ISPE
Connecting a World of Pharmaceutical Knowledge

Carolina-South Atlantic Chapter

CaSA News

Volume 22 • Number 1

February 2015

President's Message

Heather Denny

The countdown is on...the 2015 ISPE CaSA Life Sciences Technology Conference is less than 5 weeks away. As with other events that have taken place this year, the Tech Conference is on track to set a new standard for ISPE CaSA. On March 10, the only place you will want to be is the Raleigh Convention Center! Where else can you find such a diverse gathering of industry leaders and suppliers in one location in the Carolinas? There is no other local venue with exposure to more than 150 companies in the life sciences industry. Exhibitor tables have sold out, and we thank all of our partners who are supporting this event with their participation. Our keynote address will be delivered by John Cox, Executive Vice President, Pharmaceutical Operations & Technology, Biogen Idec. This presentation promises to be standing room only, so make sure you get your seat early. We have also incorporated our Leadership Symposium into the conference this year, providing a Student/ Young Professionals Career Development Track. Check out our website www.ispe-casa.org for more information on all educational sessions.

Looking for an opportunity to network? Stop by Bucks Billiards on your way home on February 23 for Billiards and Brews, brought to you by the Young Professionals Committee. Register through the home page of the website www.ispe-casa.org. Also, check out an upcoming Therapeutic Thursday event in the Triangle or the Atlanta area.

So are you now wondering how many more times I will mention the website address? One question the board continues to ask is how do we best communicate with you, our members? We are in the process of working on a social media plan to increase the flow of information through Linked In, Facebook, and Twitter. We have a couple of questions for you:

How do you prefer to receive information?

Are you interested in becoming part of the CaSA Communications Team?

Please submit your answers or interest to me at president@ispecasa.org.

Enjoy the remainder of winter, and make it a point to attend an ISPE CaSA event.

Heather Denny
President, ISPE CaSA Chapter

Featured Sponsors

22nd ANNUAL ISPE-CaSA Technology Conference
March 10, 2015

Visit **www.ispe-casa.org/2015** to register your company to attend or check out the details of the Conference.

INSIDE THIS ISSUE

Upcoming Events

Young Professionals' Billiards and Brews - February 23, 2015, 5:30-8:30 pm, Bucks Billiards, Raleigh, NC

ISPE-CaSA Therapeutic Thursday - February 26, 2015, 5:30-7:30 pm - location TBA

NCSU/ISPE Career Fair - Friday, March 6, 2015 - McKimmon Center, Raleigh, NC

Technology Conference - March 10, 2015 - Raleigh Convention

ISPE-CaSA Therapeutic Thursday - March 26, 2015, 5:30-8:30 pm - Mystic Grill, 1116 Clark Street SW, Covington, GA

Tri-Sci Expo - April 11, 2015 - NC Museum of Life Sciences - Raleigh, NC

Golf Event - May 18, 2015 - Prestonwood, Cary, NC

Membership Corner

$40 DISCOUNT NOW AVAILABLE FOR NEW INDUSTRY MEMBERSHIPS!

By Terence Morrison, P.E., LEED AP BD+C, ISA 84 SFS

$40 DISCOUNT NOW AVAILABLE FOR NEW INDUSTRY MEMBERSHIPS! Applications can be made online at www.ispe.org/join. Click on Join Now under Industry Membership, and enter **CASA2015** in the promotion code box. Please remember ISPE's Refer-A-Friend Program! Earn one free month of membership for every friend you refer. All the details are available at http://www.ispe.org/membership-referral-program

This discount is not applicable to Students, Young Professionals, Academics, and Regulatory Authority / Government as these are already discounted memberships. If you have any question about ISPE or the CaSA Chapter, please contact me at membership@ispecasa.org.

Welcome New Members

New Members who joined November 26, 2014 through February 10, 2015

Amanda Mellenberger
Atiya Moses
Chiang-Sheng Chang
Dr. Barb Eppler
Dr. William P. Jackson, Ph.D.
Ivy Sweeney
Lee Carroll
Marc W. Haakenson
Abdul Kamalpasha
Adam Holferty
Alan Lash
Alexandre Jassoud
Ariel Macari
Bhavani Prasad
Brandon S. Jones
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Clive Finney
Edwin Martinez
Eric M. Newman
Evan D. Frazier
James H. White
Jason Denton
Jay Reed
Justin Rothwell
Kevin McGough
Kyle Fahrland
Mark Petyak
Minh-Thi Ton
Nathan Zeidler
Nicholas F. Weidle
Noe Rodriguez Rivera
Paul Jacob Howland
Peter Waddleton
Richard B. Eason
Robert A. Wolff, PE
Robert B. Brown
Ryan Staton
Shawn Geisel
Thomas M. Woo
Timothy M. Wilson, CFM, LEED AP
Tully Erwin
William J. Ulmer, III
Ann Grant
Beth J. Haas
Brandy Jacic
Keri Concannon
Mona Saffarzadeh
Amanda P. Hiester
Amber M. Oakes
Ashley A. Lynch
Claudine R.C. Clarke, ASQ,CQA
Diana Wright
Elise Krankoski
Heather N. Chambers
Jiabao Wen
Kate Harmon
Katherine L. Wagner
Kathy Powell
Kristine Huynh
Lisa Pieramico
Liz Wilson
Monika Gavireddi
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ISPE
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Young Professionals

You're invited to ISPE's Young Professional Virtual Book Club!

Here's our first book! *Creating Personal Presence: Look, Talk, Think and Act Like a Leader* by Dianna Booher. Buy it here

When? March 9, 2015

Where? On the new YP Networking Community – more details coming soon!

Check us out on Linked-In, Facebook & Twitter

"Thousands of dollars in personal coaching in a book!"

"Making a strong Personal can make the difference as your move forward in your career!"

"Full of practical tips! Immediately increase your credibility! "

Student Corner

An Interview with Ryan Boehm, Jane Brown ISPE-CaSA Scholarship Winner

By Tracey Ryan, ISPE Manager of Affiliate/Chapter Relations

Ryan Boehm, a graduate student pursuing a PhD in biomedical engineering at University of North Carolina at Chapel Hill, recently shared his ISPE journey with ISPE Manager of Affiliate/Chapter Relations Tracey Ryan after winning the Jane Brown ISPE-CaSA Scholarship.

Tracey: Let me start by congratulating you on receiving the inaugural Jane Brown ISPE-CaSA Scholarship.

Ryan: Thank you. I am honored to be selected as the first recipient of the Jane Brown ISPE-CaSA Scholarship. I owe a lot of thanks to the great people who have made an impact early in my career – especially Jane Brown, Wendy Haines and all of those involved in the scholarship process.

Tracey: You have been an active student member of ISPE for some time now, how did you find ISPE?

Ryan: I first joined the University of North Carolina at Chapel Hill student branch of ISPE-CaSA at the suggestion of my graduate school advisor in the spring of 2012. Not knowing much about the organization at the time, it seemed like a good opportunity for networking, sharing my research and the opportunity to attend professional meetings as a graduate student. When I presented a poster on the research of the antibacterial properties of microneedle devices for drug delivery applications at the 2012 Technology Show in Raleigh, NC, I quickly saw the benefits of being a part of ISPE from an educational and professional perspective.

Tracey: Your poster was then selected as the winner of the regional poster competition and you were able to present the research at the 2012 ISPE Annual Meeting in San Francisco, CA. What was your ISPE Annual Meeting experience?

Ryan: The trip to San Francisco for the Annual Meeting was rewarding. I not only had the chance to present my research again, but was able to meet with a number of industry professionals, get to know more of the ISPE-CaSA leadership, interact with the Young Professionals group and talk to fellow students from around the country. The networking sessions and educational programs gave me a better idea of the wide reach of the organization and the numerous disciplines associated with ISPE within the life sciences. Getting to do some sightseeing around San Francisco was not a bad perk, either.

Tracey: After presenting your research to industry leaders at both the 2012 Technology Show and 2012 Annual Meeting, you returned to North Carolina with passion and excitement to expand your involvement with ISPE. Would you tell us a little more about your experience with the student branch and the chapter's activities for increasing interest in STEM careers?

Ryan: I've been serving as the treasurer of the student branch since spring of 2013. The leaders of the ISPE-CaSA chapter and student branch work together to create opportunities for students to engage with industry professionals at local meetings and learn about the research and career prospects during site visits a number of life sciences companies in the area. We also participate in outreach events in Raleigh, NC, at the North Carolina Museum of Natural Sciences. The museum and ISPE-CaSA have partnered over the last several years to put on an annual STEM outreach event, for which our student branch has been able to create a booth to provide science demonstrations and activities for the event patrons. It allows us to meet with young people who are interested in and enthusiastic about STEM activities.

Tracey: As you continue your studies and involvement with ISPE community, what are you looking forward to the most?

Ryan: I have had positive interactions with everyone I have met through ISPE and the CaSA chapter. Mostly, I am looking forward to continuing my involvement with the organization, increasing the reach of the student branch and enhancing my knowledge and network.

Membership Corner

CaSA Chapter Annual Automation Forum - CaSA Chapter Board

The CaSA Chapter Annual Automation Forum represented many emerging and hot topics in the automation field. The Education Committee set the bar high with an evening of quality speakers, networking and giving back to the community through contributions to the Toys for Tots Foundation. Multiple speaker tracks permitted attendees to select topics of interest relevant to their needs. The event brought together automation professionals, designers, project managers and owners to hear various presenters discuss real world examples of project implementation and share details of their roadblocks to success. Of particular interest were the topics of serialization and high level integration of ERP software systems into manufacturing platforms. This trend of automation solutions that combine traditional business and production sectors will only accelerate as manufacturers struggle with issues such as counterfeiting and tracking of resources from raw materials to finished product.

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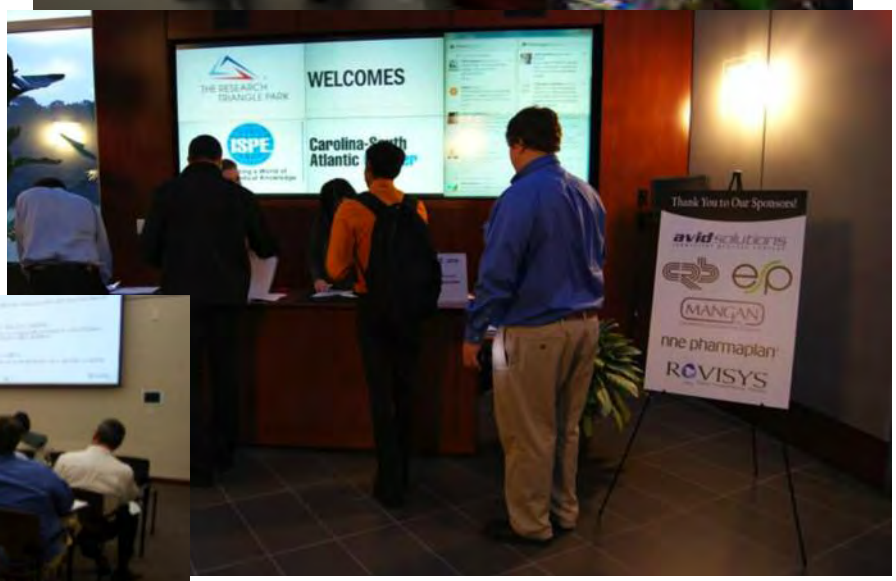

Connecting a World of Pharmaceutical Knowledge

Carolina-South Atlantic Chapter

2015 ISPE CaSA Poster Competition

CALL FOR ABSTRACTS!

Want to present your research to Industry Professionals and show off your knowledge?

Want to WIN a free trip to the 2015 ISPE Annual Meeting in Philadelphia?

When: Monday March 9th 2015 @ 6:00pm

Where: Raleigh Convention Center

Submit your abstract by March 1st 2015 to ISPECASASAC@gmail.com

Technology Corner

22nd Annual ISPE-CaSA Life Sciences Technology Conference

By Mike Putnam, Chair, 2015 ISPE-CaSA Technology Conference

Don't miss the best life sciences gathering in the Southeast! Register today for the 22nd Annual ISPE CaSA Life Sciences Technology Conference! **On March 10, 2015**, over 1,000 attendees and 200 exhibitors are expected to converge on the downtown Raleigh Convention Center for what's quickly becoming the Southeast's largest gathering of life sciences professionals. Educational seminars for this year's conference include everything from 'Risk-Based Asset Management' to 'Testing and Validation of Mobile Apps'. Conference pre-registration cost is $65 for members and $75 for non-members. Admission includes breakfast, lunch and dinner as well as full access to exhibitor area, educational seminars, and networking reception.

Quick Facts About The 2015 Conference:

- 22nd Annual Technology Conference date is **Tuesday, March 10, 2015**
- Hosted at the **Raleigh Convention Center**
- New for 2015…**CaSA Pavilion** area
- **6 Educational Tracks** featuring industry leading professionals
- **Keynote Presentation** featuring Biogen Idec Executive VP John Cox
- **Networking Reception** following conference featuring Vegas-style casino gaming and gourmet food 5-7 pm

Please make plans today to attend the Technology Conference on March 10, 2015. Visit http://www.ispe-casa.org/2015/ to register. Thanks and I'll see you there!

Call for Volunteers!

The Student Affairs committee is searching for a graduate from Virginia Tech to represent and lead their student chapter membership – Please send your information to info@ispeCaSA.org, subject line "GO HOKIES!"

Sponsors Needed!

Sponsors needed for 2015 Therapeutic Thursdays! A great way to get your company into the hearts and minds of the chapter membership – Please send your information to info@ispeCaSA.org, subject line "Cheers!".

CaSA COMMITTEES 2014-2015

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Technology Corner

CREATING A SOLID CALIBRATION PROGRAM

BY JON DOYLE, PCI

IMPORTANT ASPECTS OF A CALIBRATION PROGRAM

There are many hot topics on Quality Systems of a Life Sciences company, such as emerging technologies and data integrity. An often neglected topic that is of great importance is Calibration Programs. An effective calibration program ensures that all instruments are assessed and calibrated properly, specifically in production areas.

A robust calibration program provides the necessary controls to ensure instrumentation accuracy. However, the calibration program is not a stand-alone program but rather one of several departments that work together to ensure consistent batch-to-batch product quality. The effectiveness of this program relies heavily on the cooperation amongst groups. A company's calibration program is not a revenue generator but if it is run efficiently, it can make audits easier and improve production throughput. The following information covers the many aspects of setting up and running an "Audit-Ready" calibration program

STAFF

This is the most important aspect of running a solid calibration program. Hire the best people you can get and invest in your team. This can be said for any department but the best calibration staff are able to both understand the technical aspects of instrumentation and how a calibration program runs and interacts with the company's various Quality Systems. Staff need a high level of integrity to ensure calibrations are completed properly and correctly. Plus they must be able to quickly recognize and resolve any issues. The Calibration Supervisor must show dedication to delivering quality work and ensure that dedication flows to the team. Instrumentation is constantly evolving, as is regulatory guidelines, so a good program will allow time for mentoring and training.

There are a few training outlets that allow for recruiting staff members, including experience from life science companies, governmental agencies and other regulated industries, such as the nuclear industry. Staff that have been trained in regulations such as FDA, MIL, EPA, ISO and other regulatory agencies tend to better understand the meticulous and collaborative nature of a calibration program. An excellent training guide for your new staff is "Calibration – A Technician's Guide" by Mike Cable. This guide is published by the International Society for Pharmaceutical Engineering (ISPE) and can be obtained online at the ISPE Bookstore (visit www.ispe.org for more information).

While there is no "one size fits all" staffing model, one common approach is for an organization to use contractors initially and then graduate to a blend of internal and external staff. This minimizes risk and maximizes flexibility. A small calibration program may have one Subject Matter Expert (SME) per site who oversees all aspects of managing the calibrations. As the company grows, this SME may become Lead

Technician or Supervisor to several technicians, a data analyst, and a planner/scheduler who coordinates with the Production and Maintenance departments.

In an analytical setting such as Quality Control, a Full-Time Equivalent (FTE) can execute approximately 50 to 60 calibrations per month. Analytical calibrations are generally more complex in nature and take longer to execute than other types of calibrations found in a production setting. In a production setting, an FTE can handle between 100 and 200 calibrations per month depending upon One-point versus Multi-point calibrations. Contractors can typically perform a greater number of calibrations due to the fact that they are not working on continual improvement activities, corporate objectives, or other internal corporate requirements.

COMPUTERIZED CALIBRATION MANAGEMENT SYSTEM (CCMS)

CCMS discussions are multifaceted and discussed at length in many resources and publications. Any small calibration department will eventually move from a primitive yet often effective excel/logbook based schedule and install/qualify a more robust asset management system. Along with this transition you will find the organization also moving from a paper based system to a hybrid of paper work orders and electronic database, and then into a fully electronic system that establishes work flow processes. This transition can be very disruptive and require significant internal and external resources. Upper management must drive the change while ensuring the culture and processes are being implemented at a reasonable pace. Users of the system must have time to "test drive" and train before the live transition. In most cases, a cultural change is a far larger issue than the technical change. Continual improvement is not done with one change, but many contiguous, sometimes overlapping, smaller changes.

In less demanding environments a CCMS is primarily used to capture basic asset information as well as the associates instrument calibration schedule. As an organization grows and becomes more sophisticated and efficiency focused, a good CCMS allows for additional functionality, such as Maintenance program needs. Functionalities that a growing organization may want to capture (best practices) include:

- ✓ Advanced asset information such as GMP Classification, device Status, asset characteristics
- ✓ Electronic Work Orders
- ✓ Bill of Materials (BOM)
- ✓ Inventory Control
- ✓ Calibration Data Templates with setpoints/tolerances
- ✓ Maintenance Job Plans (step-by-step service instructions)
- ✓ Planning and Scheduling functionality
- ✓ Key Performance Indicators (KPI's or Metrics)
- ✓ Queries and Reports
- ✓ Purchase Orders
- ✓ Labor tracking
- ✓ Service requests
- ✓ Management of Change

Some companies utilize both a CCMS and a CMMS (Computerized Maintenance Management System), but due to cost reductions and IT requirements, it may be more beneficial to select one "system" which is capable of meeting the majority of both department's requirements. Increasing in popularity is a system that can be deployed across multiple sites. This is a significant task and requires much collaboration

(development, process flows, qualification, etc.) and coordination from all levels of an organization. It is key to remember the difference between "bells and whistles" and "needs and wants" when purchasing and configuring a new system. A User Requirement Specification is the best first step, along with communicating the design to the end users so they understand corporate goals.

When researching CMMS options, it is wise to investigate the systems for their strengths and weaknesses as well as identifying an implementation partner who can assist with rollout. Simple installations using preconfigured software may take 3-4 months and less than $200k. More complex rollouts could take significant internal and external resources, collaboration, millions of dollars to implement, and several years to rollout effectively.

WORK ORDERS

While work orders (WO) could be mentioned within the CCMS component of the calibration program, it is a critical topic worthy of separate discussion. Work orders are not taken as seriously as they should be. First and foremost, work orders are the most important document the calibration department generates. It ensures quality and proves to regulatory agencies that calibration is performed routinely. A work order must have the proper information to be effective. It must contain a unique ID, instrument information, standards used, calibration data, tolerances, pass/fail indication, and technician performing the work. It also must contain all relevant dates, such as due date, start date, and completion date. For unscheduled calibrations, there should always be a comment on the work order with an explanation why the calibration was performed out of sequence. Additional work order aspects are:

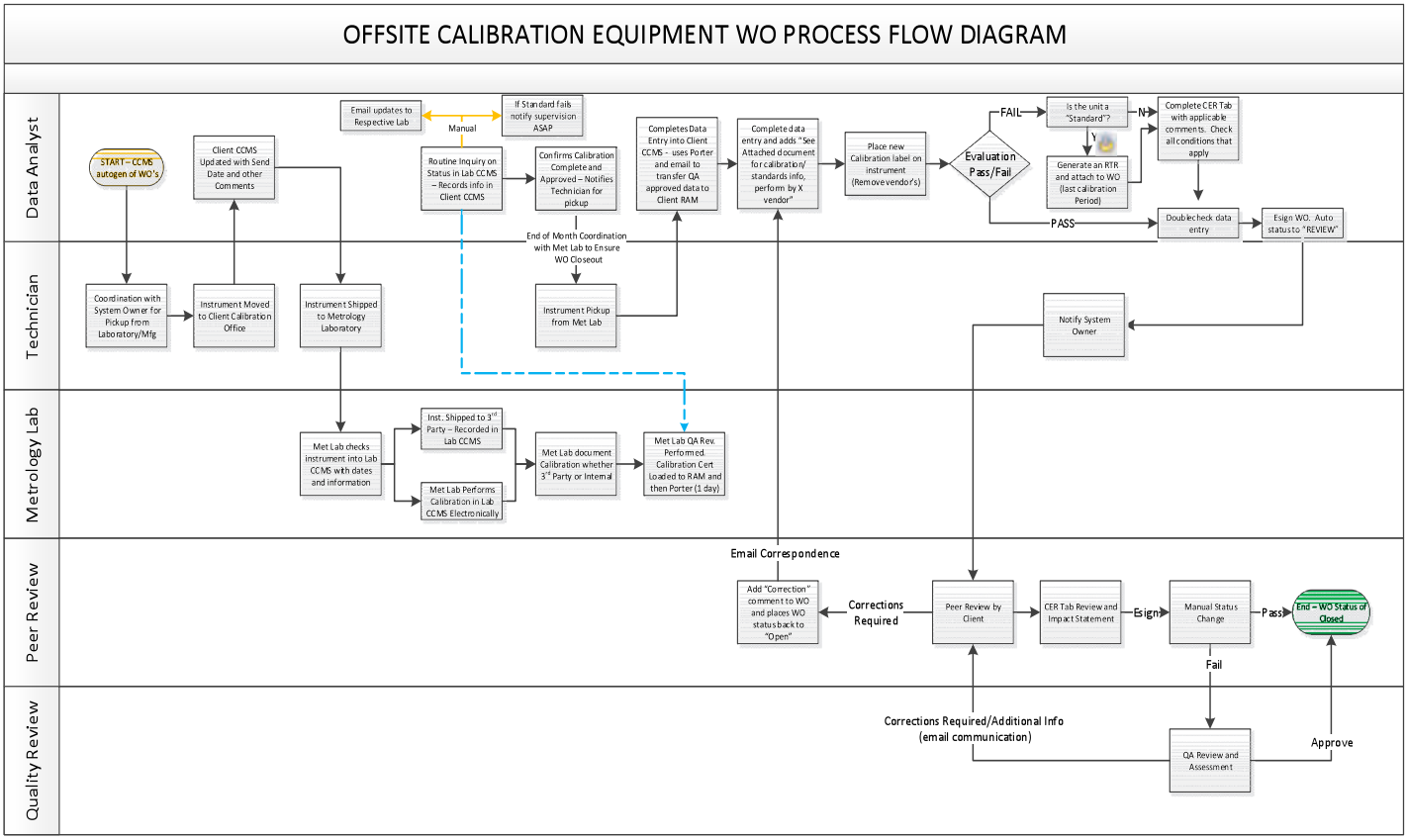
- Generate WOs before the work is to be performed. This provides a place for the technician to record important data and also ensure work gets captured real-time. It is very common for work not to get documented after it has been performed. Avoid this common compliance gap.
- Establish an efficient process flow diagram for all types of WOs, including filing if using paper-based WOs. Having a well establish process flow for all WOs is critical to ensuring WOs are planned, properly handled, executed, contain at least the minimum data, and are reviewed and filed (if paper-based) appropriately. There is nothing worse than having a missing or incomplete WO when inspectors are reviewing equipment service records.
- Peer Review of WOs is critical. Many organizations simply "Rubberstamp" calibration WOs and leave highly visible errors open for discovery during a subsequent regulatory agency audit. In small calibration departments (single person) one person may be responsible for peer review of all work orders. In larger organizations this may not be feasible due to the sheer volume of work orders. In larger calibration departments the calibration supervisor should review all WOs related to calibration of standards and instrument WOs that did not meet instrument tolerances. This is a "Risk-Based" approach.
- Ensure timely peer review of WOs. Many organization do not perceive the peer review of WOs a critical activity and will allow several months of WOs in an "Open" status. Timely review allows for errors to be correctly immediately (reduced risk of prolonged process impact) and/or when the information is fresh in the technician's mind. In some cases a WO that would have been sent back for rework is no longer a viable option since a more current WO has already

been executed or the technician is no longer available. Best practice is to track closure of WOs and ensure that no more than a certain number are open at any given time. Refer to "Metrics" below.

STANDARD OPERATING PROCEDURES (SOP)

Regulatory requirements provide high-level governance for calibration programs (example: calibration is required of all critical instruments) but these regulations will not explain how to develop or manage a calibration program compliantly or efficiently. Many organizations turn to industry guidelines published by international groups such as the International Society of Pharmaceutical Engineering (ISPE), American Society of Quality (ASQ) and others. Organizations such as these are always updating publications based on current industry and regulatory trends. Investigate these sources as much as possible. In many cases these groups will explain how to perform certain tasks in a compliant manner. The ISPE GAMP guide for calibration programs even provides detailed process flow diagrams. Never forget to reach out to other industry professionals to see what they do (benchmarking). Refer to Diagram 1 for an example of a process flow diagram.

Diagram 1. Process Flow Diagram Example



At a minimum, every calibration program needs one SOP that governs the critical aspects of the program and one SOP that explains the CCMS/CMMS system. Another necessity is for general SOPs on how to calibrate different parameters such as temperature, pressure, humidity, etc. As a program expands, there

may be a need for more specificity, adding SOPs that explain how to calibrate specific/critical instruments, how to process out-of-tolerance (OOT) findings, the swapping of "Instrument Twins", among others that will create consistency. It is highly important to not repeat certain information in these procedures, such as what CCMS is used, calibration frequencies, test points, or tolerances. All of this can be found in the CCMS, and by keeping the information in one location (CCMS), the accuracy of the data will be intact. By tracking the same information in more than one location there is a great risk of inaccurate information being discovered during a regulatory audit. A common litmus test for SOPs is to ask "Is the SOP written specific enough to be helpful, but not too detailed to require immediate revisions or compliance gaps." Constant revision of SOPs add significant overhead to an organization.

CLASSIFICATION OF INSTRUMENTATION (CRITICALITY/GMP RISK)

In today's fast paced, ever-changing economic landscape, there is always a limit to the amount of resources a calibration department has available to execute their scope of responsibility. As such, it is highly advantageous to group all instruments into certain "Risk" categories based on GMP impact (safety, identity, strength, purity, and quality) and also safety/business impact. Performing the assessment before an instrument is put into use allows the company, specifically the calibration department, to focus the majority of their resources on the instruments that carry the most associated risk. This process, well defined by the ISPE GAMP guide for calibration programs, is a multidisciplinary effort that typically consists of representatives from engineering or calibration, production (system owner) and quality.

First, the team must agree and document the instrument risk classification names and definitions in their program SOP. ISPE gives good examples, but it is important to be creative to meet specific business needs (GMP critical, non-critical, safety, for reference only, etc.). Next, assemble multidiscipline representatives and assign each instrument a classification and other variables such as operating range. The classification is typically recorded as part of the asset information in the CCMS. Based on risk and other factors, the calibration department can identify calibration frequency, calibration tolerances, and other information helpful for calibration including selection of calibration standards. Finally, the organization must agree what actions are required when the instrument fails calibration or has other performance-limiting factors. An example can be found in Diagram 2 below.

Diagram 2. Instrument Classification and Actions

Instrument Classification/Actions				
Calibration Issue	GMP Critical	Business Critical or Non Critical	Safety	For Reference Only
Instrument Missing	Immediately notify system owner and Quality, initiate deviation, and inactivate instrument if it is not found.	Immediately notify system owner and inactivate instrument if it is not found.	Immediately notify system owner and EH&S, initiate deviation, and inactivate instrument if it is not found.	Immediately notify system owner and inactivate instrument if it is not found.
Past Due for Calibration and not tagged "OOS"	Immediately notify system owner and Quality. Initiate deviation and tag instrument "OOS".	Immediately notify system owner and Quality. Initiate deviation and tag instrument "OOS".	Immediately notify system owner and EH&S. Initiate deviation and tag instrument "OOS".	N/A
"As Found" calibration data cannot be obtained	Immediately notify system owner and Quality. initiate repairs and/or corrective actions. Initiate deviation and tag instrument "OOS".	Immediately notify system owner and initiate repairs and/or corrective actions. Tag instrument "OOS".	Immediately notify system owner and initiate repairs and/or corrective actions. Tag instrument "OOS".	N/A
Inside "Adjustment Tolerance"	No adjustment is required. Peform and complete calibration as per procedures.	No adjustment is required. Peform and complete calibration as per procedures.	No adjustment is required. Peform and complete calibration as per procedures.	N/A
Outside "Adjustment Tolerance" but inside "Calibration Tolerance"	Adjust instrument. Perform and complete calibration as per procedures.	Adjust instrument. Perform and complete calibration as per procedures.	Adjust instrument. Perform and complete calibration as per procedures.	N/A
Outside of "Calibration Tolerance"	Immediately notify system owner and Quality, initiate deviation. Adjust instrument to within "Adjustment Tolerance"and complete calibration as per procedures.	Immediately notify system owner. Adjust instrument to within "Adjustment Tolerance"and complete calibration as per procedures.	Immediately notify system owner and Quality, initiate deviation. Adjust instrument to within "Adjustment Tolerance"and complete calibration as per procedures.	N/A
Instrument cannot be adjusted to within "Adjustment Tolerance"	Immediately notify system owner and Quality. initiate repairs and/or corrective actions. Initiate deviation and tag instrument "OOS".	Immediately notify system owner and initiate repairs and/or corrective actions. Tag instrument "OOS".	Immediately notify system owner and initiate repairs and/or corrective actions. Tag instrument "OOS".	N/A

CALIBRATION STANDARDS

If calibrations will be performed onsite, a set of calibration standards (sometimes referred to as transfer standards) will be required. This special set of instruments that belong to the calibration department usually have a high degree of accuracy and are typically quite expensive to purchase and maintain. The average cost of a standard is $200 to $7,000. However, some standards can be significantly more expensive. Before purchasing a standard, the calibration department has to make sure that it is accurate enough and has a suitable range of operation. Generally, the accuracy of these standards should be three or four times greater than the instruments being calibrated. This common industry best practice is a way to reduce the error associated with making measurements using a calibrated instrument.

It is quite typical for a department to buy standards in duplicate and stagger the calibration dates so at least one of the two standards is always onsite and ready for use. The typical calibration cycle for standards is 6 to 12 months; however, some calibrations may be more often (such as humidity standards) or less often (optical standards and weights such as NIST Class F). Standards can be sent back to the Original Equipment Manufacturer (OEM) for calibration or an accredited third party calibration laboratory. OEMs calibration cost tend to be higher, however, they can typically perform more advanced repairs. Non-OEMs offer one-stop

shopping for standards and sometime have quicker turn-around times at reduced cost. Depending on quality system and accuracy requirements, look for an accredited lab which can provide the uncertainties associated with each type of calibration (pressure, temperature, humidity, etc.). Also, some standards are easily checked between calibrations. This helps limit the number of calibrations that are subject to investigation if the standard is found OOT when it comes due to routine calibration. Humidity standards can be checked against saturated salt solutions (Various %RH environments between 10 and 90%RH) or in an environmental chamber. Temperature standards can be checked against an equilibrated ice bath (0°C).

Larger companies will often purchase the capital equipment and train dedicated staff to calibrate transfer standards in-house because it is cost effective. Calibration of transfer standards by OEM or vendors can be quite significant, so calibrating in-house can reduce cost and turn-around time.

Be certain to remove from service all transfer standards which are not being used. It's very common to stockpile standards and continue to calibrate them even though they are not being used. This can be a significant overhead expense related to cost of ownership, vendor management, and metrics. It is common that the percent OOT for standards will be higher than the percent OOT for operating instrumentation. This is due to the fact that the standards are designed to be mobile and may take more abuse than a permanently installed instrument.

PERFORMANCE METRICS

There is a phrase "If you can't measure it you can't control it". This is very true for calibration programs. At some point a calibration department must initiate routine trending of important data. Trending not only shows what the calibration department is doing well but also what needs improving.

Metrics can be generated by using either database queries to generate key numbers or by writing a CCMS key performance indicator (KPI) using built-in software tools. When using database queries (least expensive route), it is a good idea to pick a certain point during the month and generate a query to export to a spreadsheet. Post the numbers in the spreadsheet and trend the data in a graph. Post metrics so management and the calibration team can see the trends. Monthly trending and corrective action (when needed) will contribute to a "continual Improvement" mentality and generate further ideas/calibration team involvement. Important metrics that could be tracked routinely include:

- Number of Instruments in the calibration program
- Percentage of active instruments being calibrated
- Percent of instruments out of service, inactive, etc.
- 30, 60, 90 day projection of calibration WOs (or FTEs required if there is data to support)
- Backlog (unscheduled calibration WOs with FTE data if possible)
- Overdue calibration WOs
- Calibrations completed
- Percent of calibrations OOT

- Percent of calibrations adjusted
- Percent of calibration WOs returned for corrections
- Percent of calibration WOs completed (Weekly metric to track/coordinate resources)
- Technician hours per calibration WO

Reviewing metrics and setting goals can significantly improve various operational efficiencies. For example, one organization continually experienced an OOT rate of 13%. This organization also put the internal cost of each OOT investigation at $5k (investigation, impact statement, review and document time, tracking time, etc.) If there were 100 calibrations due in a month and the cost of each OOT occurrence was approximately $5k, then the 13% OOT was costing the company about $65k per month in additional overhead. Various corrective actions finally achieved a 1% OOT rate after about two years of focus (purchasing better instrumentation, assigning better tolerances, selecting better standards, staff training, better planning and scheduling, etc.).

In another example, calibration departments can gain significant efficiency simply by reviewing the common classes of instrumentation (same manufacturer and similar use) and permanently extend the calibration periodicity from 6 to 9 months (example) if historical calibration indicates the instrument will remain in tolerance at the new periodicity. SMEs should review the calibration due list for cycle change candidates every month and identify instruments that can be extended. Organizations that do this can sometimes reduce their calibration workloads by up to 20% in one year alone. These efficiency gains will make the calibration department shine but also allow time for new projects, training, and other cross-functional activities. This will also improve morale if the calibration technicians are overscheduled.

INSTRUMENT TOLERANCES

Before discussing instrument tolerance it is important to discuss purchasing suitable instrumentation. A best-in-class organization will allow the calibration/engineering department to help specify instrumentation before it is ordered/arrives onsite. This ensures the instrument will meet the process requirements. At a minimum, this collaboration increases the site's instrument uniformity while minimizing staff training needs, calibration methods, standards, and service vendors. It also provides a unique opportunity for increased instrument reliability. However, in many organizations (especially smaller organizations) the task of specifying instrumentation falls to the instrument owner without calibration department/SME consultation. As such, the instrumentation arrives on site before an engineer or calibration SME has had time to provide input. This causes "reactive" responses instead of "proactive" efforts, adding to the company's direct and indirect costs.

Generally, when an instrument does not meet calibration tolerance there is a potential risk to product quality, business efficiency, and sometimes risk to personnel safety. When developing calibration tolerances the calibration group must follow their internal/corporate procedures which usually act as a guide to determining a tolerance. Some organizations expect their instrumentation to perform to the OEM tolerances. While it is easy to find these tolerances (found in OEM manual and cutsheets) this is often a problematic way

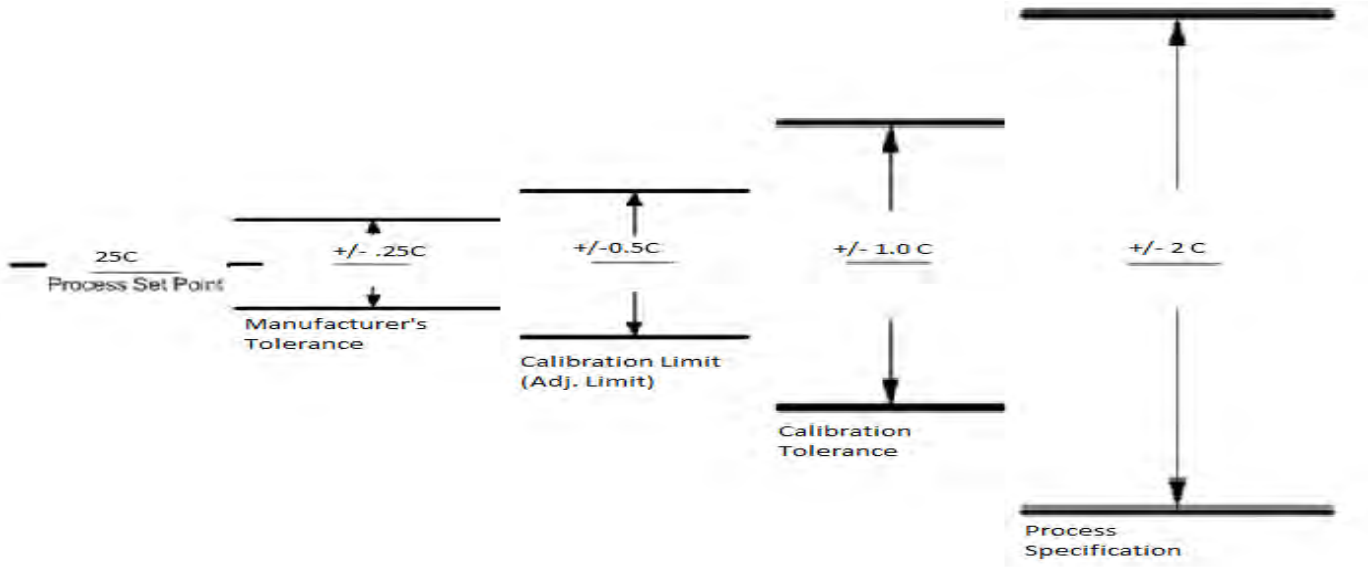
to establish tolerances since OEMs specify tolerances typically under “Best-case” conditions. Calibration to OEM tolerances will sometimes result in two unnecessary and costly reactions. First, a high accuracy standard may be required or a standard of unsuitable accuracy will be used for calibration. Second, the instrument will not routinely pass calibration causing more “reaction-based” organization behavior such as spending significant time investigation failures and even potentially replacing good instrumentation. One of the best ways to establish instrument tolerances is to allow the calibration group to factor in other important variables such as:

- OEM established tolerances
- Historical data from other identical/similar instruments onsite
- Instrument classification (how critical is instrument)
- Use of instrument (high usage or other physical risks of damage)
- Accuracy of the standard
- Process requirements

If this preferred method for establishing tolerances can be put into effect, there will be various organizational gains such as reduced instrument adjustments and reduced OOT conditions. Having to make unnecessary adjustments can double, even quadruple, the expected amount of time it takes to calibrate an instrument. The tolerances must be documented and approved. Refer to Diagram 3 for an example of setting temperature tolerances. Approval should include at least the system owner and a representative from Quality. A change in tolerance should include re-approval by the assessment team.

Some organizations also document and approve a Process Specification (usually only when the process is well-defined and not subject to frequent changes). Process Specifications (Diagram 3, far right) are usually set wider than the calibration tolerance. Setting a Process Specification requires a little more “Upfront” effort when the instrument is purchased but it will significantly minimize the investigating effort related to a calibration OOT finding. Essentially, an organization (based on written procedure) may not have to investigate every OOT instrument for product impact unless the calibration data is outside the Process Specification.

Diagram 3. Instrument Tolerance Levels



OUT OF TOLERANCE INVESTIGATIONS

As noted above, there are many ways to reduce the number of investigations for instrumentation found OOT. There is significant cost savings in reducing this effort which allows the organization to focus on their value stream. Keep in mind that when an instrument OOT does occur it should be "noteworthy" in that the failure is significant and should be evaluated with a corresponding level of effort. Many organizations generate significant numbers of insignificant OOT events and as such each one may not be investigated as thoroughly as it otherwise should have been. This happens all too often and can represent a significant compliance gap.

A few key facts regarding investigations must be noted. The OOT reporting follows a workflow that is formally documented and adhered to rigorously (software process flow is best). Once an OOT condition is realized, notification to the relevant parties (System Owner, Validation, and/or Quality) should be immediate and can consist of verbal and/or written communication. The OOT should be investigated by a calibration SME first (within 1 business day) to ensure there are no technical errors and to review the instruments prior calibration history. Sometime a subsequent follow-up calibration is warranted or even instrument replacement. In some cases these investigations are first performed by an Engineer or a Quality representative. The investigation needs to be thorough and follow a standard practice such as RCA (Root Cause Analysis) or MEEPS (Method, Environment, Equipment, Personnel, and Systems). This investigation needs to be documented in the CCMS or other quality system as defined by approved procedures. Ensure that a good CAPA (Corrective Action and Preventative Action) system is in place to ensure all corrective actions are recorded, tracked, executed, and effective. Regulators have continued to focus on the effectiveness of a company's CAPA program. Furthermore, sound investigations and corrective actions can significantly reduce the OOT rate, and therefore reduce overhead costs for an organization.

PLANNING AND SCHEDULING

In a smaller company, the scheduling of calibration work orders is fairly simple and commonly does not take significant effort. There are fewer people in the organization, fewer processes, and typically larger periods of process equipment downtime in which the calibrations can be performed. As the organization grows it becomes increasingly difficult to schedule the work orders for various reasons (spare part availability, equipment availability, projects, staff availability, etc.). These issues cause inefficiency and, in some cases, compliance gaps when critical service activities are not performed on time. At some point the organization will want to conduct routine scheduling meetings to better understand and resolve these issues to maximize organizational and equipment efficiency. These routine meetings may involve a couple of staff members who review at a 1-week, 1-month, and/or a 60-day outlook. At some point production and maintenance will be involved as well. Larger organizations will have well-coordinated shutdowns for invasive maintenance and significant repairs. This will ensure equipment service activities are complete, on schedule, and execution efforts have minimal impact to critical equipment uptime.

VENDOR MANAGEMENT

A typical life sciences company will have either a corporate policy on vendor management or a site specific standard operating procedure - sometimes both. These documents are put in place to confirm that critical service vendors are performing as they should and to hopefully weed out service organizations that may not perform to expectations. These vendor management programs are typically risk-based (i.e. active ingredient suppliers get audited more often with increased scrutiny since the risk of product impact is higher).

In some cases calibration vendors require approval (or conditional approval) by Quality before a calibration department can utilize the vendor's services. In a majority of cases the OEM is considered "approved" by default and does not need routine auditing unless an audit is warranted for another reason such as a CAPA. Non-OEM vendors will require some form of an audit and subsequent approval. Due to the various "Accrediting" programs and their rigorous lab requirements it is much easier to identify and select a good vendor today than in times past. Commonly, these service providers will have Quality Systems in place and also have a current ISO or A2LA certificate of accreditation. Associated with this certificate is a "Scope" of accreditation that will provide specific details regarding the vendor's measurement capabilities. A calibration SME can review this scope and determine if the service provider is technically competent to perform specific calibrations.

It is important to understand an organization's policies and procedures on vendor management. The calibration department needs to be aware of who the vendors are and be vigilant to close any gaps. Many companies do not have the systems in place to control their use of vendors and all too often the calibration department can used an unapproved vendor. Past experience indicates that vendor control is important. But just as critical is to review service vendors' calibration documentation thoroughly when calibrations are performed. This documentation will often highlight when a vendor is having internal issues (turnaround time, data inconsistency, delays, training issues, mix-ups, unexpected failures, issues with standards, etc.).

SUMMARY

Hopefully this article has provided several ideas on improving an organization's calibration program. Joining ISPE and reading the latest edition of the GAMP guide for calibration programs will also help generate ideas and practices that create better programs and positive results. Reach out to like-minded individuals in the industry, learning how their calibration program operates. Understanding what works and doesn't work before implementing changes help avoid negative impacts to a company's calibration program.

Finally, ensure that company procedures are followed. This is by far the most common regulatory finding when a calibration department is audited.

Questions can be emailed to Jon Doyle at jdoyle@pci-llc.com. Jon Doyle is a Sr. Consultant with Pharmaceutical Calibrations and Instrumentation (PCI). Jon has worked for PCI several years and is located in Raleigh, NC. He has been in the life-sciences industry for over 15 years primarily building, managing, remediating, and streamlining several life sciences calibration programs. He has experience in Quality Control and Maintenance systems as well as various computerized asset management systems. PCI is a full scope calibration service provider which has several locations throughout the United States. Visit www.pci-llc.com for more information.

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