rating of 3 are capable of an explosive reaction or detonation if subjected to a strong initiating source such as heat or shock. A 4 indicates substances that are readily capable of explosive decomposition or detonation at normal temperatures.

For illustration of the reactivity, consider the following examples. Liquid nitrogen would receive a zero rating. It is stable, nonflammable and nonreactive with water. Phosphorus (red or white) is rated a 1, since it can become unstable at elevated temperatures. Calcium metal rates a 2. Less reactive than sodium, it reacts violently with water, alcohols and other materials and burns in air. Fluorine gas is an example of a reactive material rating of 3. It is the most reactive nonmetal; it decomposes in water, producing hydrofluoric acid and other hazardous compounds, and reacts vigorously with most oxidizable substances at room temperature, usually with ignition. An example of a class 4 reactive substance is trinitrotoluene or TNT. We are all familiar with its explosive properties.





Special hazards

At the bottom of the diamond is the white section. This section is used to denote special hazards. NFPA 704, *Standard System for the Identification of the Hazards of Materials for Emergency Response*,¹ mentions only two approved symbols:

OX This denotes an oxidizer, a chemical that can greatly increase the rate of combustion or fire.

W This means the substance is incompatible with water. It indicates a potential hazard with the use of water to fight a fire involving this material.

Some organizations and manufacturers use additional symbols to indicate hazards associated with the substance. One example is the *Hazardous Materials Emergency Response Guidebook*,² a few of these are presented above.

ACID	This indicates that the material is an acid, a corrosive material that has a pH lower than 7.0.
ALK	This denotes an alkaline material, also called a base. These caustic materials have a pH greater than 7.0.
COR	This denotes a material that is corrosive (it could be either an acid or a base).
	This is another symbol used for corrosive.
	The skull and crossbones are used to denote a poison or highly toxic material. See also: CHIP danger symbols.
	The international symbol for radioactivity is used to denote radioactive hazards; radioactive materials are extremely hazardous when inhaled.
	This indicates an explosive material. This symbol is somewhat redundant because explosives are easily recognized by their Instability Rating.

Health

The final section of the diamond is the blue section on the left-hand side. This area denotes the health hazard of the compound, and is also rated from zero to 4. A zero indicates no toxicity and no additional hazard beyond that of normal combustible materials under condition of fire. A 1 means the material is slightly toxic and usually considered innocuous when used responsibly. It may cause some irritation, but only minor, even without treatment. Moderately toxic materials are rated a 2 and may cause temporary incapacitation or injury with continued exposure unless medical treatment is given. A rating of 3 indicates a serious toxic material that can cause injury upon short exposures, even if medical attention is given. Deadly or extremely toxic materials rate a 4. Very short exposures could result in death or serious injury, even with medical treatment.

I know you would be disappointed if we did not provide examples of the different health hazards as we did for the flammable and reactive chemicals above, so here goes. Peanut oil is an example of a material that would rate a zero on the health scale. Turpentine would rate a 1, being irritating to skin and mucous membranes. Ammonia gas would rate a 2, since it is definitely irritating

and corrosive but generally regarded as nonflammable unless mixed just right in air. Also, ammonia has an exposure limit of 50 ppm and is immediately dangerous to life and health (IDLH) at 300 ppm. Extremely corrosive chlorine gas ranks a 3 for health hazard. It can form explosive mixtures and cause fatal pulmonary edema. The OSHA permissible exposure limit (PEL) is 1 ppm and the IDLH limit is only 10 ppm. An example of a health hazard 4 substance is arsine gas. A colorless gas with a mild garlic odor, it is extremely poisonous. For comparison, the OSHA PEL is a diminutive 0.05 ppm, and arsine is IDLH at only 3 ppm.

Now you understand diamonds, those that provide colorful gems of knowledge. Be on the lookout for them and pay attention to what they are telling you. *Hill Street Blues* fans will remember that Sergeant Esterhaus said it best: "Let's be careful out there."

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

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Additional Resources

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

The Merck Index, an encyclopedia of chemicals, drugs and biologicals. 14th edition. Merck & Company, Inc. Rahway, N.J. 2006

OSHA Hazard Communication Standard. http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10099

SAFETY TIP

USE WARNING SIGNS TO DESIGNATE PARTICULAR HAZARDS

By James A. Kaufman

The use of warning signs to designate particular hazards is not just a good idea. It's the law. The OSHA Laboratory Standard 29CFR1910.1450 requires that those areas in which particularly hazardous substances (select carcinogens, reproductive toxins, and highly toxic substances) are used be clearly designated. The OSHA Hazard Communication Standard requires the labeling of hazardous chemicals in the workplace.

Hazard labeling should not be limited to chemical hazards. Mechanical, Biological, Physical, Noise, Radiation, Hi/Low Pressure, Electrical, and Stress hazards should all be clearly indicated with appropriate signs.

Good signs should go beyond hazards and extend to the facilities and equipment we use to deal with these hazards: emergency equipment and emergency facilities. OSHA regulations require the emergency equipment be identified with prominent signs.

Take a careful look at your labels and see if they can't be improved. Can you make it easier to recognize the hazard and the means of dealing with it? Are cabinets for corrosive storage clearly labeled? Are the circuit breakers in all your electric panels clearly labeled? Do preserved specimens have the identity of the preservative and appropriate hazard warnings on the labels?

The August 1991 issue of "Safety and Health News" from the National Safety Council had a good article on labeling. It contained the names and addresses of the many companies selling labeling products.

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

USE IT OR LOSE IT

PROPER DISPOSAL OR REUSE OF OLD LABORATORY CHEMICALS by John K. Borchardt, Ph.D.



Laboratories frequently accumulate bottles of old chemicals, often toxic or hazardous, that are no longer used. Laboratory managers can use several strategies to properly reuse or dispose of these chemicals. These strategies are not mutually exclusive. Laboratory managers can apply more than one to meet the requirements of maintaining laboratory safety and environmental protection. These strategies are discussed in the individual sections below.

Proper disposal can be expensive. So it is essential to minimize the need for proper disposal, by minimizing chemical purchases. Even if yours is a small laboratory, centralizing chemical purchasing is an effective way to do this. Having a single person assigned to purchase all chemicals for the entire laboratory will help ensure that duplicate orders are not made by different members of the laboratory staff. More people may be assigned to do this in larger laboratories, and departments may be set up to manage chemical purchasing, storage and waste disposal.

Maintaining a computer-searchable chemical database

The first step in proper recycling or disposal of chemicals is to know what you have. The best way to do this is by maintaining an inventory of all the chemicals in use or stored in your laboratory. Supply room personnel should record the receipt of all purchased chemicals. Among the data that should be recorded are the supplier, the amount of chemical purchased, its purity, its amount, the person ordering the chemical and the laboratory room number to which it was delivered.

“The first step in proper recycling or disposal of chemicals is to know what you have.”

New chemicals should be added to the database as they are purchased and old ones deleted as they are consumed. This last requirement means that laboratory personnel and not just stockroom personnel should be able to access the database to update information. Laboratory personnel should record when samples are completely consumed or transferred from one laboratory to another.

This inventory can be used to tell laboratory managers and staff members when samples become so old that disposal is necessary. This database can also be a money-saver by enabling lab personnel to learn from whom they can obtain a needed chemical without purchasing a new sample. Should it be necessary to purchase a fresh sample of a particular chemical, the purchaser can review the chemical inventory to identify a supplier and the chemical purity of previously purchased samples of the same chemical.

Several firms offer commercially available chemical inventory database software. Using an Internet search engine and keyword phrases such as “chemical inventory management software” can identify software suppliers and retrieve a description of their products.

These computer programs vary in sophistication and features. Software search features can include one or more of the following search options: searching by chemical name, chemical supplier, the storage location, and the laboratory department and/or individual who purchased the chemical. The chemical name can be the proper IUPAC (International Union of Pure and Applied Chemistry) systematic name designation or one or more common names of the chemical. Other search options include the CAS (Chemical Abstracts Service)

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LAB SAFETY

number of the chemical and the date of purchase. Some programs provide storage of MSDS information.

More sophisticated software can print barcode labels for chemicals that can be affixed to the chemical sample container and used to track movement of chemicals within the laboratory and their consumption. Should supply of a chemical be recorded as falling below a specified level, some software can automatically issue an alert informing the user of that particular chemical and that it needs to be reordered. Some chemicals may arrive with an expiration data beyond which the chemical should not be used. Some software offer features that include issuing an alert when a particular chemical sample usage date is due to expire.

Some software suppliers such as Chemoventory offer limited capability versions of their software for free (www.chemoventory.com) to educational and other nonprofit institutions. Other software provides more features but must be paid for. One example is Nexxis Chemical Inventory Manager (www.labtronics.com/chemical_inventory_management.htm).

Holding periodic lab cleanup days

Having periodic cleanup days during which old chemical samples and unused/nonfunctional equipment is collected and disposed of can be a useful way of putting labs in clean, tidy and safe operating condition. These cleanup days are most effective in achieving these goals if lab managers insist that all routine work stop for the day to focus on cleanup.

Sometimes only an individual laboratory rather than the entire facility needs to have a laboratory cleanup day. This situation can arise if a laboratory is being relocated from one location to another either within the facility or from one facility to another. Alternatively, the termination of a project or its relocation from one laboratory to another may be facilitated by a lab cleanup day.

If an individual laboratory rather than the entire facility is cleaning up and disposing of old chemicals, have the appropriate lab staff members advertise their lack of availability to coworkers before this process begins. Interruptions can greatly reduce the efficiency of the cleanup process and increase the time required for it.

Once old chemical samples are identified and selected for disposal, proper procedures must be followed. Lab managers can have samples packed properly by lab personnel for pickup and disposal by a qualified chemical disposal firm. Some disposal firms will perform all the work themselves. This approach may be more appropriate for large laboratories.

While any chemical to be discarded is chemical waste, hazardous chemical waste is defined by the Environmental Protection Agency (EPA) or a relevant state authority as waste that presents a danger to human health and/or the environment. The EPA defines four key properties that determine whether a chemical is hazardous waste: ignitability, corrosivity, reactivity and toxicity.

Potentially hazardous chemicals must be disposed of in accordance with federal and state regulations and procedures. EPA regulations are summarized at www.epa.gov/epaoswer/osw/conserve/clusters/schools/index.htm.



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While state requirements vary somewhat by locality, the basics remain the same. However, it is best to consult with your relevant state agency or the EPA to determine whether particular chemicals are defined as hazardous and what the requirements are for storage and disposal. These requirements should be defined on the chemical's MSDS. However, if the chemical was purchased some time ago, the available MSDS sheet may be out of date and you should consult the current version of the MSDS.

Many labs use one or more large containers labeled "chemical waste" for solvents and other chemical wastes. Extreme care must be used in combining chemicals in

such containers, as some chemicals may be incompatible. For example, addition of a strong oxidizing agent may result in oxidizing another chemical in the container and leading to heat evolution and an explosion or fire.

Because of the dangers of such chemical incompatibilities and the hazards of chemical spills occurring in a busy work area, chemical waste containers should be stored away from normal work areas and away from sinks and floor drains. Every addition of a chemical waste to a storage container should be noted in a permanent record such as an online file or a laboratory notebook.

Do not completely fill waste containers, particularly waste storage bottles. While the amount of empty headspace at the top of the container can vary with the size of the container, it is usually best to allow about 20 percent vacant headspace at the top of the container for possible vapor formation or liquid expansion due to heat evolution.

To remove chemical wastes from your laboratory site, contact professional, licensed hazardous waste haulers and transporters. Trained personnel from these firms will package waste chemicals properly for transport and disposal.

Training lab personnel

Training lab personnel in proper disposal and storage procedures is essential. This is a particular issue in academic laboratories because the students using a laboratory can change from semester to semester. Larger laboratories often have a Health, Safety & Environment Department whose personnel are qualified to conduct such training. If your laboratory does not, there are consultants who offer training programs in proper chemical storage and disposal.

When supervising students working in laboratories, professors and teaching assistants should review the safety concerns and required safety procedures associated with each laboratory exercise or experiment.

Solvents and glassware cleaning

Solvents produced as waste in laboratory equipment such as rotary evaporators and distillation apparatus are often as clean as what initially comes from a fresh solvent bottle. Do not dispose of these solvents; reuse them instead for routine laboratory operations such as glassware cleaning. Often one can filter and reuse solvents for at least initial cleaning of glassware. Laboratory personnel should limit the use of solvents and other chemicals in routine operations such as cleaning laboratory glassware.

Chromium-containing cleaning agents can be highly

effective but should be used only as a last resort. Evaluate the use of enzyme-based or detergent-based cleaners before resorting to chromium-based cleaners. Chromium-based cleaners are highly toxic, as the Julia Roberts film *Erin Brockovich* makes clear in a fairly accurate recital of a major California pollution case in which chromium-containing toxic wastes leached into a town's water supply and apparently led to birth defects in children and severe illnesses in adults.

Volatile solvents such as isopropyl alcohol routinely used for sterilizing equipment should be replaced by quaternary amine-based detergents. Replace highly toxic solvents such as benzene or carbon tetrachloride with less toxic ones whenever possible. For example, cyclohexane is often used as a substitute for carbon tetrachloride.

Mechanical cleaning methods should be used instead of solvents whenever possible. These may be as simple as using cleaning brushes in good condition or ultrasonicators instead of solvents. Large laboratories often use industrial dishwashers instead of solvents for cleaning glassware.

Keeping an adequate supply of clean glassware on

hand will reduce the tendency to rinse glassware with volatile solvents such as acetone to quickly dry glassware for reuse. So will the use of a glassware drying oven.

Neutralize aqueous acids and bases. Pour only non-toxic, pH 4 to 9 aqueous fluids down drains. Neutralize and clean up spills so that all or most of the waste can be disposed of properly.

Distill used solvents to purify them. For example, scale-up laboratories and pilot plants can accumulate large volumes of used solvents. If distillation removes all reactive compounds and impurities, distillation can both purify solvents for reuse and reduce volumes released to the environment. After all, production plants frequently distill solvents for these reasons as well as economic ones.

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

CHEMICAL DISPOSAL AND LAB STAFF REDUCTIONS

By John K. Borchardt

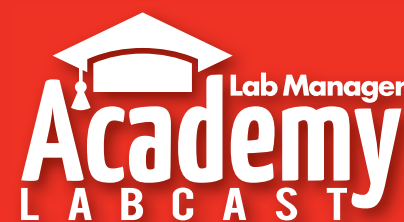
Staff reductions can result in severe challenges to proper chemical waste disposal management. In some recent cases, entire large facilities have been closed. Some areas of research have been abandoned completely and work in others has been severely curtailed. Often personnel are required to leave the laboratory immediately after receiving notice that they have lost their jobs. Even when they have a week or more to leave the laboratory for good, chemical waste disposal may be the last of their concerns in a rush to write reports, turn over projects, work with patent attorneys to write patent applications, etc.

Laboratory personnel often depart leaving their former coworkers with responsibility for properly disposing of chemicals, returning unused chemicals or partially used bottles of chemical reagents to the stockroom, and transferring ownership of chemicals recorded in the laboratory chemical inventory. Doing this is a challenge in the absence of former employees. In addition to the mass of information that must be managed and the physical transfer of chemicals, this work is uninteresting and must often be done by laboratory staff members demoralized by the departure of their former coworkers.

Some solid commercial reagents may be surplus to the laboratory's new requirements. The company's other laboratories may also have ample supplies of these chemicals. In these cases, the options are disposal or donation to a university or college. Donation is often a cost-effective alternative to disposal and appreciated by local universities and colleges. (Many of these institutions are currently under funding constraints due to state budget cuts.)

Another concern is compounds and chemical intermediates synthesized in the laboratory. Often unlikely to be commercially available, these are more likely to be retained on the chance they will be useful later.

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DEVELOPING NEW REVENUE STREAMS

THE LAB MANAGER'S ROLE IN FINDING UNTAPPED PRODUCT AND PROCESS OPPORTUNITIES IN THEIR LABS by John K. Borchardt, Ph.D.

Developing profitable new products and processes is the major mission of corporate laboratories. Professors justify their research grants aimed at developing new knowledge by describing how the research can eventually result in new products and processes to create new business, improve health, or protect the environment. Government labs justify their research in the same way.

The key to creating new revenue streams for your organization is becoming aware of new science and business developments and figuring out how to take advantage of them. Other than reading research journals in their field and encouraging their staff members to do the same, how can laboratory managers participate in the development of new revenue streams for their employers?

"The key to creating new revenue streams... is becoming aware of new science and business developments."

Read, read, read

Read business magazines, newspapers and trade magazines. Firms constructing new plants could be a source of new business. While I was heading Shell's Pulp & Paper Chemicals Group, my keeping up with general news enabled Shell to begin competing early for business at companies building or expanding their paper recycling mills. Reports of new technology developments could give you ideas for new product lines.

And read those research journals. New developments could be the basis of new businesses. For example, John Fenn received the Nobel Prize for his research developing the electrospray ionization technique for mass spectrometry. This capability is now built into many commercial mass spectrometers, enabling them to identify and analyze complex biological polymers. The instrument

companies whose scientists read Fenn's papers could have gotten a jump on commercializing this technology.

Read the patent literature, or subscribe to a service that scans patents worldwide using key words supplied by the lab manager and his/her staff members. This information can enable researchers to work around patent claims to develop competitive technology or recommend licensing of the patented technology.

Talk to sales and marketing personnel

Your firm's sales representatives are usually at the front line of communication with customers. Thus, they can bring in information on what problems customers are facing and what new technology they have under development. Lab managers and their staff members in various business areas should read sales people's customer call reports for these business areas. All this information can result in new products and additional business.

Play an active role in the sales process

You and your staff members can play a more active role in the sales process by sometimes accompanying sales representatives on sales calls to customers. Hold periodic discussions with customers to see what problems they face in their businesses. It could be that lab managers have the staff members and other resources to discover solutions to these problems and generate additional business for their employer. By the same token, lab managers should hold similar discussions with their employer's suppliers. They may be developing new raw materials that the employer could convert into profitable new products. Confidentiality agreements are sometimes needed for these discussions to be meaningful.

In these situations, the lab staff member often presents a talk based on new results that would interest the customer. Customer input can help guide the development process and give customers an emotional stake in the project outcome. They may be more willing to evaluate a new product if they feel they had a role in its development.

Lab personnel may also participate in plant evaluations of new products in the customer's plant. If things go well, your lab personnel may make valuable contributions that help plant personnel do their jobs. They could even be regarded as members of the customer's plant team. This customer familiarity helps build sales and customer loyalty.

Sometimes this positive attitude goes to the point of sharing product performance data from the customer's operation and allowing you to write a paper on the results. You may be asked to keep their company's name confidential in the paper. Alternatively, if they give permission to use the customer's corporate name, you can make their employee (or employees) coauthors of the paper. The paper can be presented at a trade association conference or published in a trade magazine. Such papers can be an effective sales tool in trying to sell the product to other customers, more effective than an advertisement.

Attend conferences

Attend conferences and see what's new in fields that are of interest to your employer. Lab managers can do some of this themselves, but should also send their scientists to meetings to scout for new developments that could result in additional business for their employer. Your people can take prospective customers out for meals and

Shell Chemical Company, the sales people had director chairs made in the company colors (red and yellow) and with the company emblem and the lab people's names on them. These matched the sales representative's chairs and contributed to the impression that the lab and sales people were on the same team. Customers felt that concerns they discussed with a sales representative would be taken to the lab personnel if appropriate. Most also really ap-

"Reports of new technology developments could give you ideas for new product lines."

business discussions during conferences. A sense of camaraderie can build as they attend presentations with customer personnel and discuss the papers with them.

If your employer is operating a trade show booth at your conference, lab personnel can participate in staffing the booth and talking with customers. When I worked for

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preciated the opportunity to discuss their problems and concerns with lab personnel.

Some of my lab managers would sit down with their staff members and with sales and marketing personnel and discuss what conferences lab personnel should attend in the coming year. They would also discuss what papers lab staff members might present at these conferences. This planning enables papers to be written more carefully than is the case when personnel decide to submit a paper with little advance notice and then rush to finish a manuscript to meet a deadline.

Talk to customers and suppliers

You can rent a small meeting room in the conference hotel and hold private meetings with customers, complete with oral presentations and slides. By reserving two or three hours for this meeting, often just before or after the formal conference, you can have detailed discussions and often agree on joint efforts going forward.

I used this approach when I headed the Pulp & Paper Chemicals Group at Shell. We often rented a small meeting room in a conference hotel and held these discussions during paper industry conferences. Shell business managers and sales representatives were also involved in these discussions. High-level business people sometimes flew into town just for these meetings.

Visit research universities

Encourage staff members to give talks at research universities, and pay their expenses. University departments strapped for funds to bring in outside speakers are often eager to take companies up on offers to provide speakers. Lab managers and their staff members can meet with faculty members doing work of potential interest to their employer. They can also meet with graduate students and postdoctoral researchers working in these areas of potential interest. Should the employer decide to develop some of this science into commercial applications, lab managers can get a fast start on the project by hiring one of these graduate students or post-docs.

Becoming a sponsor of university research can promote a closer relationship with professors eminent in technology fields important to your company and to your laboratory. Often a professor's research is sponsored by

a consortium of companies rather than a single firm. A visit to the campus for consortium meetings can provide valuable face time with customers' representatives who are also members of the consortium. Often these individuals are influential members of customers' R&D teams.

When Shell Chemical was a member of a consortium sponsoring paper recycling research in the chemical engineering department at the University of Maine, I was fortunate that my employer was the only chemical company member of the consortium. Most of the members were customers or potential customers for our paper industry chemicals. I didn't overtly sell, but I provided chemicals needed by the university team to perform their experiments and discussed chemical performance requirements with the professor and with other consortium members. Our participation and these discussions helped bolster our credibility with customers and potential customers.

Sometimes you can combine these discussions and visits with recruiting trips to the campus.

"Some of your best prospects for new business are your firm's current customers."

Increase sales to current customers

Some of your best prospects for new business are your firm's current customers. There are three main strategies to this. The first is

providing excellent customer service for the products you already sell to current customers.

When you improve current products, work with sales personnel to "up-sell" the new product. This requires the development of data that clearly indicates the superiority of the new version over the current product in terms of both performance and cost effectiveness. Remember, if you replace an old product with a new one, you have to increase both your firm's sales revenues and profit margins.

Cross-selling means selling additional products to customers already purchasing one or more of your products. Because you already provide high-performance products and excellent customer service, your firm's customers will be more open to purchasing additional products from your firm. Your firm's established credibility makes this process easier and shorter.

Develop your oral and written communication skills

Many of these strategies require lab personnel to have good oral communication skills. Therefore, it is a good strategy to have lab staff members take courses

to improve their oral presentation skills. Joining Toastmasters International can also help them do this. Some of my lab managers had staff members rehearse their conference and customer presentations by delivering them to coworkers.

Your staff members also need to create concise, well-written lab reports for your firm's sales and marketing personnel and for customers. This requires good writing skills. You can improve these skills by coaching staff members and having them take short courses.

Write reports that sales and customer personnel can understand. Remember that many of your firm's customers probably aren't chemists. Your staff members' reports should be concise and focused on the customers' interests so they will understand and appreciate the reports when they read them. Your staff members aren't writing a paper for a research journal, so excessive use of jargon and theorizing about the science behind the results probably won't be appreciated by your firm's sales and marketing personnel.

Lab personnel can also write or participate in the writing of product technical bulletins. Lab managers can work with sales representatives and marketing personnel to decide what bulletins should be written in the coming year. They should also carefully review this

"Pharmaceutical companies have cited the failure to develop... new revenue streams as the rationale for R&D cutbacks."

literature for technical correctness before it gets printed or posted on your firm's website. They can advise on the proper tone to strive for in these documents. This approach facilitates the introduction of new technical literature shortly before a major conference and its distribution at the meeting, increasing traffic at your firm's tradeshow exhibit booth.

Wrap-up

Doing a good job of increasing revenue through new product and process development and enhancing profit margins provides justification for a laboratory's contin-

ued existence and for continuing employment of the laboratory staff. Recently, big pharmaceutical companies have cited the failure to develop new products and develop new revenue streams as the rationale for R&D cutbacks and even the closure of large research centers. Preventing this sort of situation from occurring at your company is a major responsibility for lab managers at all levels of the organization.

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


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- Vulcan can be combined with a dedicated fume extraction system to provide an integrated sample preparation workstation



Analysco

www.analysco.co.uk

ATR Probe for FTIR Spectroscopy

DPR-230

- Features broad mid-IR spectral response
- Comes with an interchangeable sample compartment mounting plate to mate to any specified FTIR spectrometer
- Probe can pivot around spectrometer's sample beam axis so it can be dipped into any sample container for rapid screening or detailed analysis

Axiom Analytical

www.goaxiom.com

Double Beam UV/Vis Spectrophotometer

Libra S80PC

- Features a wavelength range of 190 to 1100 nm with accuracy of ± 0.3 nm across wavelength range (at 1 nm bandwidth)
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CRAIC Technologies

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Oxygen Flask Combustion Unit

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- Prepares samples for elemental analysis of halogens, sulfur, phosphorus and numerous metals using the Schöniger flask method
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Miniature Visible Spectrometer

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- Features a flat field optical design and reflective holographic concave grating to disperse light
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PAC

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Epsilon 3

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- Performs non-destructive quantitative analysis of elements from sodium to uranium, in concentrations from 100% down to ppm levels
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Shimadzu Scientific Instruments

www.ssi.shimadzu.com

MAXIMIZING UV LIGHT FOR LAB WATER SYSTEMS

ABSTRACT:

Conventional lab water systems use UV light by flowing water in a chamber around the bulb in a protective quartz sleeve as part of the recirculation loop. Using innovative technologies, the UV light benefits are maximized but sterilizing the water in the loop and the dispensing port as well.

INTRODUCTION:

For many years, the water industry has known the many benefits of ultraviolet (UV) light for germicidal reduction. The specific wavelength of 254 nm destroys the nucleic acids of the bacteria's DNA rendering it sterilized and prevents the colony from growing. In most lab water systems today, UV systems are installed as a single pass within the recirculating loop. Water flows around a UV bulb in a quartz sleeve sterilizing the purified water. To dispense the water, an automated or manual valve is opened and flow will enter a 0.2 micron capsule filter upon exit. As the system sits idle, a potential for bacteria growth exist on areas outside of the recirculating loop: post valve tubing and submicron filter. Most manufacturers recommend flushing water through the filter before use to purge the small standing water. To bring awareness of this potential issue, ASTM 5196 Biomedical grade specification, Section 4.5 addresses the dispensing port:

The distribution outlets or faucets must be of non-contaminating design and materials. Particular care must be given to the valve seat and joint construction. The outlet must be protected

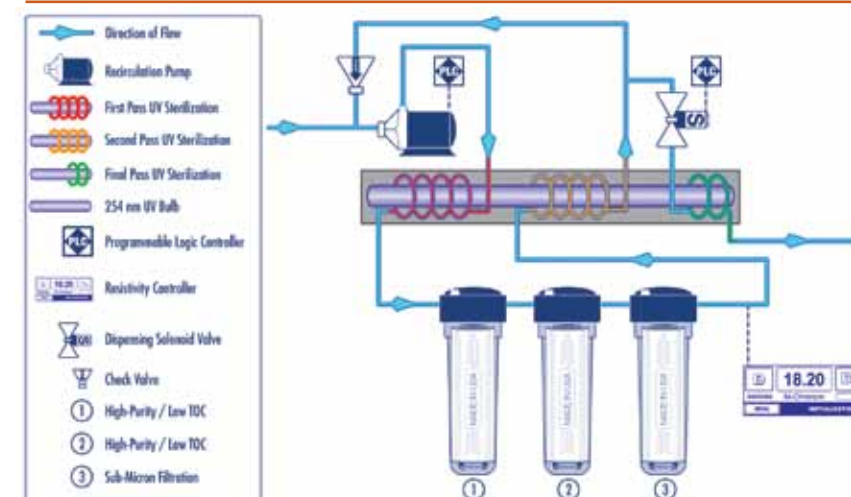
from biological contamination particularly when the use is only occasional. Ultraviolet (UV), chemical, or heat sterilization should be considered.

An innovative approach for UV sterilization has been developed to irradiate the water at multiple passes within the recirculating loop. By taking a UV bulb in an atmospheric, shielded box, Teflon coiled tubing wraps around the UV bulb with a turbulent flow and maximizing surface area irradiation. Water is UV irradiated before deionization, after DI and submicron filtration, and the outlet dispensing port thus meeting the ASTM 5196 specification for Biomedical Grade Water. The Aries Filterworks Gemini system with multi-pass UV was tested with a bacteria challenge.

EXPERIENTIAL CONDITIONS:

A pure strain of Pseudomonas aeruginosa was inoculated into a flask and incubated for 24 hours. Following incubation, enumeration was performed using diluted spread plate technique. The culture was determined to contain 2.0 x 10⁹ cultivable bacteria per ml using Pseudomonas Isolation Agar (PIA).

FLOW DIAGRAM



Following introduction of the challenge organisms, the Gemini was allowed to recirculate for one minute. After recirculation, three samples were dispensed from the Gemini outlet and collected in 1 liter autoclaved bottles. This procedure was repeated for samples collected at 30 minute and 1, 2, 3, 4, 24 and 48 hour post spike injections. No other water was dispensed from the Gemini unit during the test period. Following incubation for 24 hours and five days, bacteria on the plates were enumerated. The Gemini panel resistivity meter reading was noted and the dispensing UV lamp was checked at each sampling.

RESULTS:

During the test period, the Gemini resistivity was equal to or greater than 18.1 megohm-cm @ 250 C. The UV lamp at the dispenser port was operating during each sample event. No viable bacteria were discovered from any of the triplicate 1 liter Gemini outlet samples collected 0 to 48 hours following a P.aeruginosa spike. Samples collected twenty eight days after the spiking of the Gemini feed water with 2x10¹⁰ Pseudomonas aeruginosa bacteria cells and analyzed by the Kinetic Turbidimetric Method, was also completed for pyrogens with less than 0.003 EU/mL.

CONCLUSIONS:

Using the non-conventional methods of UV sterilization in a multi-pass arrangement provides the user with confidence that the dispensing port has not been compromised with bacteria growth. The Gemini ultrapure water system use of UV, deionization, and submicron filtration provides consistent, reliable Type I and Biomedical grade water.

REFERENCES:

ASTM D5196 - 06 Standard Guide for Biomedical Grade Water



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Petrifilm™ Aqua Plates

- Eliminate the need for agar preparation
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Purair 5

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MERLIN

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- Ideal for investigating the mixing, stirring and process flow characteristics of fluid systems
- Includes Peltier Temperature Control for all measuring systems
- Features an angular velocity range from 0.01 to 200 rad/s, a Torque range from 0.005 to 20 mNm and a temperature range from -10°C to 120°C



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Formerly Mallinckrodt Baker

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www.avantormaterials.com

ABSTRACT: Increasing the sensitivity and resolution of LC/MS instruments has been an ongoing focus for instrument manufacturers. As a result of this increased sensitivity of today's analytical instrumentation, the choice of high purity solvents can greatly influence the test results that are achieved.

INTRODUCTION: To meet the needs of the most demanding ultra-high pressure liquid chromatography (UHPLC) and mass spectrometry research and analytical testing applications, such as proteomics, drug discovery, pharmacokinetics, and clinical research, instrumentation is not the only parameter to be considered. Solvent design and selection is also very important. Performance of three specific solvents, (1) **Acetonitrile**, (2) **Methanol**, and (3) **Water** was examined in detail and the solvents were assessed for their suitability in selected LC/MS applications. In particular, the impact of packaging materials on the quality of LC/MS solvents was evaluated. The performance of LC/MS grade solvents was compared using LC/UV/MS gradient, MS infusion, and trace metals analysis. One way to ensure that high purity LC/MS grade solvents meet stringent purity requirements is by improving the packaging associated with the storage and delivery of these solvents. For example, certain containers can leach metal ions during storage, and lead to the formation of metal adducts, which can adversely impact test results.

EXPERIMENTAL CONDITIONS:

Materials:

- LC/MS grade Acetonitrile, Methanol, and Water from various suppliers

- J.T.Baker® ULTRA LC/MS™ solvents
- Standards (Sulfadimethoxine, Chloraphenicol)

Methods:

- LC/MS gradient (Waters ACQUITY UPLC® System/LCT TOF mass spectrometer)
- Positive/Negative ESI (electrospray ionization)
- Direct infusion to mass spectrometer (Waters Quattro Micro)
- Trace metals (Perkin-Elmer ICP-MS)

RESULTS: Results indicate that J.T.Baker® ULTRA LC/MS™ solvents and solvent packaging show better performance than other traditional LC/MS grade solvents. The J.T.Baker® ULTRA LC/MS™ water packaged in the borosilicate bottle maintained sodium levels < 9 ppb in two months while material packaged in amber glass bottles presented sodium levels > 150 ppb. Sodium metal adducts (m/z 333) were also reduced. The J.T.Baker® ULTRA LC/MS™ grade exhibited adducts of 40% compared to 150% for the material packed in amber glass bottles.

CONCLUSIONS:

Based on the data compiled for the study, the test results indicate that J.T.Baker® ULTRA LC/MS™ solvents are more suitable for use on UHPLC and high sensitivity

mass spectrometry instrumentation. J.T.Baker® ULTRA LC/MS™ solvents also offer better performance than the other brands tested by delivering:

- Lower trace metals
- Reduced adduct formation
- Minimal suppression

REFERENCES / TRADEMARKS

ACQUITY UPLC System™ and Quattro Micro™ are trademarks of Waters Technologies Corporation.

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Figure 1: ULTRA LC/MS Water—Sodium level (Borosilicate vs Amber Bottle)

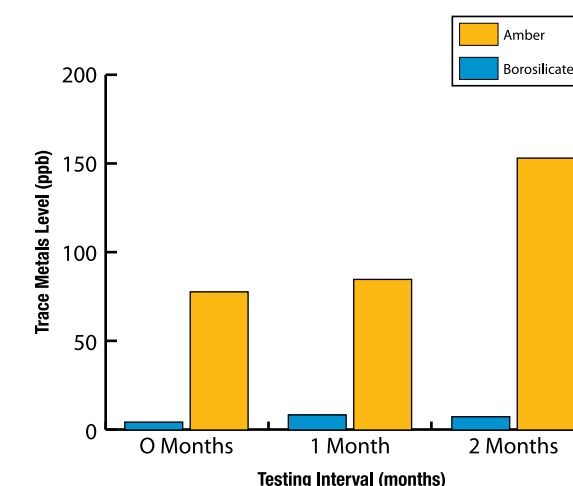


Figure 1a contrasts the sodium leaching for water packaged in amber bottles to borosilicate bottles over a two month time interval.

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- Features adjustable power head speeds from 30 to 60 rpm (250 model), or 60 to 150 rpm (300 model), both in 10 rpm increments
- Z-axis function removes material by depth instead of time

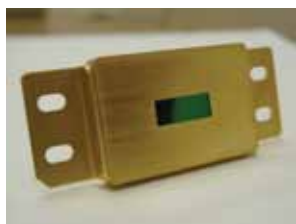
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Gas Cylinder

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- Standard 34-liter aluminum alloy cylinder contains 66 liters of precision calibration gas
- Available in standard disposable and EcoSmart refillable formats
- Employs reinforced cylinders and a proprietary manufacturing process to safely increase the gas pressure
- Holds both pure gases and gas mixtures and is approved for safe transport by the Department of Transportation



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Linear Shaking Water Bath

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- Includes drain taps, two programmable temperature and shaking presets, timer with audible buzzer, and non-drip polycarbonate lids
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- Features precision temperature control with operating range of ambient +5°C to 99°C with $\pm 0.1^\circ\text{C}$ stability and uniformity



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SAMPLE SECURITY THROUGH QUALITY MANUFACTURING

The integrity of samples is paramount in all critical laboratory processes, and important in more routine operations. The range of environmental control apparatus offered by BINDER Inc. includes full lines of ovens, incubators, CO₂ incubators and constant-climate chambers manufactured in Germany and tested using the rigorous DIN 12880 specifications. This attention to quality performance assures that products and methods are consistent and reliable and that samples are conserved and protected.

Unique features that heighten performance characteristics are implemented across the BINDER product line. APT.line™ preheating chamber technology facilitates long-term temperature stability. APT-COM™ Software is available in Basic, Standard and GLP Editions and provides monitoring, control and documentation of all vital process parameters. Construction quality, levels of insulation, reliable door locks and ergonomic displays all add to the level of comfort experienced by both user and sample.

A summary of BINDER products provides both an overview of the breadth of the product line, offering apparatus for almost every application, including: biological research; chemical precipitation; drug metabolism research; drying of non-flammable crystalline chemicals, solid materials, filter paper and glassware; moisture content analysis and moisture elimination; pre-heating glassware and other containers; protein and starch digestion; tissue fixation or drying; quality assurance; stability testing; microbiology; pathology; and many others.

Ovens in natural, forced-air and gravity-convection designs find application in both rapid and routine drying and in sterilization. Units are available in 0.7 to 25 cu/ft capacity and cover a temperature range of 5 C above ambient to 300 C. Controller functions run from simple for constant temperature drying ovens to programmable with viewing windows for testing applications. Like all BINDER apparatus, the ovens incorporate user-friendly and easy-to-operate all-digital PID controller technology.

Incubators are offered in gravity and mechanical convection and refrigerated models, all told covering a temperature range of -5 to 100 C. There are units designed

for long-term and stable, continuous operation that are ideal for the gentle incubation of organisms and for conditioning of heat-sensitive materials. Premium models process large numbers of samples at high throughput while keeping required temperatures virtually stable irrespective of how many times the door is opened. Various models offer capacities from 0.7 to 28.6 cu/ft.

CO₂ incubator features protect rare and expensive samples while providing conditions that promote cell proliferation. A hot-air sterilization cycle initiates a 180 C, 9-1/2-hour cycle that provides a completely sterilized interior for incoming cultures. A condensation-free, seamless, deep-drawn interior and real-time CO₂ measurement with homogenous CO₂ distribution are representative of the cell-friendly environment. Models are offered for hypoxia research.

BINDER environmental chambers are available in capacities from 4.1 to 25.4 cu/ft, with temperature ranges from -10 to 100 C, with and without humidity (humidity range 10 to 90 percent). Select chambers incorporate homogenous light conditions along with temperature and humidity control. Shining in pharmaceutical stability testing and food and beverage monitoring, these units are also valuable for materials testing in electronics, plastics and other fields.

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▲ A BINDER CO₂ incubator with double-door, seam and weld-free interior, perforated shelves and water pan visible.

HIGH-THROUGHPUT SAMPLE FILTRATION

SIMULTANEOUS VACUUM FILTRATION OF UP TO EIGHT SAMPLES

EMD Millipore's new Simplicity™ filtration system was designed to ease the strain researchers typically experience when preparing samples for chromatography.

The device, which can simultaneously filter up to 8 samples—even those with high viscosities or particulates—provides a high-throughput alternative to syringe-tip filtration, which can slow down an entire workflow.

Samples are easily loaded into filter units using a pipette, and are filtered directly into LC vials. The filtered samples are then immediately ready for subsequent analyses. The entire filtration process takes a few seconds.

"As we move from HPLC to UHPLC, runtimes significantly go down," said Vivek Joshi, Senior Scientist, Bioscience Business Unit, at EMD Millipore. "Now you're running your analysis in one minute and your sample prep is taking longer and becoming a bottleneck."

Vivek added that the device addresses the unmet need for medium-throughput users. Syringe-tip filtration is slow and tedious, but the only other option is the use of robotic systems, which can be too elaborate and expensive for labs running a few dozen samples a day.

"Something like this is not necessarily breakthrough technology—it's filtration," said Greg Hoff, Media Relations Manager at EMD Millipore. "But it takes away a major pain point and it saves an enormous amount of time for people."

Simplicity is designed for use with Millex Simplicity™ filter units, which allow processing of samples as small as 200 μl . The unit is available in two colors: bold blue and glossy green.

"What researchers have told us is that everything in the lab is drab and boring—white, beige, grey," added Joshi. "Sample prep to begin with is not something people love to do. We thought we would make it bright and stand out in the lab."

For more information, visit www.millipore.com/breakfree



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- HQd meter permits easy switching and set-up of multiple smart probes
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- HQd system can test ammonia, pH, dissolved oxygen, conductivity, BOD, ORP and sodium
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96-channel Electronic Pipette

VIAFLO 96

- Features proprietary Touch Wheel™ interface for easily programming various pipetting modes including repeat dispense, serial dilute and sample dilute
- Four pipetting heads with pipetting volumes up to 12.5 µl, 125 µl, 300 µl or 1250 µl are available
- Compatible with VIAFLO GripTips, which provide a perfect seal and won't fall off during use



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Coulometric Titrator for Trace Water in Battery Materials

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- Reduces the use of expensive KF reagents
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- Features an ultra-trace moisture measurement mode with an accuracy of $\leq 10 \mu\text{gH}_2\text{O}$



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- Both models can be controlled as either stand-alone systems or via PC



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- Q2 model automatically dispenses the compound to a target weight
- QL2 model adds solvent in the exact amount to achieve target concentration



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- Contains no moving parts and no flow obstructions
- Can be used in areas where flow sensors with moving parts cannot be applied due to contamination in the media
- Ideal for water, chemical and cooling industries



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ULTRAPURE WATER FOR PCR

ABSTRACT

PCR techniques are in widespread use for the amplification of genetic material. The need for reagents and solutions free from nucleases (DNase, RNase) is widely recognized, however, it is vital to also ensure the absence of other waterborne contaminants which could cause problems with test results.

INTRODUCTION

PCR-based methods, such as reverse transcription PCR (RT-PCR) and quantitative PCR (qPCR), are essential in medical and biological research. DNA amplification by PCR uses DNA polymerase enzymes to synthesize double-stranded DNA molecules from single-stranded 'templates', using oligonucleotide primer sequences to target the gene of interest. Both the target specificity and efficiency of the enzyme-catalyzed reaction are highly dependent on the composition of the reaction mixture¹. The presence of nucleases — enzymes which cleave the phosphodiester linkages between nucleic acid subunits — will lead to severe disruption of the PCR process, as genetic material will fragment under reaction conditions. It is vital to ensure that all reagents and solutions used in PCR applications are 'nuclease-free'; however, a number of other contaminants commonly found in water can also impede DNA amplification², including:

BACTERIA

Many bacteria release nucleases and other molecules which interfere with DNA polymerization. The presence of bacterial DNA can lead to errors in qPCR, and amplification of non-target sequences.

IONS

The concentration of Mg^{2+} , which is a co-factor for effective substrate binding, is crucial for optimization of polymerase activity³. Other divalent cations interfere with co-factor co-ordination and disrupt substrate binding and trace amounts of heavy metal ions will inhibit enzyme activity.

ORGANIC COMPOUNDS

Negatively charged bio-molecules can reduce substrate turnover by steric interference with substrate binding at the positively charged active sites.

PURIFYING WATER FOR PCR

PCR requires the use of water free from nucleases, micro-organisms, organic compounds and trace elements for all reagents and buffers. Ultrapure grade (Type I) water — with 18.2 MΩ cm resistivity, < 20 ppb total organic carbon (TOC), < 1 CFU/ml bacteria levels and < 0.01 EU/ml endotoxins — is highly recommended⁴.

ELGA's PURELAB Ultra Genetic uses UV photo-oxidation, high capacity purification cartridges, combined with an ultrafilter, to reliably deliver ultrapure water for PCR work. Real time resistivity and TOC monitoring ensure verifiable removal of inorganic and organic contaminants and the system offers validated traceability.

CONCLUSION

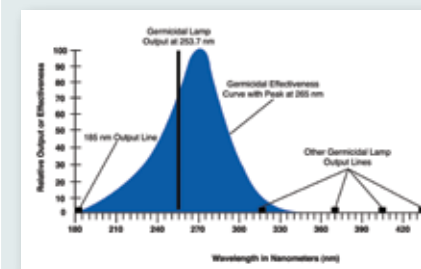
Ultrapure water with a high resistivity (18.2 MΩ cm) and free from nucleases, organic compounds and endotoxins should be used for all PCR applications, to ensure optimized amplification of target sequences. To find out more about ELGA LabWater's water treatment technologies and solutions for life science applications, visit www.elgalabwater.com

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ELGA

5 Earl Court
Woodridge, IL 60517
(877) 315-3542
Email: elga.usa@veoliawater.com
www.elgalabwater.com



▲ Figure 1: Germicidal efficiency of UV radiation

	Product water Endotoxin (EU/ml)
Pre-challenge	< 0.001
During challenge after 1 Liter	< 0.001
During challenge after 2 Liters	< 0.001
During challenge after 3 Liters	< 0.001
During challenge after 3 Liters	< 0.001
During challenge after 5 Liters	< 0.001
Post challenge after 5 Liters	< 0.001
Post challenge after 15 Liters	< 0.001
Post challenge after 25 Liters	< 0.001

▲ Table 1: Efficiency of endotoxin removal

PURELAB Ultra Genetic challenged with 5 Liters of partially purified water spiked with 10,000 EU/ml endotoxins, achieving a residual endotoxin level of < 0.001 EU/ml, even after 25 Liters.

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Supercritical Fluid Extractor SFT-110XW

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Nils Gerke, Eppendorf AG, Hamburg, Germany
Stefan Roth, Eppendorf Instrumente GmbH, Hamburg, Germany
Eppendorf North America

eppendorf

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ABSTRACT:

The new heated lid technology, vapo.protect™, featured by the Eppendorf Mastercycler pro, achieves improved evaporation protection even at the corner and edge positions of the thermoblock. The tighter sealing of the newly developed fluid filled cushion incorporated in the heated lid, leads to an improved evaporation protection. With its demonstrated minimization of technical variance on PCR**, the Mastercycler pro makes a significant contribution to higher comparability and reproducibility.

SYNOPSIS:

A major criterion for efficient and robust PCR is the minimization of evaporation of the sample volume. There are various sealing methods such as tube caps, adhesive tape or foil, or heat-sealing film or foil that are used to combat evaporation. The successful sealing of the reaction vessel is highly dependent on the correct intensity and uniformity of the pressure applied by the lid of the thermocycler. In order to test the effectiveness of the new vapo.protect™ heated lid technology of the Mastercycler pro, the same PCR reaction was performed on the Mastercycler pro as well as five other thermocyclers. All reactions were identical; this includes the same 96-well plate, same sealing method, same reaction, and the same protocol was followed. The results clearly show a marked reduction of evaporation with the Mastercycler pro in comparison to the other five thermocyclers. There was an observed evaporation of 0-3% with the Mastercycler pro in comparison to 30% or greater evaporation seen with the other thermocyclers (Table 1 and Figure 1). The data presented in this report highlights the significance of improved evaporation protection provided by the Mastercycler pro with regards to obtaining optimal and reproducible PCR conditions.

▼ Table 1: Observed evaporation of reaction solution on the Mastercycler pro and 5 thermocyclers of other manufacturers.

THERMOCYCLER	PCR PLATE: MEAN EVAPORATION [%]		
	CORNER (4 WELLS)	EDGE (32 WELLS)	CENTER (60 WELLS)
MASTERCYCLER PRO S	3	2	0
A	45	32	10
B	30	5	1
C	4	3	6
D	49	5	0
E	>50*	30	0

* Thermocycler E: Since the measured signals of 2 corner positions correspond approximately to the background value it can be assumed that there was not enough reaction fluid left for transferring 5 µl to the MTP. This complies with the visual observation. Therefore, a mean evaporation of more than 50 % was estimated for the corner positions on this thermocycler.

Mastercycler pro:



Thermocycler A:



▲ Figure 1: Fill levels of the well positions A1-A12 of the PCR plate after a run on the Mastercycler pro and Thermocycler A.

* Practice of the patented polymerase chain reaction (PCR) process requires a license. The Mastercycler is an Authorized Thermal Cycler and may be used with PCR licenses available from Applied Biosystems. Its use with Authorized Reagents also provides a limited PCR license in accordance with the label rights accompanying such reagents.

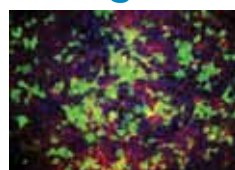
** The Polymerase Chain Reaction (PCR) is covered by U.S. patent numbers 4683105 and 4683202 held by Roche Molecular Systems and requires a license for use.

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HOW TUBES CAN AFFECT YOUR EXPERIMENTS

By Matthew Lieber, Dr. Lars Borrmann, and Daniela Marino

INTRODUCTION

It has been known for several years that chemicals (e.g., BPA and phthalates) can leach out of the plastic, such as toys and baby bottles. The impact of these chemicals on human health is well known. Recent scientific reports have now noted that chemicals used in the manufacturing of disposable plastic labware, such as slip agents or plasticizers, can leach out of the plastic and affect laboratory experiments leading to erroneous results.¹⁻⁴

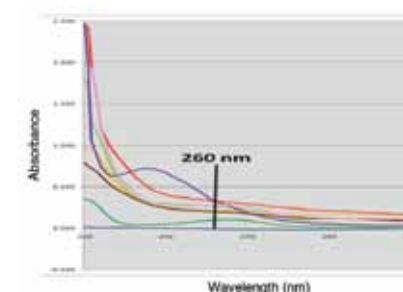
WHAT COMES OUT OF YOUR TUBES

During incubation (e.g., enzymatic assays at 37°C or DNA denaturation at 95°C) chemicals used in the manufacturing process can leach out of the plastic and contaminate your sample.³ Figure 1 shows the absorbance spectra of water after incubation in tubes from several different manufacturers. As you can see, in contrast to other brand tubes, the water incubated in Eppendorf tubes (blue line) shows no significant UV/Vis absorbance. This suggests that no UV/Vis active substances are released from the tube into the water. This is one of the examples of Eppendorf's commitment to minimize sample contamination. Besides highly automated manufacturing under clean-room conditions and purity testing of each production lot, Eppendorf doesn't use any slip agents, plasticizers, or biocides during the tube manufacturing process (certificate upon request).

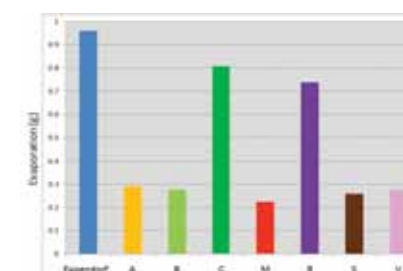
The next question to ask is how does leaching affect my experiment?

HOW THE TYPE OF TUBE CAN AFFECT YOUR ASSAYS

It has been shown in several publications that the chemicals used during manufacturing of plastic consumables can affect assay results from DNA quantitation³ to enzymatic assays.^{1,2}



▲ Figure 1. Chemicals released from different brands of 1.5mL tubes can contaminate your sample. Shown are UV absorbance spectra of pure water incubated (30min, 95°C, 1,400 rpm mixing) in tubes from different manufacturers.



▲ Figure 2. The brand of tube can affect evaporation rates. Chemicals, for example oily slip agents, released from the tube plastic can slow down evaporation. Some of these slip agents (e.g., oleamide) have also been shown to negatively affect the outcome of biological tests like enzyme activity or receptor-binding assays.^{1,2,4} Shown are the evaporation volumes (in grams of water) after 3 h incubation in a vacuum concentrator. Pre-incubation for 1 hr at 70°C.

In a *Science* paper from 2008, researchers showed that chemicals released from plastic tubes inhibited the activity of human monoamine oxidase-B (hMAO-B).¹ Important to note that the researchers used an amber-colored Eppendorf tube in that paper. When they switched to a clear Eppendorf tube, the results showed an absence of significant inhibition of hMAO-B.² Another common lab application is sample concentration. When samples need to be concentrated, it is common to use a vacuum concentrator to accelerate the evaporation of aqueous solutions. Figure 2 shows how incubating water in different brands of tubes can affect the evaporation rate of water. Samples incubated in Eppendorf tubes had the highest evaporation rate, consistent with the data shown in Figure 1. Both of these experiments and the *Science* paper lead you to the same conclusion: If you have a leachate you never know where it will affect you.

CONCLUSION

Not all tubes are created equal. If a chemical leaches out of the tube, it can carry over to all of your downstream applications and you will never know when it might affect your assays. One good summary on the importance of leaching comes from Reid et al. (2009): "There are several steps researchers can take to minimize the likelihood of their data being compromised by leachates. Some manufacturers provide information on the additives content of their plastics; for example, Eppendorf use virgin polypropylene for their colorless pipette tips and microfuge tubes, and no slip agents or other additives are present. Although the associated costs may be slightly higher, researchers should purchase plastic ware from a manufacturer that does not use additives and avoid buying from suppliers that refuse to confirm the absence of additives."²

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2. Reid G. et al., *Git Laboratory Journal* 9:10, 2-4 (2009)
3. Lewis, L. K. et al., *BioTechniques* 48, 297-302 (2010)
4. Watson J. et al., *J Biomol Screen* 14(5), 566-572 (2009T)

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Transforming bacteria to amplify recombinant DNA is often achieved through chemical transformation. Though reliable, this process is time-consuming and the efficiency can be too low. The new Eporator from Eppendorf provides transformation efficiencies ten times higher than is achieved with the heat shock method.

The instrument is designed to be user friendly, with simple one-button operation for faster sample handling—just set the voltage or choose a preset parameter and insert a cuvette.

"[Eporator] is very simple to perform and saves valuable time," said Jaimie McLaughlin, Product Manager, PCR, Detection & Cell Technology at Eppendorf North America. "Typically a manual is not even needed and you can start an experiment immediately."

In addition, the unit features freely programmable function keys and two program buttons that allow storage and recall of most commonly used parameters. Added safety features maximize user protection, such as safe electronics and an integrated electroporation chamber to prevent voltage leaks and potential misuse.

The compact design simplifies storage and transport, and the USB port allows experiment data to be exported for GLP-compliant documentation and analysis.

For more information, visit www.eppendorf.com/eporator



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INTRODUCTION

LECO Corporation continues its history of innovation in high-speed time-of-flight mass spectrometry with the introduction of new High Resolution TOFMS (HRT) instrumentation, available in LC and GC configurations. Based on LECO's exclusive Folded Flight Path™ (FFP™) technology, the HRT systems provide mass accuracy, acquisition speed, dynamic range, and resolution, all in one instrument and at the same time.

HIGH RESOLUTION LCMS AND GCMS

Recognized with the 2011 Pittcon Editors' Gold Award, the Citius™ LC-HRT offers several API sources and acquisition of 50-2500 m/z, 200 spectra/second, at 100,000 resolving power (FWHM) and < 1 ppm mass accuracy. Its novel ion optics provide the capability to generate and analyze fragment ions in a comprehensive fashion. Ions are effectively fragmented, similar to traditional in-source CID (isCID), with the same mass accuracy and resolution as available to parent ions in a distinct data channel. The GC-based Pegasus® GC-HRT provides acquisition capabilities of 200 spectra/second over the mass range of 10-1500 m/z, with 50,000 resolving power and < 1 ppm mass accuracy.

In both HRT systems, signal acquisition is achieved using patented KADAS™ technology to provide information-rich, high-integrity output under demanding acquisition conditions. The combination of KADAS and FFP provide the capability for high-accuracy relative isotope abundance measurements for greater confidence in analyte identification. These advances in technology are paired with LECO's

exclusive ChromaTOF-HRT™ software, which utilizes True Signal Deconvolution® for accurate peak definition.

VERSATILE MS OPTIONS

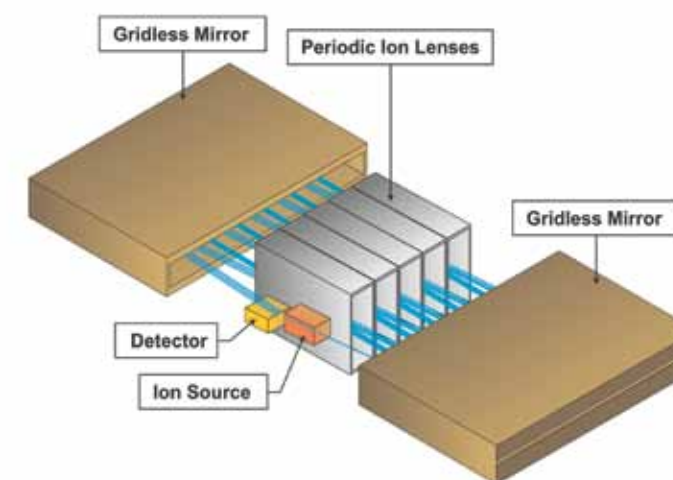
In addition to HRT instrumentation, LECO's existing portfolio of mass spectrometry products includes the TruTOF® HT GC-TOFMS, a high-throughput, benchtop GCMS that combines a fast acquisition mass spectrometer (80 Hz) with ChromaTOF® software, to provide revolutionary Time-Compressed Chromatography, Automated Peak Find, and True Signal Deconvolution®. No other benchtop system can match the speed and accuracy of TruTOF, with the reliability customers expect from LECO.

For a higher performance system which can be upgraded to GCxGC, the Pegasus HT GC-TOFMS is available. This system combines LECO's Time-of-Flight Mass Spectrometer with ChromaTOF® software to provide revolutionary Time-Compressed Chromatography, Complex Sample Resolution, Automated Peak Find, and True Signal Deconvolution in a high-throughput GCMS.

For a more rigorous approach to GC separations, and to achieve higher information content, LECO offers the Pegasus 4D with comprehensive two-dimensional gas chromatography (GCxGC). The 4D offers two dimensions of chromatographic separation, the information content of TOFMS, and the power of award-winning ChromaTOF software and True Signal Deconvolution, all in a seamless, easy-to-use package. When MS detection is not needed, GCxGC FID and/or ECD systems are available, with resolving power unmatched by traditional GC.

CONCLUSION

The LECO portfolio provides high-performance tools to answer the most demanding separation science challenges. Building on the success of LECO's existing products, new HRT instrumentation makes it possible for laboratories to combine speed, resolving power, mass accuracy, isotopic abundance, and dynamic range in a single instrument.



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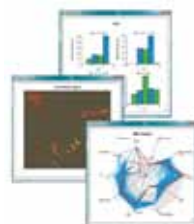
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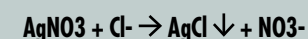
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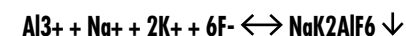
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ANALYSIS OF SODIUM IN FOODSTUFFS BY THERMOMETRIC TITRATION

Consumers and regulatory agencies are expressing more and more interest in the true amount of sodium contained in food products. Sodium has traditionally been indirectly tested using a silver nitrate precipitation reaction:



The amount of sodium would be calculated by assuming a 1:1 molar ratio of chloride ions to sodium ions in the food. This assumption is not necessarily the case when common sodium containing food ingredients such as sodium benzoate, mono-sodium glutamate or chloride containing ingredients such as potassium chloride are present in the food matrix as well as sodium ions that may be present in the food itself. Common methods of testing the true amount of sodium directly have typically been atomic absorption spectroscopy or inductively coupled plasma spectroscopy. Although specific to sodium for analysis, these techniques typically involve significant capital investments in equipment and infrastructure, costly ultra-pure reagents and lengthy sample preparation and system calibration. Metrohm USA is excited to announce a method of direct thermometric titration of sodium in food stuffs that is specific, rapid, robust and economical. Thermometric titration is a form of titration using the heat of enthalpy of entropy produced by a chemical reaction to determine the endpoint. This method of titration is free from the electrochemical and solvent effects that are present in many types of titration making them difficult to adapt to some food matrices. To determine the amount of sodium the food is first masticated or homogenized to make a homogeneous mixture. The prepared mixtures is then titrated with a standardized solution of aluminum containing a stoichiometric excess of potassium ions in the presence of ammonium hydrogen difluoride at ~pH3 to give an exothermic reaction, forming insoluble NaK₂AlF₆.



The titrant is standardized against a solution prepared from anhydrous sodium sulfate.

Equipment Required:

Metrohm 859 Titrotherm Sodium Analysis Kit with PC

Reagents Required (included with kit):

Titant: Mixed 0.5mol/L Al(NO₃)₃, 1.1mol/L KNO₃ solution.

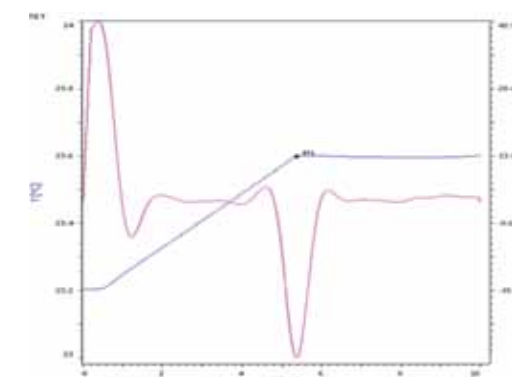
Complexation reagent: 300g/L NH₄F.HF

Waste neutralization solution: Boric acid solution

Representative Experimental Results:

Sample I.D.	ICP Average Sodium %	Titrotherm Average Sodium %	RSD
Ketchup	1.3	1.3	0.008
Yellow Mustard	0.9	1.2	0.005
Green Beans	0.2	0.3	0.011
Jamaican Jerk Seasoned Potato Chips	0.4	0.6	0.113
Mini Pretzels	1.1	1.0	0.078

Analysis of Sample



Titration Curve for seasoning sample

Sample I.D.	Sample Size, g		Sodium %
827102-107	~ 1g	Mean % Sodium	30.51 %
		Std. Dev.	0.19
		% RSD	0.63 %

Typical time to endpoint: 65 – 90 s

Conclusion

- These data show that the thermometric analysis of sodium is a robust, precise and accurate test method.
- Enables a QC lab to analyze sodium quickly and accurately.
- Current sample preparation techniques for chloride titrations may be kept for ease of integration into existing methodology.
- Robustness of maintenance free probe allows for simplified sample prep if desired.
- Simple to use software that is readily integrated into existing LIMS and other software systems.
- Very rapid analysis.
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- Enables numeric, free text, calculated value, data and time, colour, etc. to be used to record test sample data
- Allows final reports to be produced to look like original forms



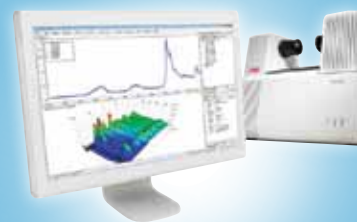
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FLASH DSC 1 – A QUANTUM LEAP IN DSC TECHNOLOGY

JUERGEN E. K. SCHAWÉ*, MICHAEL R. ZEMO**

The commercialization of the DSC (Differential Scanning Calorimetry) technique in the 1960s led to a rapid expansion of this method for the thermal characterization of materials. The great strength of DSC is that complex information can be quickly and easily obtained about physical transitions, the structure of materials as well as the kinetics and composition of chemical reactions.

Conventional DSC instruments allow measurements to be performed at heating rates of up to 500 K/min and cooling rates of 200 K/min with a signal time constant of about 1 to 2 seconds. This is not adequate for the investigation of the structure and morphology of polymers and polymorphic substances or of meta-stable materials in general. Semi-crystalline polymers are meta-stable; their structure, thermal and mechanical properties depend on their thermal history. Different cooling rates can lead to changes in the meta-stable structure when they are cooled from the melt. This specific reorganization often cannot be measured in the DSC because the result curve consists of exothermic and endothermic events that take place simultaneously. A new technology is needed to further investigate these systems and simulate high speed production processes such as injection molding that use cooling rates of up to several hundred Kelvin per second.

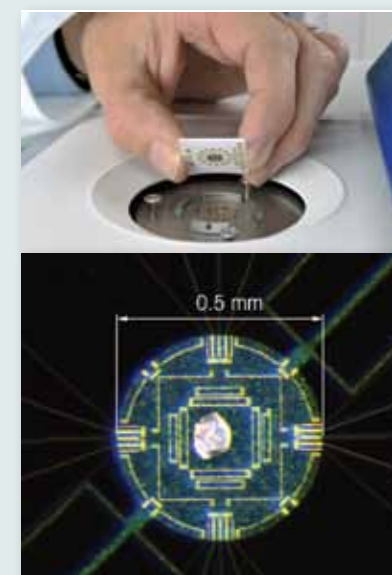
The Flash DSC 1 (Fig. 1) is a completely new type of commercial DSC with a signal time constant of less than 1 millisecond. This allows very high heating and cooling rates to be achieved in the range is 1 K/s to 40,000 K/s (60 K/min to 2,400,000 K/min). The heating rate overlap with conventional DSC is complimentary and offers over six decades of heating rate for experimentation. The

UFS 1 MultiSTAR sensor is based on MEMS technology (MEMS: Micro-Electro-Mechanical Systems) and is made up of two separate calorimeters on a removable sensor chip (Fig. 2). It consists of two identical quadratic silicon nitride membranes with a length of 1.6 mm and a thickness of 2 µm. The sample area with a diameter of 0.5 mm is in the middle of the membrane and is coated with aluminium so that a homogeneous temperature profile is obtained. The temperature of this area is measured by means of eight thermocouples and resistive heaters are used to heat very quickly. Samples can be prepared and cycled many times to understand the effect of high heating and cooling rates, stored for archiving purposes and re-investigated again at a later date. Typical polymer samples for the Flash DSC 1 have a thickness of 10 to 50 µm and small disks are first cut from the bulk material. Organic materials typically have a mass between 10 ng and 10 µg and the mounted stereo microscope aids sample preparation and placement.

The Flash DSC 1 opens the door to the wider experimental parameters required to investigate the meta-stable and time-dependent transitions of materials. Very fast cooling and heating rates allow researchers to generate material under real process conditions (cooling) and then measure those material properties (heating) to gain a never before seen perspective into their materials.



▲ Figure 1



▲ Figure 2

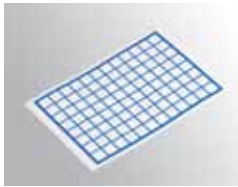
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MULTI-PARAMETER ANALYZER FOR PH, BRIX AND ACIDITY, TORE FOSSUM, METTLER-TOLEDO, INC.

ABSTRACT
This application note describes an automated method for the measurement of pH, Brix and acidity, incorporating a METTLER TOLEDO T90 Titrator, DM45 Density Meter, Rondo60 autosampler and LabX® titration software (Figure 1).

INTRODUCTION:

In quality control of juices, pH, acidity and sugar content affect both taste and shelf life. Discrete separate analyzers for each of these parameters have been used for years. Presented here is an analyzer which will measure these three parameters on a series of samples and deliver the results to a LIMS system.

EXPERIMENT:

The sample is pulled from a test tube on a multi-sampler by a peristaltic pump through separate flow-through density and pH measuring cells. After measuring these two parameters, it is transferred to a fixed volume loop where the contents of the loop are pumped into a titration beaker. The acidity is determined by potentiometric titration with sodium hydroxide. The workflow is as follows:

1. The analyst selects a method by one click on the shortcut. The sample list opens.
2. The sample ID is entered or bar-coded in. Sample is poured into a 30 mL test tube and placed in the first position on the Rondo sample changer. Up to 120 samples can be entered this way. The titrator can be started at any point after the first sample is entered.
3. The Rondo sample changer brings a sample to the tower position. The sampling tube goes into the test tube, whereby a pump transfers sample from the test tube into the density meter or refractometer cell, then into the flow through pH chamber.
4. The titrator signals LabX to start the density or refractive index measurement.
5. When the reading is stable, the result is posted to LabX and sent to the titrator. The titrator then records the pH in the flow through chamber.

6. The sample is pumped through the 10 mL sample loop. The TV6 valve is switched to transfer the sample into titration vessel and to allow solvent to be added.
7. The water pump pushes the sample in the loop to the titration vessel and follows with about 40 mL water.
8. The acidity in the sample is titrated with sodium hydroxide to an end point of 8.2 pH.
9. The result of the pH measurement and the acidity are sent to LabX.
10. LabX prints a report and sends the results to a LIMS system.
11. The Rondo advances to the next sample and the workflow repeats.

RESULTS:

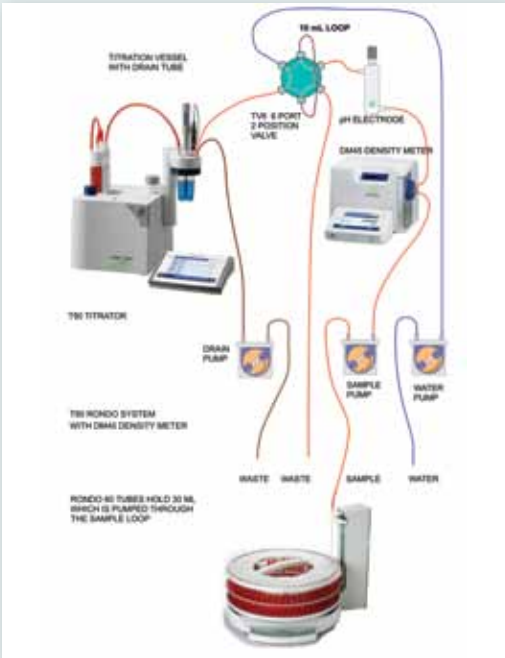
Table 1 to the right lists the results of some samples that were taken for analysis.

CONCLUSIONS:

This procedure provides a reliable method for the automated analysis of these parameters and requires minimal user interaction. The system can also be modified to incorporate color measurement, an additional parameter often measured in the quality control of flavors and fragrances.

METTLER TOLEDO

Mettler-Toledo Inc.,
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▲ Figure 1

Sample	pH	TA (%)	Density (g/cm3)	Brix
Lemonade	2.74	0.544	1.0412	10.75
	2.76	0.543	1.0413	10.77
	2.74	0.543	1.0412	10.75
	2.74	0.543	1.0413	10.77
St. Dev.	0.01	0.001	0.0001	0.01
Apple Juice	3.18	0.256	1.0226	6.28
	3.15	0.255	1.0226	6.27
	3.16	0.256	1.0225	6.25
	3.18	0.255	1.0226	6.27
St. Dev.	0.02	0.001	0.0000	0.01
Grape Juice	2.94	0.281	1.0442	10.99
	2.95	0.279	1.0423	11.01
	2.94	0.280	1.0422	10.99
	2.93	0.281	1.0423	11.01
St. Dev.	0.01	0.001	0.0001	0.01

▲ Table 1

NUAIRE INCUBATOR STERILITY TEST

Incubator contamination is a potential for all incubators. Laboratories have thousands of airborne contaminants that may enter a culture incubator during a door opening and enter the growth environment.

High Efficiency Particulate Air (HEPA) filters remove airborne contaminants. NuAire incorporates a HEPA large capacity capsule filter into the Autoflow CO₂ Water-jacketed Incubators to remove contaminants that enter the chamber during door openings. The HEPA filter is incorporated into the recirculation system (See Figure 1). The chamber air is drawn into the inlet tube, to the pump, through a 0.3 micron HEPA inline capsule filter, through a 0.3 micron Hydrophobic HEPA filter to the IR Sensor and returned to the chamber. The recirculation provides filtration to remove airborne contaminants reducing contamination.



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Website: www.nuaire.com

To test the incubator's ability to filter the airborne contaminants, a biological test was developed.

MATERIALS & METHODS

A NuAire CO₂ Water-Jacketed Incubator with set-point parameters of 5% CO₂, 96% humidity and 37 C was tested. The incubator was set and stabilized for 24 hours. The incubator shelf placement was standard with four shelves equally spaced in the chamber. On the middle shelf, covered soy agar plates were placed on the center plane from the side access port (See Figure 2).

A nebulizer was used to deliver *B. subtilis* var. *Niger* spores prepared to a concentration of 1.0 x 10⁴. The nebulizer was mounted next to the side access port to distribute the spores.

A wire hook was also present at the side access port to remove the agar plate covers.

PROCEDURE

- Remove (2) control agar plate covers.
- Place nebulizer over side access port. Connect air source and run nebulizer for one minute.
- Remove nebulizer and agar plate covers per the following:

Plate 1 - 5 minutes
Plate 2 - 10 minutes
Plate 3 - 15 minutes
Plate 4 - 20 minutes
Plate 5 - 25 minutes
Plate 6 - 30 minutes

- Allow agar plates to incubate for 24 hours. Remove agar plates and record.

RESULTS

Three test results indicated below. Each plate was analyzed for colony forming units (CFU) of the *B. subtilis* var. *Niger* spore.

Test #1: Plate 1 - 122 CFU
Plate 2 - 69 CFU
Plate 3 - 27 CFU
Plate 4 - 19 CFU
Plate 5 - 16 CFU
Plate 6 - 4 CFU
Control Plates - TNTC

Test #2: Plate 1 - 67 CFU
Plate 2 - 35 CFU
Plate 3 - 20 CFU
Plate 4 - 7 CFU
Plate 5 - 3 CFU
Plate 6 - 1 CFU
Control Plates - TNTC

Test #3: Plate 1 - 200 CFU
Plate 2 - 150 CFU
Plate 3 - 75 CFU
Plate 4 - 16 CFU
Plate 5 - 7 CFU
Plate 6 - 1 CFU
Control Plates - TNTC
TNTC - Too numerous to count

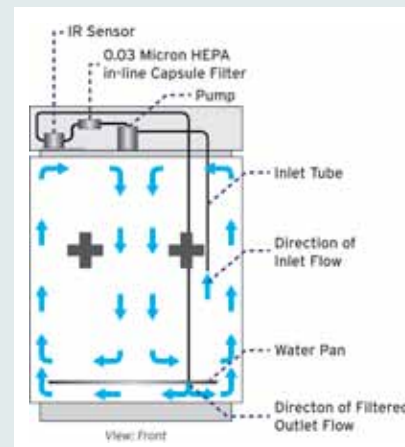
Control plates were evaluated to check spore concentration was an acceptable challenge. The control plate should contain greater than 300 CFU's to be valid.

CONCLUSION

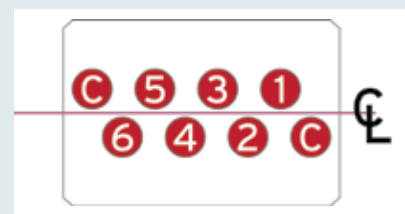
Results indicate a reduction in chamber spore concentration. The reduction of spores can be directly attributed to filtration through the HEPA filtered recirculation.

Results also indicate cleanliness level of class 100 or better 15 minutes after the chamber has been exposed to airborne contaminants. The filtration system reduces the chance for contamination.

The NuAire CO₂ Incubators offer a substantial reduction in contamination potential.



▲ Figure 1: HEPA Filtered Recirculation System



▲ Figure 2: Soy Agar Plate Distribution on Shelf

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Recently, the demand for low-cost DNA sequencing has driven the development of high-throughput sequencing technologies that are based on several parallel instances of the sequencing process. This approach produces thousands or millions of DNA sequences at once, followed by algorithmic analysis and alignment of the data. The challenges of this approach are associated with handling massive amounts of the generated information.

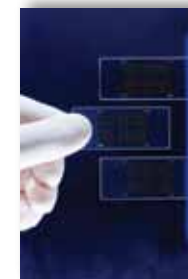
Next generation high-throughput DNA sequencing technologies are widely used by the scientists who embark on a monumental task of deciphering genetic information from a statistically significant population group. With the emergence of Epigenetics as one of the frontiers of biological science, the researchers face even greater challenges of piecing together genetic information and DNA-protein interactions. These research projects are insurmountable without a flexible laboratory data management system capable of storing, analyzing and sorting the data generated as a result of several experimental work-flows.

In order to communicate results, manage processes at various stages or make common decisions, a software like LIMS 24/7 used in all labs could help to coordinate the work. The goal is to retain result achievement, elaboration, further decision and final review directly at the workplace. Indeed, all laboratory users can login and use this software from any-

where on the network. Projects are organized by type, subtype, priority and other criteria and all the related information is recorded within such projects. Moreover, instruments can send data directly to LIMS that is configured to guarantee the traceability of the work. With LIMS it is possible to save time and money, and to improve rate and productivity.

LIMS 24/7 is an easy to use yet provides powerful analysis tool for streamlining the overwhelming sequencing process. It is an excellent solution for data management and sharing that can handle complex ChIP-Seq data including collaborators, donors, cohorts, antibodies, samples, DNA libraries, raw ChIP-Seq data files, and analysis results. Powerful data mining capabilities help lab managers to make decisions on the next steps in the process, find bottle-necks and track performance. RURO is making genomic data easier to share, search and archive.

We have presented one possible application of LIMS 24/7 in sequencing, but this software could also be successfully employed for the management of clinical trials, preclinical and animal research, drug discovery, microarray, genotyping, gene expression, biobanks and proteomics labs.



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Rapid Microbial Screening Systems

Problem: The traditional method of testing for microbial contamination has changed very little in the past 100 years. A sample of product is added to a growth medium in a plate or sample container. The samples are then put into a warm incubator and allowed to sit for several days to encourage the growth of any microorganisms that might be present. In a typical manufacturing lab, hundreds of plates are checked manually, day after day, until a specified number of days have passed without growth. Test times average 4 to 7 days for microbial limits and a minimum of 14 days for sterile products at each point of testing. Meanwhile, drums of raw ingredients, huge vats of in-process work and pallets of finished goods occupy valuable space in the warehouse and keep working capital tied up in inventory. Traditional methods are simply out of step with today's more streamlined, modern manufacturing facilities, where products are within spec 99% of the time or more.

Solution: For materials and products typically free of bioburden, a simple absence/presence primary screen offers the ideal solution for safely releasing the vast majority of products quickly. Rapid microbiological screening with adenylate kinase (AK) technology, such as the AKuScreen assay from Celsis Rapid Detection, combines the reliability of growth-based ATP, the gold standard of rapid testing, with a patented signal amplification that makes use of AK present in all living things.

Because AK is an enzyme and not a metabolite, it can generate an almost unlimited supply of ATP when it is presented with an adequate supply of ADP. This strengthens the bioluminescence signal and, therefore, the assay's sensitivity, shortening time to result.

Like the traditional method, sample preparation for the growth-based



◀ The Celsis Advance luminometer fits easily on the benchtop.

AKuScreen assay also starts by adding product samples to a medium and then incubating them. However, instead of waiting 4 to 7 days for microbial limits test results, the AKuScreen samples can be prepped, incubated and assayed all within 18 to 24 hours.

The rapid screening assay also reduces prep time and is more environmentally friendly: a single broth enrichment is typically used to detect bacteria, yeast and mould in all products. This reduces the amount of selective media that must be mixed and stored, as well as the various plates or jars needed to hold the different media for each replicate.

Whereas traditional samples are individually inspected for visual—and often very subjective—indicators of microbial growth, the Celsis screening system includes a sensitive luminometer with software that automatically controls the timing and volume of reagent injections. The instrument measures the light output of the AK-amplified ATP reaction, providing results in a color-coded table or graphical view. The standardization provided by automation makes this a simple, yet state-of-the-art approach that is easy to operate without the need for extensive training or an advanced degree. It can test up to 120 samples per hour, including a mix of product types and batches.

Definitive, objective results are generated within 24 hours for limits testing. It is this fast time to a negative result that is most critical: the “no to go” information needed to release products quickly. Such systems can be justified

by the operational reductions in inventory and working capital as well as by the environmental savings in the lab. Celsis offers a financial and environmental impact assessment to help companies estimate these savings in advance.

For more information, visit www.celsis.com

When choosing a rapid method, be sure to evaluate the system to make sure it delivers on these criteria:

1. Provides critical information when you need it, to keep your business running. Idle goods and materials cost money and take up space in the warehouse.
2. Tests the majority of your products. Find a system that can test a full range of product types, including opaque, viscous, high or low pH, non-filterable and highly pigmented materials.
3. Environmentally friendly. Your system should enhance your lab's sustainability initiative by using less energy and water and by reducing the amount of liquid, solid or hazardous waste you must dispose of daily.
4. Easy to validate. By its nature, an absence/presence test requires fewer steps to validate. But don't stop there. Ask about the validation support and resources available from the manufacturer.
5. Global support. Once you have a system in place, you won't want to go back to the traditional method. So make sure the company has maintenance contracts, technical support and service available every place you need it, whenever you need it.

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EXPERTS: Tamie Webber & Anne Sefried Seamlessly Integrate MSDSs with Chemical Inventory Management



Tamie Webber

Director of Product Management at 3E Company, is responsible for product management initiatives, product planning and strategies and product development, including MSDS Distribution and Management, Emergency Response, Regulatory Reporting, Training and Waste Services.



Anne Sefried

Technical Specialist/Inventory Consultant for ChemSW, provides implementation, data migration, custom reporting, and general technical support to ChemSW customers. She graduated from Chapman University with a B.S. in Computer Information Systems.

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HOW TO SEAMLESSLY INTEGRATE MSDSs WITH CHEMICAL INVENTORY MANAGEMENT

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The average R&D laboratory typically has thousands of materials on site and each one requires a Material Safety Data Sheet (MSDS). But having a MSDS is just the beginning because those MSDSs are frequently updated by the supplier, meaning that the lab manager must keep track of not only where each MSDS is and which MSDS need updating, but also any new MSDSs that need to be attached to new chemicals being ordered by the lab. Keeping up with those changes can be a complex, time-consuming, and costly task.

“Historically, MSDS management has not been integrated with chemical inventory management, so two separate processes and databases are maintained,” says Tamie Webber, Director of Product Management at 3E Company. “However, the two workflows are integral to each other, so it makes logistical and financial sense to integrate the two tasks.”

“The most efficient R&D labs typically automate as many manual processes as possible to optimize lab productivity,” adds Anne Sefried, Technical Specialist/Inventory Consultant for ChemSW. “Integrating MSDS and chemical management processes streamlines the lab's workflows, eliminates duplicate work across locations, provides an accurate picture of chemicals in lab inventory, and reduces operating costs.”

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TUNE INTO OUR LIVE WEBINAR to hear Tamie and Anne explore the challenges involved with juggling MSDS and chemical inventory management, and different approaches that reduce the financial burden and streamline the associated workflows.

Integrated Sample Management Across Several Labs

Problem: It is essential for medicinal chemists to have access to analytical instrumentation for reaction monitoring and product analysis. However, due to the associated high capital cost and maintenance overheads, it is not possible to install and support instrumentation in every lab across a research site.

As a result, submission of chemical and biological samples to equipment such as HPLC and GC/MS requires substantial manual effort. Typically samples are formulated and collated into racks before manually being entered into analytical instrumentation. This can be a time-consuming, error-prone and inefficient process.

Solution: The Horsham Sector of Novartis Global Discovery Chemistry initiated a project with TTP LabTech to develop a system for connecting remote medicinal chemistry labs on different floors of the building to LCMS instruments in a central analytical chemistry lab. The result is LAB2LAB from TTP LabTech.

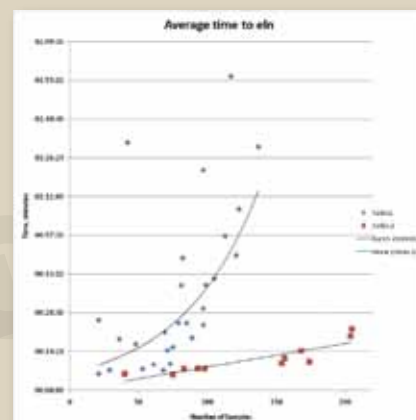
operation of equipment, thereby reducing sample queues, optimizing instrument use and increasing the speed of data generation. It is simple to install, easy to customize and easy to expand.

The system connects labs from anywhere in the building to analytical instrumentation via a low-pressure compressed air system. Each sample tube has a unique 2D barcode. To submit a sample, the chemist scans the tube and selects one or more methods. An ELN reference is assigned and the tube is placed in a LAB2LAB Sender. LAB2LAB transports and directs samples to the most appropriate analytical instrument available and results are automatically returned to the originator's ELN. In addition, LAB2LAB can prioritize and hold samples in a buffer/holding space if the analytical equipment is busy or otherwise unavailable; this allows low-priority analyses to run overnight.

The initial phase of integration of the LAB2LAB system into the Novartis Horsham site involved linking six medicinal chemistry laboratories to one Agilent 1200 HPLC. Next, a Waters ACQUITY UPLC-MS instrument was added for reaction monitoring. Sample throughput increased dramatically to 100+ per day. In the final phase, a second ACQUITY UPLC-MS of the same configuration was added. Both the 1200 HPLC and ACQUITY UPLC-MS analyzers were existing instrumentation owned by Novartis and neither required modification for use with the LAB2LAB system.

These three analyzers now support in excess of 250 sample submissions per day. LAB2LAB provides the chemist with a 'virtual instrument' in every laboratory, capable of running a variety of methods.

Figure 1 shows the results from an analysis of the time taken for a chemist to physically submit a sample vial to UPLC-MS instrumentation and to receive data in his Electronic Lab Notebook (ELN). The data show the response of a single UPLC-MS (Series 1) and two UPLC-MS instruments (Series 2) in managing a queue of samples. The data include samples that have been submitted for multiple methods, including samples submitted using methods which would take longer than the standard 2 minute reaction monitoring time set by the machines. Additionally, outliers show the effect on queue times as a result of taking an instrument offline for maintenance. As the number of samples per day increases to more than 100, a single UPLC-MS instrument struggles to cope. The addition of a second analyzer within LAB2LAB, which manages the queuing and distribution, is shown to reduce the queue time significantly. More than 250 samples per day are being run with an average queue time of < 30 minutes.



▲ Figure 1: Average time taken for sample submission to data arriving in the Electronic Notebook (ELN) using LAB2LAB.

For further information or to request a demonstration please contact sales@ttplabtech.com



▲ LAB2LAB, An automated transport and management system, is in use at Novartis.

LAB2LAB is a novel laboratory sample transport and management system for linking laboratories to existing analytical instrumentation. LAB2LAB transfers samples from remote laboratories to existing HPLC, LCMS, GC/MS, UPLC and NMR equipment, and allows unattended

LAB2LAB

Do you need to maximise your analytical capabilities?



LAB2LAB is an automated sample management system that provides on-demand reliable, secure and rapid microtube transportation, analysis and data generation using your existing analytical equipment.

Today's scientists need easy access to analytical instrumentation. Ideally this instrumentation should be as close as possible to work areas to provide efficient workflows. However it is uneconomic to install in every laboratory. LAB2LAB offers you a virtual analytical lab on each lab workbench.

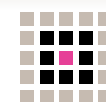
LAB2LAB Application Areas

LAB2LAB will connect your labs directly to your existing HPLC, LCMS, GC/MS, UPLC and NMR analytical equipment

Examples of where LAB2LAB can be used:

- Analytical testing of synthesised samples
- Identification and quantification of compounds
- Quality Control of stored chemical compounds: checking for crystallisation, precipitation, degradation, concentration and decomposition
- Biological, clinical or forensic sampling
- Drug testing and contaminant identification
- Characterisation of unknown compounds
- Large molecule analysis such as peptides and proteins
- Cell metabolism using NMR
- Industrial applications checking for sample purity and content
- Non destructive composition analysis
- Remote sample collection and delivery

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T T P L A B T E C H

Eliminating the Edge Effect

Problem: When culturing cells for use in, for example, drug screening assays, maintaining consistently high throughput is essential. However, in order to achieve this while obtaining reliable data, evaporation and consequent well-to-well variability must be significantly minimized. This is commonly experienced as the result of the 'edge effect', where medium from the wells during incubation is evaporated. As a phenomena which is especially prominent in the wells close to the perimeter of the plate (the edge wells), this can be highly problematic. As the medium evaporates, concentrations are altered and differential rates of evaporation across the plate results in variability. When a volume loss as small as 10% can concentrate media components and metabolites enough to alter cell physiology, this can have a detrimental effect.

In an attempt to alleviate the edge effect, researchers often decide not to culture cells in the outermost wells but to fill these with sterile water, and use only the inner wells of each plate for cell cultures. However, by rendering these wells unusable, throughput and efficiency become compromised instead.

Solution: In order to increase the throughput and efficiency of cell culture protocols, researchers need to be able to use all of the wells of a plate with confidence. As such, the Thermo Scientific Nunc Edge Plate has been designed with an evaporation buffer zone built into its perimeter. This can be filled with sterile water or 0.5% agarose, providing an additional reservoir that effectively eliminates the edge effect.

The Nunc™ Edge plate reduces the overall plate evaporation rate to <2%

following seven days of incubation, making it ideal for high-throughput cellular assays requiring repeatable results. Thus, more viable and healthy cells are obtained for use in downstream applications. By significantly reducing the occurrence of any media evaporation, sample concentrations are maintained over long periods of incubation. The prevention of cell death and toxicity in the plates' outer wells allows results to remain more true to the population phenotype, for more efficient high-throughput analysis.

By filling the evaporation buffer zone with 5% agarose, a more solid, jelly-like moat is provided, eliminating the potential for any spillages. This provides the same low plate evaporation as water, maintaining evaporation rates at <2% after seven days of incubation,

in comparison with over 8% observed with a standard plate. As a result, the plates can be used as standalone, or combined into a fully automated workflow, without the risk of liquid spillages by robotic arms.

By combining advanced optical properties with a low evaporation rate, the Thermo Scientific Nunc Edge Plates enable researchers to obtain quality data from automated fluorescence imaging and quantitative analysis protocols. The dramatic reduction in evaporation enables concentrations to remain consistent across all wells and thus, efficient cell growth is obtained across the entire plate.

For more information, please visit www.thermoscientific.com/edgeplate.



◀ The Thermo Scientific Nunc Edge Plate greatly reduces the edge effect, which is commonly experienced during cell culture. By reducing well-to-well variability, results remain consistent across the entire plate, enabling the confident use of the outer and corner wells to increase throughput.



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PARTING POINTS

Takeaways from this month's issue:

LABORATORY ETIQUETTE

Laboratory etiquette describes the preferred if not required conduct in the laboratory, and keeps all other pieces working together, in the form of written or unwritten rules. Some general guidelines for ensuring proper etiquette in the lab:

- Punctuality: ensures common areas are used efficiently and smoothly
- It's considered egregious to interfere with experiments set up by fellow lab workers
- Be conscientious about status of supplies—re-order or bring to the proper person's attention when needed
- Apologize for impolite conduct and provide positive feedback on good performance

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EMPOWERING YOUR STAFF

An empowered staff enhances the laboratory research culture and potentially decreases the managerial burden, costs of mismanagement and research inefficiencies. Improving your staff's skills through training can provide various benefits to your organization.

- Employees can gain skills through mentoring, coaching, classes, seminars and e-learning
- A 2011 study says that the best labs have development plans for all researchers
- Managers need an arsenal of techniques to help out visual learners, auditory learners, kinaesthetic learners, etc.



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THE NFPA HAZARD DIAMOND

The four properties that form the foundation of the NFPA hazard diamond are the four basic categories of chemicals: toxic, corrosive, flammable and reactive. There are many chemicals that exhibit a combination of properties. Here is a breakdown of information on a NFPA diamond.

- The top section (red) indicates the flammability hazard, via a rating from zero to 4
- The right section (yellow) indicates the material's reactivity, via a rating of zero to 4
- The bottom section (white) denotes special hazards (oxidizer, incompatible with water, etc.)
- The left section (blue) denotes health hazards, and is also rated from zero to 4



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CELL CULTURE CONTAMINATION

When culturing cells, sources of contamination are ubiquitous as well as difficult to identify and eliminate. There are a variety of ways to limit and prevent sample contamination in the lab to effectively maintain experiment integrity.

- Clothing can harbor and transport microorganisms from outside the lab, so wear a lab coat
- Moving around creates air movement, so the room must be cleaned often to reduce dust particles
- Frequently used equipment are reservoirs for microbes and fungi; clean them regularly
- Each cell type should have its own solutions and supplies and should be manipulated separately from other cells



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DEVELOPING NEW REVENUE STREAMS

The key to creating new revenue streams for your organization is becoming aware of new science and business developments and figuring out how to take advantage of them. Here are some ways to do this:

- Read business magazines, newspapers and trade magazines; firms constructing new plants could be a source of new business
- Talk to sales reps; they can bring information on new technology customers are developing
- Attend conferences to see what's new in fields that are of interest to your employer
- Encourage staff members to give talks at research universities

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