



# Carolina-South Atlantic Chapter

ENGINEERING  
PHARMACEUTICAL  
INNOVATION

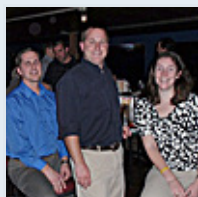


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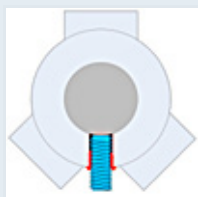
Engineering Pharmaceutical Innovation

SPRING 2011

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## Don't miss it!



## CaSA ISPE's 18th Annual Life Sciences Technology Show

### April 5, 2011

See page 5 for details...

# President's Message



Scott Billman  
CaSA President

## Spring into Volunteerism!

Sorry for the obvious pun. I just couldn't resist! It was between that and another bad pun about March Madness. As we get into the swing of the Spring events in CaSA, we are looking for volunteers. It's a great way to get more involved in your local ISPE chapter and network with

your peers in the industry. I hope you take the time to come to some of the events planned by our various committees. If you see anything that interests you please reach out to one of the Board Members or Chapter Managers to start getting involved.

First up is CaSA's ISPE Therapeutic Thursday Networking Event on March 31 from 5:30-7:30 PM at the Carolina Ale House in Cary, NC. Therapeutic Thursday will occur on the last Thursday of every month at the Carolina Ale House in Cary, NC. This relaxing networking event is hosted by the Membership Committee.

On April 1, the Annual CaSA ISPE Student Poster Competition (4:30 PM) will be held at NC State's BTEC Center. Undergraduate and graduate student abstract submissions are due by March 28. Judges are still needed for this event. Abstract submissions from students and volunteers interested in being a judge, contact Amy Lineberry at the following email address: [ispecasasac@gmail.com](mailto:ispecasasac@gmail.com).

On April 5, the 18th Annual Technology Show will be held at the RBC Center. This year's show includes many great programs led by industry experts from our region.

The RBC Center offers the perfect accommodations for the class room settings, the Career Development Fair, and ample space to network with the exhibitors. Take the time and come out to see it.

On April 12, the Young Professional Spring Social/ Bowling and Networking Event will be held at Sparians in Raleigh, NC. Students, and both young and seasoned professionals are welcome to attend this event. There is a \$5 discount if you register prior to April 1 (Students and YP are \$15 and Professionals are \$20). On-line registration for the event is at : [www.ispe-casa.org](http://www.ispe-casa.org) and registration includes the following: bowling cost, show rentals and food. There will be a cash bar available.

On May 16th the Annual Golf Outing is moving to a new venue. This year Prestonwood Country Club will host the event. Prestonwood allows us the opportunity to open the event to many more golfers. So I challenge the membership to try and fill out two full courses!

I want to congratulate the NCSU Student Chapter for winning the ISPE International Student Chapter of the year award. This was well deserved as they have been one of the most active student chapters I have seen in my 15 years of ISPE involvement. A special thanks to Amy Lineberry for leading our Student Affairs Committee for the past two years. Her dedication and leadership for the student chapters is amazing.

Our Young Professionals and Programs Committees continue to keep busy. We look forward to seeing you at one of the many events they have planned over the next several months. Thanks for your continued involvement with ISPE.

*Scott Billman*  
Chapter President



## Carolina-South Atlantic Chapter

ENGINEERING  
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### 2010-2011 Board of Directors

#### Officers

- Scott Billman, President
- David Brande, Vice President
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- Wendy Haines, Communications
- Heather Denny, Membership
- David Knorr, Programs
- Amy Lineberry, Students
- Blake Derrick, Young Professionals
- Alan Tucker, Technology Show

# Young Professional Committee Update

By: Blake Derrick, YP Committee Chair

The ISPE Young Professionals group had a great initial year in 2010, and was able to have several events in the latter half of the year that helped to build the group from the ground up. Prior to the Summer of 2010, we had a few social events including a picnic, dinners at local restaurants, and a small educational event focused on continuing education programs offered at N.C. State University. Our YP group finished out the summer season strong with a fun bowling event in August, in which over twenty ISPE young professionals gathered together for an evening of networking at Pleasant Valley Lanes in Raleigh, NC. We had an excellent turn-out and it was great to participate in conversations among industry professionals from several local biopharmaceutical firms. With a majority of the attendees being first-time participants in the group, it was encouraging to see new relationships form and opportunities to meet colleagues from various organizations.

In October, a group of YPs met at Vintage Lounge in downtown Raleigh after work for a time to catch up and networking. What I've found to be most encouraging about these events is the mix of attendees each time we meet. There never seems to be the exact same group, as we've regularly seen new people who have recently moved to the area for a new job opportunity, or some who are just recently heard about the new YP offerings through ISPE-CaSA.

In November, we held an educational event at the BTEC amphitheater at NC State, in which we gained some valuable insights into the topic of business ethics. Our speaker facilitated the meeting with thought-provoking discussion in a highly interactive atmosphere. This was also our first event that was open to all of ISPE-CaSA, and reflects the new initiative for 2011 to provide opportunities for the YPs to become more involved with ISPE as a whole.

We finished 2010 with our biggest YP event yet in December with a brewery tour and networking social at Aviator Brewery in Fuquay Varina. This event brought a mixture of students, Young Professionals, and experienced ISPE members together as we closed out the year. Looking back, it's encouraging to see the progress we've made in drawing together a community of young professionals in the pharmaceutical/biotechnology industry that can participate together in local ISPE events.

On February 5, 2011, the Young Professionals Group, led by Jennifer Lauria Clark, put on the CaSA Leadership Symposium at the McKimmon Center at NC State University. This year's focus was driven towards the issues most relevant to Young Professionals, and speaker topics included: networking, preparing for performance reviews, conflict resolution in the workplace, personal finances,

and the Myers Brigg Personality assessment. The event was followed by a networking dinner at Busy Bee in downtown Raleigh.

Our next big event occurs on April 12th, as the Young Professionals Committee invites you to come join your colleagues in ISPE for an evening of bowling and networking at the brand new Sparians Bowling Boutique and Bistro near the North Hills shopping area in Raleigh, NC. We'll have our own ISPE bowling room with private catering, event staff, and unique entertainment atmosphere including huge projection screens and black-light illuminated bowling. Be sure to visit [http://www.ispe-casa.org/2011\\_html/spSprSoc.html](http://www.ispe-casa.org/2011_html/spSprSoc.html) for registration details.

We've also considered new ways to provide more consistent opportunities to connect the next generation of ISPE professionals with industry veterans within ISPE-CaSA. The Young Professionals Committee is partnering with the Membership Committee to hold "Therapeutic Thursdays" on the last Thursday of every month.



The next networking social will be held at the Carolina Ale House in Cary on March 31 from 5:30-7:30. If you're interested in hearing about these and other ISPE CaSA YP events we'll be holding this year, please send an email to [casayoungprofessionals@gmail.com](mailto:casayoungprofessionals@gmail.com). We'll be happy to add you to our list to receive email announcements as events are planned throughout 2011.

# Bray®

*The CaSA ISPE Therapeutic Thursdays are proudly sponsored by Bray.*





# Student Perspectives

## Student Activities 2010 Year-In-Review

By Amy Lineberry, Student Activities Chair for CaSA ISPE

The objective of the Student Activities Committee is to provide support, events and networking opportunities to the students at our colleges and universities. We had several wonderful events during 2010 and added new chapters as well. East Tennessee State University, Meredith College, and NC A&T were all chartered in 2010. NC A&T was an existing school that had gone dormant. East Carolina should be officially chartered in the coming weeks. If you would like to help with the events or speak at a school please let us know by emailing [ispecasasac@gmail.com](mailto:ispecasasac@gmail.com)

Below are Highlights of the 21010 CASA ISPE Student Events:

### The Career Coaching Workshop

The workshop was held at the McKimmon Center at NC State University. With over 150 students and professionals in attendance, the students made many great connections. This gave the schools a chance to mingle with other students and many professionals. We talked about resumes, interviewing skills, Email & Social Networking Etiquette, and How to keep the Job once you get it.

### Career Fair & Poster Competition

The Career Fair is held each year in partnership with BTEC at NC State. The fair has booths in the lobby but also has a unique format of question and answer team interviews. Several of the students from all universities are invited and many walk away with further interviews and internships. The Poster Competition is held after the last interview session. For 2010, the undergraduate winner was Juan Cueva from NC State University and the graduate winner was LeAnna Pearson from NC Central University. They both received an all expenses paid trip to the 2010 Annual Meeting in Orlando and presented at the International Level.

### Student Trip to the 2010 Annual Meeting

Every year CaSA helps to send students from our local universities to the Annual Meeting and 2010 was our best year yet! The students put their heads together and came up with transportation and hotel ideas to reduce the cost for the trip. This year 19 students attended the meeting for the CaSA Chapter. Every year we receive so many wonderful comments from everyone at the Meeting about how professional our students are and this year was no different.

To top off the year, NC State won Student Chapter of the Year. We are so proud of them! CaSA also won the Grand Award for Innovation in Student Programs. Winning these awards would not be possible without the help of the wonderful volunteers in the CaSA Chapter. We are looking forward to more wonderful events in 2011!

### Upcoming Student and Young Professional Events in 2011

#### CASA ISPE Student Poster Competition (Undergraduate and Graduate Students)

**Date:** April 1, 2011 at 4:30 PM  
**Location:** NC State BTEC Center 850 Oval Drive, NC State Centennial Campus  
**Abstract Deadline:** Abstracts due March 28th, send to [ispecasasac@gmail.com](mailto:ispecasasac@gmail.com)  
**Judges:** Need more judges, send email to: [ispecasasac@gmail.com](mailto:ispecasasac@gmail.com)

#### Young Professional Spring Social—Bowling and Networking

**Date:** April 12, 2011  
**Location:** Sparians, 141 Park at North Hills St, Suite 120, Raleigh, NC 27609  
**Registration:** Required and includes bowling cost, show rentals and food, go to: [www.ispe-casa.org](http://www.ispe-casa.org) for registration details  
**Cost:** (Cash Bar)  
 —YP \$15 before April 1, 2011 and \$20 after April 1, 2011  
 —Professionals \$20 before April 1, 2011 and \$25 after April 1, 2011

# Student Perspectives

## Overview of the 2010 ISPE Annual Meeting

From a North Carolina State University Student

*By Nick Butterbaugh, Treasurer of NCSU ISPE Student Chapter*

Being a board member of NC State's ISPE chapter offers several unique privileges. My involvement as the treasurer has allowed me to meet industry professionals, plan and organize events, and participate in team building. I was excited when the opportunity to attend ISPE's 2010 Annual Meeting presented itself, because it ultimately involved all these great aspects and more.

The first day of the meeting, the International Young Professionals held an introduction luncheon for the students and Young Professionals at the Meeting. I enjoyed this time, because it not only allowed me to begin networking, but it eased my nerves. Knowing that I was surrounded by distinguished professionals involved in the career path I am pursuing is daunting. However, this lunch was casual and informal and eased me comfortably into the situation. Later that day, I enjoyed the opening of the vendor show. I learned about technology, equipment, and services that are being used in the pharmaceutical industry that are new and novel or tried and true.

I also attended a few educational sessions including a regulatory issues discussion panel and both of the Facility of the Year Awards presentations. These provided insight into specific topics and breakthroughs in the industry. One of the best moments of the meeting came when NC State won "Student Chapter of the Year" at the membership luncheon. It was fantastic to get recognized

for being involved in an outstanding group. Personally, I have only been involved with ISPE for two years, and this is only my first year on the executive board. However, I am very grateful to my predecessors who have put in so much time and effort to establish a student organization that is so effective. I am proud to be involved with this group and help continue the tradition.

After the fun time during the Tuesday Night Party, another unexpected honor and surprise came when the NC State students were invited up to Mr. Andre Walker's suite. Winning the Student Chapter of the Year award granted us this opportunity. This was a great privilege and allowed us to mingle with important professionals in an uncommon setting.

The Annual Meeting provided an excellent opportunity to develop professionally. This being my first conference of this type, I learned a lot about engaging in networking, trends and happenings in the pharmaceutical industry. It was an honor to meet so many great people who work in a diverse array of areas within the pharmaceutical industry. I am very appreciative for CASA in helping to facilitate the students of NC State and NC Central to attend this event. Being a student amongst so many professionals was a wonderful opportunity, which I hope many future peers are able to experience.



## CaSA ISPE's 18th Annual Life Sciences Technology Show April 5, 2011

*By Alan Tucker, Technology Show Committee Chair*

The 18th Annual ISPE-CaSA Life Sciences Technology Show is being held April 5, 2011 at the RBC Center in Raleigh, NC (home of the Carolina Hurricanes and NC State Men's Basketball). Doors open at 9:30.

The Show is approaching "Sell Out" status with only 8 tabletop exhibit spaces remaining. There are over 150 exhibitors registered to display equipment, services and innovations for the life sciences industry. The event remains FREE of charge to all attendees who preregister online at [www.ISPE-CASA.org](http://www.ISPE-CASA.org) and promises to include a fantastic curriculum and a Career Development Fair! The Career Development Fair will be our largest ever with major operating companies and colleges and universities represented.

## Another Successful Toys for Tots Drive!

*By Jane Brown, Membership Committee Member  
Heather Denny, Membership Committee Chair*

On December 10, 2010, the CASA Chapter sponsored its Annual Toys for Tots drive at GSK in RTP. Members came together once again and made the event a huge success. Those who attended enjoyed a continental breakfast and shared good conversation with each other, making it a nice break from year-end work schedules and the busy holiday season. They also enjoyed displaying (and in some cases playing with!) the toys as they were delivered. Stuffed animals, dolls, games, building blocks, and lots of other toys were collected by member companies, student chapters, and at various drop locations throughout the Triangle.

The United States Marine Corps developed the Toys for Tots outreach program so that no child or parent in financial need would have to face disappointment on the holiday celebrating the spirit of giving. In spite of challenging economic times, our members helped to ensure that many children found something special from Santa under the tree on Christmas morning. Due to an unexpected emergency, the Marines were not able to at-

tend to collect the toys, and it took several cars/trucks to deliver the toys to their Headquarters following the breakfast.

**A big thank you goes out to the companies and members that participated to make this year's event a success. Your demonstration of kindness and community spirit is something that CASA prides itself in maintaining year after year.**





# Membership Update

## Membership Committee Update

*By Heather Denny, Membership Committee Chair*

### Casino Night

We rolled the dice and won! With a 12% increase in attendance 130 members and guests enjoyed the evening. Thank you to our premiere sponsors CRB, McDonald York Building Company and PCI. Thanks also to table sponsors Avid Solutions and Bahson Environmental Specialties. The event was held in downtown Raleigh at the Capital City Club with gaming and music provided by All-In Entertainment. Our top three “fake” money winners participated in a reverse raffle to take home Visa Gift Cards. Congratulations to Chris Marrow, Dr. George Berg and Suzanne Schappell.

### Golf Tournament

Come out and enjoy a day of golf at Prestonwood Country Club, Monday May 16th. Watch for details the 1st of April.

### Therapeutic Thursday

The last Thursday of every month come out and unwind with fellow CASA members. March 31st from 5:30 - 7:30pm at the Carolina Ale House at Crossroads in Cary, NC. Food sponsored by Bray.

### New Member Orientation

**Who:** New Members

**What:** New Member Orientation

**When:** Tuesday, April 5th, 8:30 - 9:30 am

**Where:** RBC Center, Varsity Club Room  
(Same day and location as the Tech Show!)

**What:** Come grab a cup of coffee and pastry. Start your Tech Show Day off with an introduction of the ISPE CASA Chapter from our president Scott Billman, meet the committee chairs, and learn how to make the most of your Tech Show Experience.

**Cost: FREE OF CHARGE** – You must be registered for the Tech Show to attend the New Member Orientation.



# Technical Section

## Calibration Discussion Group takes on more than Instrumentation

By Natalie Carrick of PCI

Wednesday, February 16th, 2011 marked the 10th Annual PCI sponsored Calibration Discussion Group event, co-hosted by Novo Nordisk Pharmaceuticals. This one-day event was held in Clayton, NC. This event pools instrumentation, engineering, and quality professionals from the pharmaceutical and biotech industries to share common approaches, issues, and solutions for the everyday obstacles associated with managing a quality instrumentation program. Over 55 attendees from over 25 life science companies traveled to attend this event. Participants this year were eager to share ideas and explain the processes and course of actions used at their facilities.

The day started off with a site overview of Novo Nordisk Pharmaceuticals by Troy Woelfel, Director of Production Support. He discussed the background and history of Novo Nordisk including Balancing the Triple Bottom Line and the Balanced Score Card = Sustainability, Product Supply Mission, as well as the site layout, products, and processes keeping Novo Nordisk the leader in diabetes care. For more information about Novo Nordisk Pharmaceuticals, go to [www.novonordisk.com](http://www.novonordisk.com).

Mike Rooney, Ph. D., Senior Manager in Analytical Services, of BioTech Logic was the next presenter with vast knowledge of the PAT Instrumentation Challenges. He explained the what, when, and why of Process Analytical Technology (PAT) as well as the PAT tools including Multivariate Analyses, Process Analyzers, Process Control Tools, and Continuous Improvement. Mike also came equipped with 2 case studies which led into a great discussion.

Jim Bufano, PCI Senior Consultant, then spoke about the FDA Warning Letters on Calibration Issues. His insight in Food and Drugs, Current Good Manufacturing Practice for Finished Pharmaceuticals, and Automatic, Mechanical, and Electronic Equipment was greatly appreciated by all who attended.

Next up was Dr. Wes Tew, Staff Physicist, of NIST with a presentation on Calibration: What's Good Enough. He discussed Temperature Sensor Types and Performance, Standard Specifications & Quality Management, Calibration Uncertainty and Error, and Accreditation: NVLAP and Proficiency Testing.

Jim Bufano, PCI Senior Consultant and Jim Erickson, President of Blue Mountain Quality Resources then spoke about the Features, Benefits, and Lessons Learned of a Paperless Calibration System. They discussed the Productivity Improvement, Higher Levels of Quality, and Increased Compliance within a Paperless Calibration System.



CDG Presenter - Troy Woelfel of Novo Nordisk Pharmaceuticals

Lastly, a panel discussion was led by Phil Smith, Public Affairs Manager, of A2LA about the A2LA Accreditation.

A few of the companies represented included: Almac Clinical Services, APP Pharmaceuticals, Argos Therapeutics, Avid Solutions, Biogen Idec, bioMerieux, Eisai, Hospira, Johnson Controls, MedImmune, Merck, Metrics, Microbac, Novartis, Pfizer, RTI International, Statesville Process Instruments, Talecris Biotherapeutics, and USP.

Pharmaceutical professionals who have process, laboratory or utility instrumentation responsibilities who would like to participate in future annual events should email Andy Ferrell at [aferrell@pci-llc.com](mailto:aferrell@pci-llc.com) or join the CDG LinkedIn page at <http://www.linkedin.com/groups/Calibration-Discussion-Group-2755997?mostPopular=&gid=2755997>. This is not limited to instrumentation & controls personnel. This forum is also for those in quality assurance, quality control, engineering, and production.





# Technical Section

## Reduce the operating costs of your HVAC system by Using Pressure Independent Variable Flow Control Valves

By Joe Seufert P.E. Griffin Engineering and Technical Services, Inc.

Low system  $\Delta T$  (differential temperature) can often result in high system operating costs and low system efficiency. This often occurs at lower demand loads where the system instability results in over pumping of the coils. Pressure independent control valves can help resolve this issue by ensuring that the coil operates at the correct  $\Delta T$  throughout the operational range. Remember in our region of the country, the HVAC systems operate at maximum design load only about 1% of the time so the opportunity for part load savings are considerable.

We first need to understand what pressure dependent and independent control valves are and how they operate.

Pressure dependent control valves (butterfly, ball, and globe) rely on the differential pressure provided by the pump to control the amount of hydronic fluid provided to the load, as other control valves open and close the system pressure changes this results in a change in the amount of chilled or hot water delivered to the coil. If the system differential pressure increases the flow through the valve increases (fixed Cv balancing valve coupled with two way, open/closed, control valve) resulting in over flow conditions.

Pressure independent control valves are actually two valves in one housing. The first valve is typically a characterized ball or shoe valve and the second valve is an automatic pressure compensating valve. This creates a control valve that automatically compensates for fluctuations in the system pressure delivering the correct amount of chilled or hot water to the coil. This results in better load matching increasing system performance and efficiency.

In the early years most hydronic systems were designed as pressure dependent constant volume systems. This meant that the pumps ran at the same speed and moved the same volume of water all of the time. This is accomplished by installing three way control valves

that either ported the water to the coil, bypassed it to the return line or some combination of supply/return. This system is very inefficient resulting in high operating costs.

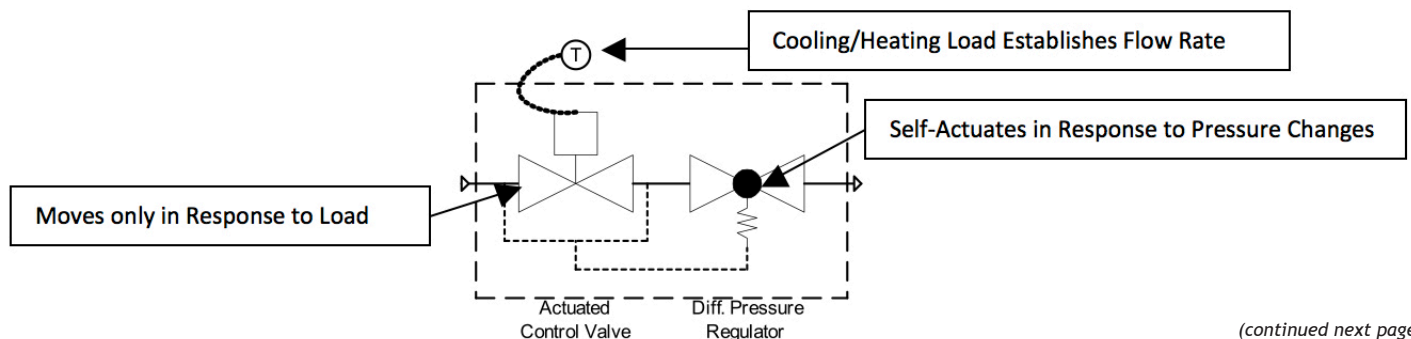
The next type of system to come along was the variable flow pressure dependent system. This system adds a variable speed drive to the pump, a remote differential pressure transmitter to the control system, and two way control valves to control the hydronic flow at the load. While this system was more expensive to design and install it significantly reduced operating costs resulting in a payback over the life cycle of the system. This is the most common type of system used in the HVAC industry today.

Both of these systems are pressure dependent because they rely on the pressure differential of the system to develop the proper flow through the control valve. This can result in under pumping and over pumping of the hydronic system reducing system performance and efficiency.

Water balancing the system can't resolve the issues with system pressure changes, balancing the system only proportions the hydronic flow at maximum flow values.

- Traditional Balancing
- Limits the flow to design when every branch is flowing at full design flow rate
- Is difficult to achieve with traditional products and methodology
- Does not address part load issues
- Has a high labor cost associated with it

The newest type of high efficiency systems use variable speed pumping coupled with a pressure independent control valves resulting in a more efficient operating system. Typical system efficiency increase with pressure independent control valves are 5 to 15%.

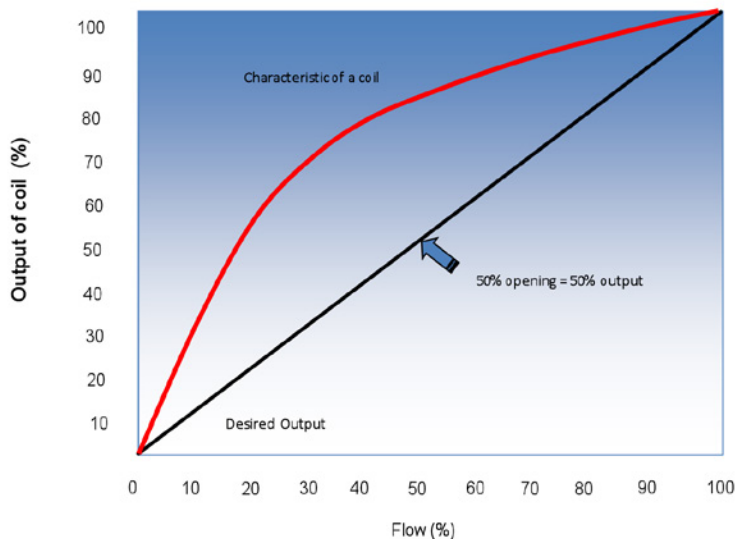
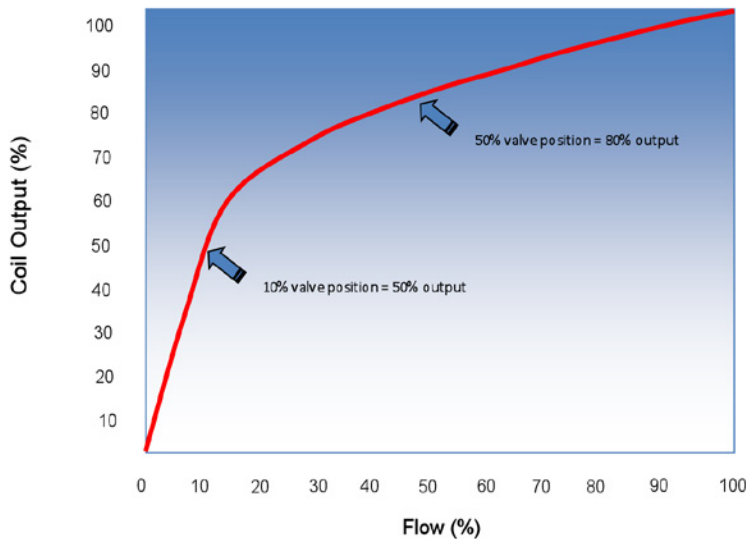


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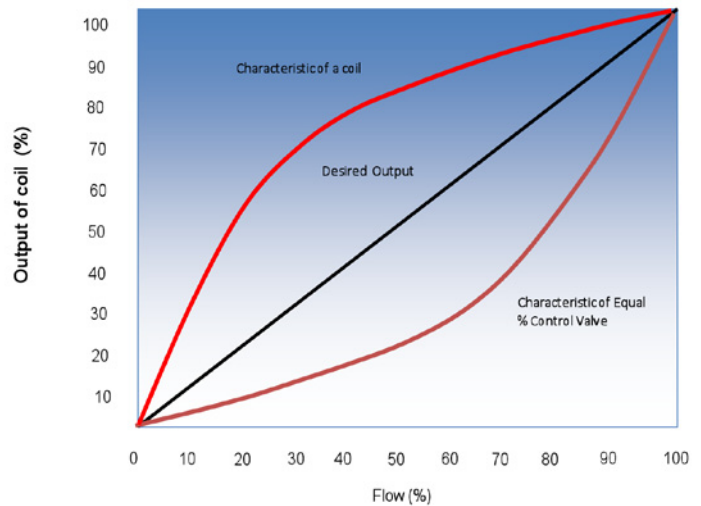
# Technical Section

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To better understand how pressure independent control valves can save energy we need to understand the typical coil characteristics. In the typical coil 50% flow will deliver approximately 80% output (80% of design heat transfer).



Coil Characteristic Vs Desired Heat Output



Equal Percentage Control Valve Counteracts the Quick Opening Coil Characteristic  
Result - 50% Control Signal = 50% Output

The result is that by using the Characterized valve (Equal Percentage) we can get the linear output we desire. This results in better control of the coil  $\Delta T$  giving us increased coil efficiency. This in turn will reduce pumping requirements saving energy at the central utility building.



# Technical Section

## Resolving Cleanability Issues with Aseptic Design

By Keith Bader, Director, Technical Services, Hyde Engineering + Consulting

### Background

Nearly 50% of warning letters posted on the FDA website contain citations for cleaning or contamination-related issues. While a manufacturer's natural first response to a cleaning issue is to increase the cleaning agent concentration, temperature, or cleaning cycle duration, this might not address the problem. Instead, a review of the hygienic design of the existing process equipment might be required to solve the cleanability issue.

CIP systems are engineered to provide cleaning solutions at the appropriate concentration, temperature, and flow rate for a length of time that removes production residues from process equipment surfaces. The system design must provide adequate turbulence to remove the residue, the system must drain well to prevent pooling of the solution, and the design must account for hard-to-clean features such as side drain ports and agitators. When a cleanability issue is identified, each of these design considerations must be looked at in detail.

### Imparting Energy to the Cleaning Process through Turbulent Flow

To remove all production residue, the cleaning system must be designed to deliver an adequate amount of turbulent solution flow in the pipes and in the falling film that flows down the sidewalls of the process vessels (see Figure 1). Turbulence is measured by a quantity known

as the Reynolds number. In pipes, a Reynolds number of 20,000 or greater is desirable for adequate cleaning. A Reynolds number greater than 2000 is required to achieve adequate turbulence in the uniform falling film created by the cleaning solution flowing down the sides of the vessel.

Ensuring adequate turbulence is required for proper cleaning, but it is not sufficient. Many other factors play a part.

### Ensuring Drainability

To maintain a turbulent film over the process vessel surface, it is important to minimize the amount of fluid pooling in the bottom of the vessel. Cleaning rates are significantly reduced in laminar flows and quiescent pools. Accordingly, equipment design must ensure that cleaning solutions drain freely from all product contact surfaces, thereby assuring that production residues cannot be retained or carried over from batch to batch.

Commonly, draining problems lead to what is known as bathtub ring cleaning failures. To diagnose whether excess solutions accumulate in the tank, note the amount of liquid collected in process vessels during washes and drain steps. When a draining problem is identified, the root cause of the problem must be diagnosed to determine the appropriate corrective action. The inability to sufficiently drain solutions from process vessels during CIP cycles can be caused by several factors:

**Improperly sized drain valves.** If the drain is undersized and cannot keep up with the CIP flow, the obvious solution is to replace the tank bottom valve with a larger one; however, this might not be necessary if the vessel is pressure rated. Creating a small amount of head or overlay pressure can possibly increase the flow through the drain enough to solve the pooling issue.

**Piping Restrictions.** Even though the vessel drain is adequately sized, downstream reducers or valves can lead to restricted flow out of the vessel. If this is the case, restrictions must be eliminated to facilitate flow from the vessel.

**Pipe Sloping.** Improper pipe sloping can lead to conditions in which a column of water can back up into the vessel after the completion of the CIP cycle. The situation can be corrected by increasing the pipe slope downstream of the vessel.

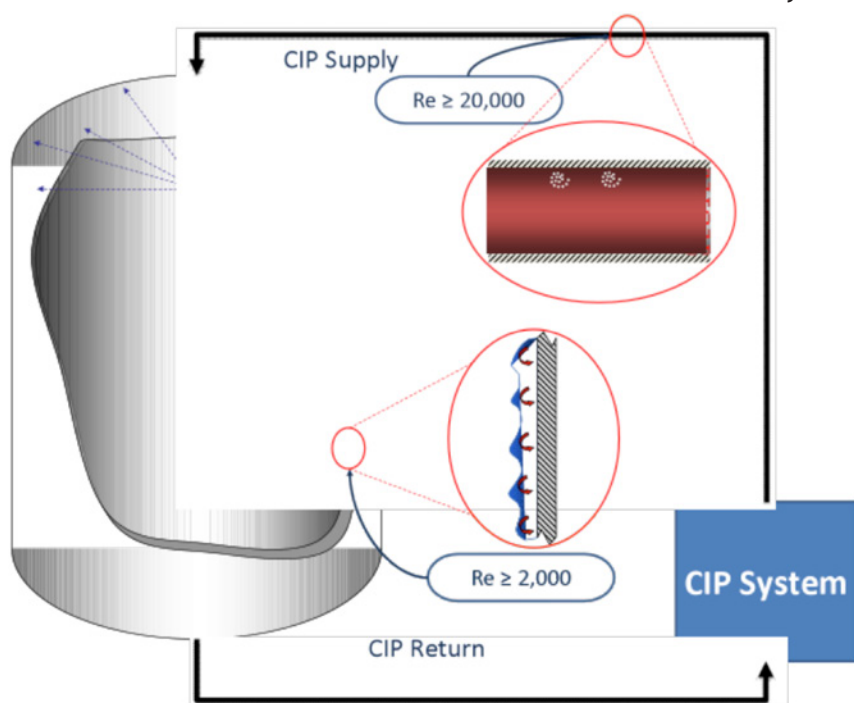


Figure 1: Ideal tank CIP circuit conditions

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# Technical Section

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**Dead legs.** Dead legs (low, stagnant spots) can lead to a small pool of solution that is still in the vessel after completion of the CIP cycle. The situation can often be corrected by equipping the pipe with a low-point drain valve.

**Inadequate drain times.** Barring any physical problems with process vessels, incomplete draining can be a result of a cleaning circuit with improper hydraulic balancing. Make sure that the drain steps in the CIP cycle are long enough to permit full evacuation of cleaning and rinsing solutions from process vessels. In addition, the evacuation rate from vessels should meet or slightly exceed the rate at which cleaning solutions are supplied.

After drainability issues with process equipment are addressed and corrected, it is time to look at components with complicated geometric configurations that have the potential to retain residue.

## Issues with Side Ports and Incorrectly Placed O-rings

Side ports can present a problem when they are not designed with an angle adequate enough to allow them to drain freely. For side ports that are poorly drained or have residue issues, the solution is to fabricate and install specialized spray devices that adequately clean the port and blow out any cleaning and rinsing solutions.

Valve and plug assemblies with incorrect O-rings can also cause residue issues. Frequently, cleaning failures occur at the O-rings on the Ingot fittings. To be effective, the O-rings must be correctly positioned as well as properly sized for the retaining gland.

- O-rings located too far from the internal tank wall prevent cleaning solutions from effectively reaching and removing residues.
- O-rings too small for the retaining gland are prone to retain residues forced into the annular gap between the Ingot port walls and the inserted probe.
- Overly large O-rings can lead to deformation and pinching of the seal, which can render it ineffective.

Specific O-ring design heuristics to accommodate cleaning requirements are contained in the ASME BPE; O-ring seals should be fitted in grooves located at a distance of less than  $6d$  from the nearest major cavity where the seal is at its point of maximum travel. The distance  $d$  is defined as the radial gap between the Ingot plug or sensor and the Ingot port wall (see Figure 2). The

grooves must also accommodate seal expansion without causing extrusion.

To properly size an O-ring, the gland volume (O-ring groove) should be between 60-85% filled with an ideal fill of 75%. The percentage of gland volume that an O-ring cross-section displaces in its confining gland is called gland fill. Seals specified or selected should allow at least a 10% void in any sealing gland to account for swelling of the elastomers used to seal the ports.

## Agitator Design

Agitators also present a unique challenge to the cleaning process. The specific measures necessary to ensure proper cleaning of an agitator are dependent on the agitator design. Agitators can be either top or bottom mounted. Bottom-mounted agitators can either be directly driven by a driveshaft penetrating the vessel or magnetically driven without directly penetrating the vessel.

For top-mounted agitators, the cleaning process must remove residues from the impellers, shaft, seals, and agitator collar. The specific design of each agitator should be evaluated to ensure that it meets hygienic design criteria. For example, an agitator mounted to the shaft by means of a set screw is undesirable, because threaded fittings are difficult to clean and invite bioburden growth. While this sort of issue is relatively easily to resolve by permanently welding the agitator blades to the shaft and filling the set screw hole to seal gaps and crevices that compromise overall hygienic design (see Figure 3, page 13), this seemingly inconsequential detail can have extremely negative results. Vessels should not be flooded to maintain a turbulent falling film on the sidewalls, so for top-mounted agitators, spray devices must be designed to distribute spray along the shaft and in the top collar of the agitator.

By nature, bottom-mounted agitators have minimal clearance between the bottom of the agitator and the vessel bottom. This area of low clearance can also retain contaminants unless the cleaning process is configured to address this issue or the design is specifically engineered for CIP. The solution is

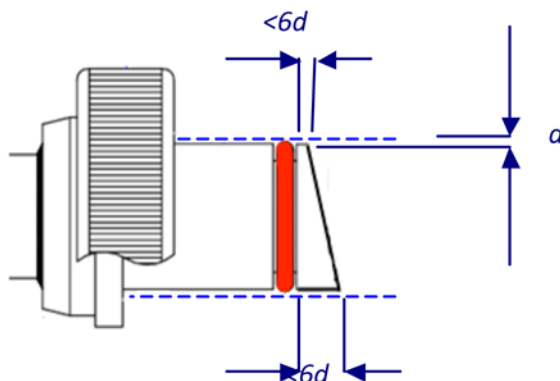


Figure 2: O-ring sizing and placement

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# Technical Section

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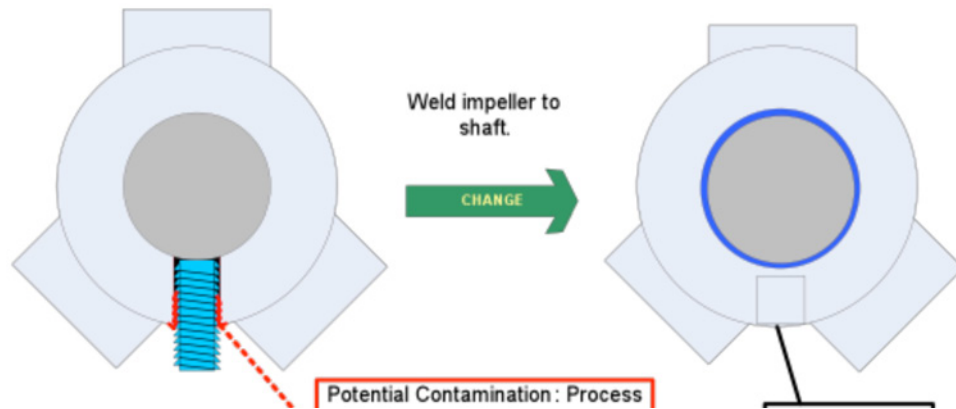


Figure 3: Remediation of a non-hygienic agitator design

to adjust the CIP flow rate or tank drain rate so that the agitator is submerged during cleaning. This submersion enables effective cleaning of the underside of the agitator and coupling pin.

Agitators designed specifically to combat cross contamination of batches incorporate an open mixing head structure. An open structure permits cleaning solutions to contact all surfaces of the agitator, including the bearing surfaces. In addition, because the dimension between bearing surfaces is small in most agitators, the open structure allows process fluid into the interstitial space as a lubricant. For agitators with this design, immersion is unnecessary if spray devices are designed to direct cleaning solution into the open head structure.

## Spray Device Design


Finally, close attention must be paid to spray devices to ensure that they are both properly designed and used in accordance with manufacturer specifications. Frequently, spray devices are employed at supply pressures below those recommended by the manufacturer.

This type of error can cause or contribute significantly to cleaning failures. When conducting spray coverage testing or developing cleaning cycles, it is of paramount importance to confirm that cleaning and rinsing solution supply pressures meet the manufacturer specifications.

Confirmation of proper spray device orientation can also be critical, especially in the case of custom-designed spray devices. To ensure optimal performance, spray devices should be physically keyed to the specific port and orientation for which they are designed.

In this short article, we have listed the most common design issues that affect cleanability and how to address them. Of course, less common problems do exist. But the important thing to remember is, without a cleanable and aseptic design, no combination of cleaning cycle parameter enhancements can produce satisfactory results.






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