ISPE
Connecting a World of Pharmaceutical Knowledge
Carolina-South Atlantic Chapter

CaSA News

Volume 20 • Number 4 AUGUST 2013

Featured Sponsors

Past President's Message

Jennifer Lauria Clark, CPIP

Four years ago when I was asked to join the Executive Board I was very humbled that the leaders of ISPE CaSA chose me to one day lead our ISPE CaSA Chapter. I have continued to be amazed during this four year journey by our outstanding Membership and volunteer leaders.

Thank you to our Membership, including our volunteer leaders, for making our educational and networking events successful. Without your attendance, support, input, guidance, willingness to speak, plan or host an event we would not have:

- Met our Membership goals of signing up 300 new Members this year
- Had the support of our outstanding sponsors
- Held highly successful Therapeutic Thursdays every month

(continued next page)

INSIDE THIS ISSUE

MARK YOUR CALENDARS!

August 21, 2013 – Durham Bulls Game
August 26-28, 2013 – ISPE International Training, GMP Training
August 27-28, 2013 – ISPE International Training, Biotech Training
September 12, 2013 – CaSA Annual Planning Session, Cary, NC
October 10, 2013 – CaSA ISPE Gala, Cary, NC
November 3-6, 2013 – Annual ISPE Meeting, Washington, DC

President's Message

(continued from previous page)

- Continued our services to students and young professionals with our 7th annual CaSA Leadership Symposium
- Helped send twelve Student Members to the 2012 ISPE Annual Meeting
- Implemented a Sponsorship Program
- Launched a new website
- Continued our outstanding Newsletter with relevant news and technical articles
- Hosted a sold out Plant Tour
- Held a successful Golf Tournament… in the rain
- Hosted our best Technology Conference ever at the Raleigh Convention Center

The time and effort our Chapter put into making our year a success is outstanding. As we move into the next year, I am pleased to pass the torch to my friend, Matt Gilson. His willingness to guide and listen gives him the ability to lead the Chapter to an even more successful next twelve months. As we transition, I am confident that your 2013-2014 Board of Directors will deliver educational programs and networking events that will not only support your companies' needs, but your needs professionally as individual Members.

If you are not a Member or have let your Membership lapse and want to renew it to participate and be the first to know about these special initiatives and what ISPE CaSA has to benefit you and your company, we are offering a special discount from **August 1 to August 14**. Please use code **CaSA0813** when renewing your Membership this month.

As the new year kicks off, I wish Matt and our new Board of Directors congratulations and great luck in the next twelve months. I know our momentum will continue throughout the next year as you offer your time and talent to the ISPE CaSA Chapter.

Jennifer Lauria Clark, CPIP
Past President, ISPE CaSA Chapter

Incoming President's Message

Matt Gilson

It's been a great year for ISPE CaSA. We've had some great events and accomplishments as Jennifer has summarized in her letter. One of the biggest challenges we face is trying to predict what you, our customer, want from this Chapter. As communication technologies have changed over the years, email varies in its effectiveness to communicate as we are all inundated with so much. But email remains our primary way to contact you, even though we are also using Facebook, Twitter, and LinkedIn, so I encourage you to read the weekly email update. What types of events would you like? What topics would you like to learn about? How would you like to interact with your fellow Members? We want to hear from you to better understand your answers to these questions. At our core, our goal is to gather people in the pharmaceutical realm to meet, network, and learn. Toward that end, I'm happy to hear your ideas on how we can improve CaSA events. A great place to make your opinions known and meet the people making the events happen is at our Annual Planning Session for Members and potential Members. This event will

(continued next page)

ISPE Connecting a World of Pharmaceutical Knowledge

Carolina-South Atlantic Chapter

2013-2014 Board of Directors

Officers
- Matt Gilson, President
- Heather Denny, Vice President
- Lisa Kerner, Treasurer
- Bruce Craven, Secretary
- Jennifer Lauria Clark, CPIP, Past President

Directors
- Ben Hund
- Chip Chappell
- Ken Ewan

Committee Chairs
- Wendy Haines, Newsletter
- Ash Patel, Education
- LeAnna Pearson, Student Affairs
- David Knorr, IT Communications
- John Marr, Networking
- Jerry "Patch" Paciorek, CPIP, Membership Development
- Jon Doyle, Young Professionals
- David Smith, BEST Fest Committee
- Mike Putnam, Technology Conference

President's Message

(continued from previous page)

be held at Prestonwood Country Club in Cary, NC on Thursday, September 12. It is free to attend and we'd love for you to come out and network and hear about what's in the works for the coming year. Look for registration details soon.

- I would like to thank our outgoing Board Members: Amy Lineberry, CPIP; Patrick Buckner; and Andy Ferrell. I appreciate the time and service you've given CaSA and hope to see you soon at the next event! I'd like to welcome our new Board Members: Ash Patel, Ben Hund, Chip Chappell, Ken Ewan, and Mike Putnam. I'm looking forward to getting to know you and working with you. And last but not least, I'd like to thank our continuing Board Members (listed above and Committee Chairs listed to the right) for their ongoing service to the Chapter. We've got a great group of Board Members and additional volunteers who spend a lot of time working for our Membership and I'm fortunate to have them on the Board and involved in each committee.
- There are a variety of events planned in the near future including: the Durham Bulls game on August 21, the Annual Planning Session on September 12, and the Gala on October 10, which will feature Facility of the Year Award Winners Biogen Idec and Novartis.
- I look forward to your participation and support of ISPE CaSA over the coming year!

Matt Gilson
President, ISPE CaSA Chapter

CaSA COMMITTEES

Education Committee
Ash Patel
ash.patel@biogenidec.com

IT Committee
David Knorr
david.knorr@grifols.com

Technology Conference Committee
Mike Putnam
mike_putnam@sequencevalidation.com

Membership Development Committee
Jerry "Patch" Paciorek, CPIP
paciorek@cagents.com

Networking Committee
John Marr
john.marr@crbusa.com

Newsletter Committee
Wendy Haines
whaines@manganinc.com

Young Professionals Committee
Jon Doyle
jdoyle@pci-llc.com

BEST Fest Committee
David Smith
davidglennsmith@gmail.com

Student Affairs Committee
LeAnna Pearson
ispeCaSAsac@gmail.com

Membership Corner

Membership Development

By Jerry "Patch" Paciorek, CPIP, CaSA Membership Development Chair

Wow! What a year! We set a goal to have 300 new CaSA Members for the year, which was from July 1, 2012 to June 30, 2013 and we finished with 301. We made it! Thanks for your effort and support throughout the entire year in spreading the word about ISPE and our Chapter. We enjoyed signing up 23 new CaSA Members who joined since our last newsletter was published.

If you have any questions about ISPE or the CaSA Chapter, please contact me at paciorek@cagents.com

International ISPE Update

Jennifer Lauria Clark, CPIP, Director, International Board

ISPE International is evolving its operational structure as well as implementing new approaches for (Communities of Practice and continuing to serve Members, Chapters, and Affiliates as things change.

ISPE International led an initiative this year, requested by the FDA and using ISPE's manufacturing Members' expertise, to provide the initial full report on the Causes/Mitigations for Drug Shortages in our industry. ISPE is working on:

- Patient Initiative
- How clinical trial packaging is used
- Quality metrics development with the FDA and Members
- Increasing awareness of our society's capabilities and expanding our Member base into a new space by joining PharmaExpo in 2014

These are all exciting initiatives to look forward to as we as Members get firsthand knowledge of what is coming next for our industry.

For more information please visit www.ispe.org.

Welcome New Members

These new Members joined May 20, 2013 through July 19, 2013

Andrew Babian
Erica Monique Brown
Shannon Chase
John Davis
Alexander Ewald
Matthew Fekete
John Franklin
Lauren Freeman
Mark Huff
Wes Johnson
Thomas Kelleher
Charles Lickfold
Josh Liptak
Dan Miller, CMRP
Tarik Monteiro
Lisa Olson
Dr. Kimberley Parker
Smaran Patel
Leo Perskii
Nicholas Roberts
John Schulz
Tatyana Touzova
Rob Venditto

Membership Corner

A Tribute to Jane Brown: Founder of Student Chapters within ISPE CaSA, Past ISPE CaSA President, and Past Chair of ISPE

Jane retired from GSK in May, 2013

"Besides being a great friend, Jane was instrumental in me becoming more involved in ISPE both locally and at the international level. I am grateful for her advice and guidance over the years and will definitely miss her at GSK. Congratulations and all the best Jane!"
—Matt Gilson, ISPE CaSA President

"Dear Jane, your dedication, leadership and heart have been an important part of shaping the ISPE family. Many thanks for your support and your personal commitment to all that is good about our industry. On behalf of the ISPE Board of Directors and Members worldwide, thank you. May the energy you always shine on ISPE be what illuminates the next exciting stage in your life. PS: I will also never forget the advice you gave me in a smoky karaoke bar in Hiroshima: "Nancy, if you are going to be any good at all to ISPE, chill out, get yourself a drink and come on out to the dance floor. Woo-hoo!"
—Nancy Berg, President & CEO, ISPE

"Jane Brown is the reason I became a Member of ISPE when she started a student Chapter at Campbell University in 1994. She "took me under her wing" as an undergraduate student and provided me with the tools to start a student Chapter at UNC-CH, where I attended graduate school. I learned so much from Jane whenever we were together – from driving

Jane Brown with the Polytechnic University of Puerto Rico Student Chapter and their 2007 Student Chapter of the Year Award.

Jane Brown speaking at a Tampa meeting in Feburary 2011.

the beverage cart together at ISPE CaSA Golf events, attending the Student Leadership Meetings in Washington D.C., to eating Mexican with my parents when they came to visit NC. One of my proudest moments was when Jane said, "Wendy, when we first met our relationship was that of a mentor/mentee, now I am glad to call you my friend." Jane, your spirit and enthusiasm are infectious and I wish you many relaxing days on the beach with Jenny and the grandkids."
— Wendy Haines, PhD, ISPE CaSA Newsletter Committee Chair

"Jane has been one of "THE FACES" of ISPE and one of the organization's greatest ambassadors. It's natural to associate people with a brand sometimes, and Jane earned that notoriety long ago. Everybody knows her. She is always professional, always pleasant, always interested and always willing. I have tremendous respect for Jane and wish her well in her retirement. Somehow, I don't think we've seen the last of Jane Brown in ISPE. Good luck Jane and thank you for your inspiration and all that you have done to make this organization better."
—Wes Robbins, CaSA Technology Conference Committee Member

"When I made the transition from ISPE volunteer to "globally involved" ISPE volunteer, Jane was one of the first people in the latter group that I met. Now that I know her as I do, it is

(continued next page)

Membership Corner

(continued from previous page)

completely unsurprising that this initial encounter was in the hotel bar; her most endearing trait is the true affection that she has for her fellow volunteers, and the joy she takes from spending time with us socially even after enduring us through a full day of work. When I was first elected to the International Board of Directors, she welcomed me to that community, and her warmth and helpful nature again helped me to adjust. When I was nominated to be an officer, Jane was among the first to offer congratulations and to assure me that I'd do well, and revealed that all of my worries were the same she had felt. Throughout my tenure on the ISPE Executive Committee, Jane has always stood ready to give advice or pitch in and help if needed. I will continue to prize Jane's friendship, and I sincerely hope she is able (I know she's willing!) to continue her deep ISPE involvement during her retirement. Thank you Jane for all you have done for ISPE, but above all thank you for being my friend."
—Randy Perez, PhD, 2011-2012 Chair, ISPE International Board of Directors

"Jane is a wonderful person. It's been a pleasure working with her over the years at ISPE. I had the pleasure of sharing time on the ISPE Executive Council with Jane, and she always brought value, inspiration and much laughter to our team. Jane truly cares about people, and it shows in everything she does and has led her to great success. Jane, I wish you the best as you enter this great new phase of your life. Enjoy it and bring the same energy to your next adventure as you have brought to our travels together. I look forward to our paths crossing again in the future."
—Brian Lange, Treasurer, ISPE International Board of Directors

"Jane Brown has meant a lot to me personally and also for my "career" within ISPE. Jane was the immediate past Chair when I first joined the International Board of Directors in November 2007. And in 2009 when I was nominated to become the next Secretary, leading up to my chairmanship this year, it was Jane who brought me the good news. Jane has always been very engaged, committed and fun to be around and I count her as one of my good friends in ISPE. I wish her all the best in her new life."
—Charlotte Enghave Fruergaard, PhD, Chair of ISPE Board of Directors

A cruise in the Baltimore harbor in June 2012 with Charlotte Enghave Fruegaard, PhD (left) and and Jane Brown (right).

"I am pleased that one of my final duties as President of ISPE was to present the Distinguished Achievement Award (ISPE's "Hall of Fame") to Jane Brown. Jane never said "no" to an ISPE request despite her hectic job and family situation. She was a pioneer and champion of the student and young professionals movements for the Society but participated in virtually every other area over the years, including being a magnificent Board Chair. Most of all Jane is a joy to be around, fully capable of coaxing a smile on even the most stressful day."
—Bob Best, President Optimus International LLC

(continued next page)

Membership Corner

(continued from previous page)

"Jane is the embodiment of the values that ISPE extols to its Membership. Whether you are a new Board Member or a young professional, she is unrelenting in her tutelage and nurturing to bring out the best in the volunteers to the Society. Everyone recognizes Jane for this unending commitment to support Membership. As I found out that she was to retire from her manager, Yvonne Stewart, I could only effuse the same message. I can only aspire to be held in such high recognition. Best of luck in this new Chapter of your life Jane! Job well done!! Congratulations."
—Stephen Tyler, Director, ISPE International Board of Directors

"Jane is such a huge part of what ISPE means to me. She has been an Ambassador not only championing students and young professionals, but also has given her time, talent and care as a Volunteer to help ISPE serve our Industry. She has put so much heart in everything she has done and I will always be grateful for her support, and friendship. One of the greatest benefits of a Membership society is the relationships that are built! From one grandmother to another……The best is yet to come!"
—Rosemary Jones

"Jane is a leader, a mentor, a friend, and a grandmother. Many of us have looked to her for career advice, industry guidance and mentoring over the years and she is always there for us. She has and continues to leave her indelible mark on us and we will miss seeing her at all of the ISPE events. Congratulations Jane on your retirement from a highly successful career at GSK. May you enjoy your new found free time with Jenny and your grand babies."
—Bo Crouse-Feuerhelm, ISPE CaSA Past President

Annual Meeting in San Francisco 2012. Front row: Jane Brown (right) Andre Walker (left). Back row right to left: Randy Perez, PhD, Jennifer Lauria Clark, Nancy Berg, and Charlotte Enghave Fruergaard.

"Jane, thank you for your support and counsel over the past decade plus. You have been a lighthouse showing me the safe path through my ISPE journeys. And when your wisdom was not shining on me, I know you were always helping anyone around you who looked your way. Best wishes on your future voyages and may all your drinks be boat drinks."
—Jim McGlade, ISPE CaSA Past President

"Jane has been the driving force that has made CaSA the strongest Chapter in the ISPE family. While it is true she didn't accomplish this alone it is also true that her guidance and fellowship with the managing team of CaSA is the core reason for CaSA's success. I wish Jane well in retirement and hope that her support and strength will carry on for both the Society at large as well as for CaSA. Thank you Jane!"
—James O'Brien, a founding father and past Chair of ISPE

"Jane, Thank you for your years of dedication and many contributions to GSK. Although I personally have failed at 'retirement', I wish you great success and much happiness as you retire. Enjoy the adventure that awaits you!"
—Bob Ingram, former CEO & Chairman of GlaxoWellcome who co-led merger to become GlaxoSmithKline

"Thank you so much for everything that you have done for the pharmaceutical industry Jane. You will be missed! Good luck for the future. With best warm wishes..."
—Heather Watson, Director, Computer Systems QA, Global Quality & Compliance, GSK

(continued next page)

Membership Corner

(continued from previous page)

(Left) Jenny Brown Chin (Jane's daughter) and Jane Brown.

"Jane Brown is a very personable person to have made acquaintance with over many years via ISPE at "vendor venues" and technical presentations. Jane is always outgoing with a great smile and vigor to help her colleagues. I enjoyed being on several committees in the past with her, and she will be missed in the organization, but I wish her well in her private life! Go Jane!"
—Rich Malfa, Sales Rep for Sartorious-Stedim

"I met Jane Brown 10 years ago when I was an ISPE Student Member at NC State University. My relationship with Jane has given me many opportunities professionally and personally over the past ten years. Following in her footsteps as she has been my mentor and friend through leadership of our Student Chapters, International Committees, and of the ISPE CaSA Chapter, I am blessed to know her and share in her life. Thank you, Jane for the many hours of guidance, ISPE discussions and for all the laughs and good times with our girls. We will miss you tremendously in the industry but wish you well as you become a full time Grandmother and Mom. Much love...
—Jennifer Lauria Clark, CPIP, ISPE CaSA Past President and Director, ISPE International Board of Directors

"I don't think it would have been possible without Jane Brown for the ISPE Campbell University Student Chapter to be established. She has helped all the way until we were independent. I don't know how she handled all of these with her busy schedule. She has always been positive on whatever things were asked. What a great lady! Small in stature but giant inside! Thanks!"
—Daniel Shin, PhD, Academic Advisor for the Campbell University Student Chapter

"I first heard Jane speak at an ISPE meeting in the early 1990s. She inspired me to want to join her in her dream of establishing ISPE Student Chapters at local Raleigh, NC universities. Jane remains an inspiration to me as a leader, someone always interested in helping others and as a good friend."
—Dan Dunbar, Owner, Dunbar Construction Consultants

"Many of us talk of how long we have known each other during our work lives. Jane and I go back to the years before we even knew what we would do in our lives. We used to hang out in the summer months at the ballpark off of Jones Franklin Road in the mid-sixties. We reconnected again when she returned to the Raleigh area working for Ajinomoto, USA where my company was providing the contract services for the facility. Jane is the epitome of service and sacrifice to the industry she has served. Jane has been an exemplary role model and mentor to countless students as they entered this endeavor. May your upcoming adventure be everything you have envisioned. Let Vickie and me know if you need any tips on cruising."
—David Brande, ISPE CaSA Past President

"Jane, it has been a pleasure to work with you, travel with you and share grandbaby stories. You are one of the hardest working women I know. I hope you enjoy your retirement and get to spend time with those little boys. Keep in touch!"
—Marsha Patterson, past Director, ISPE International Board of Directors

"Jane, your mentorship and friendship have meant so much to me. I treasure your guidance and I will be forever grateful. Congratulations on your retirement!!!"
—Amy Lineberry, CPIP, ISPE International Young Professionals Committee Chair

"Jane Brown has inspired me since I started at ISPE. Her work with the CaSA Chapter and International leaves a wonderful legacy for both. Jane has a heart of gold and soft spot for students and young professionals, who are the future of ISPE and the industry. She left her mark on everyone she touched and made a difference that will live on and on."
—Tracey Ryan, Affiliate/Chapter Relations Coordinator, ISPE

"I have always appreciated Jane's commitment to students and sharing her wealth of experience to empower others. I have known very few people that have been as willing to share and volunteer as Jane. She has been an invaluable Member of ISPE and a true blessing to the pharmaceutical industry."
—David G. Smith, ISPE CaSA BEST Fest Committee Chair

Membership Corner

CaSA Member Spotlight: David Brande

By ISPE CaSA Newsletter Committee

Q: What is your full name?
A: David Elan Brande

Q: Birth Place?
A: I was born at Annie Penn Hospital in Reidsville, North Carolina.

Q: College?
A: I attended NC State University beginning in January 1973. I spent my first two years in the School of Engineering but graduated May 1977 with an Honors degree in Life Sciences.

Q: Tell me a little about your personal life.
A: Even though I was born in Reidsville, my parents relocated to Raleigh in the summer of 1960, so I actually "grew up" here in Raleigh, just off of Buck Jones Road. I attended Francis Lacy, LeRoy Martin and graduated from Broughton in 1969 (back in those days, you only "graduated" from high school and college). I spent the next few years being introduced to the "world" through the guiding influence of the US Navy. During my service, I had the opportunity to spend 13 months off the coast of Vietnam, which is why I entered NC State in the middle of a school year. Shortly after graduating from NC State, I went to work with the NC Dept of Air Quality. It was about this time, April 1980, that I met Vickie who has been both my wife and best friend for 32 years. The two of us have lived in Cary for the last 22 years after bouncing around North Raleigh for a few years. We have no children, but with my older brother and Vickie's six siblings, we have countless nephews and nieces (who now have children of their own).

Q: What is your present position? What do you do at your job?
A: I am currently a member of the Board of Directors for PSCBiotech, Inc. and I oversee the company's interests in controlled environments (cleanrooms).

Q: How long have you been with your current employer?
A: Fourteen (14) months

Q: Tell me about your career path, and how you ended up where you are today.
A: When I started with the Dept of Air Quality, the EPA was still in its infancy and there were no college degrees in the environmental sciences at that time. Therefore, government agencies would hire a person with a math or statistics degree and "pair" them up with someone who had a life science degree, as we tried to get a handle on the pollution in the US. I always said, "the government put someone who knew how to count with a person who knew what to count." It worked out pretty well for everyone. I later left the Dept of Air Quality and went to work directly for the EPA in RTP as a contractor for the Division of Stationary Enforcement (DSSE). It was here I had my first experience with the government's enforcement of the Code of Federal Regulations not realizing how it would help me later. In August of 1987, I started Contamination Control Technologies, Inc., a company that specialized in certification of HEPA filtered environments in the bio/pharma industry. In August of 2005, my company was acquired by nnepharmaplan and I retired 2 years later. Over the next six years I spent more time trying to perfect the game of golf (still an unfinished task) and traveling without the burden of unfinished work building up while I was gone.


David Brande

Q: What is your favorite part of your job?
A: My favorite part is being a Subject Matter Expert and consulting without having to "run" a company.

Q: How long have you been a Member of ISPE/when did you first join ISPE?
A: I joined in 1993. I have a four-digit Membership number.

Q: What benefits have you realized from being a Member of ISPE?
A: I have made contacts from the industry that I admire greatly and treasure the privilege to call them my friends.

Q: Why are you still involved with ISPE?
A: Those friends I made are still here, so I am too. Additionally, there is always a new person to meet around the next corner or at the next meeting.

Q: Any Mentors/Role Models that have helped to shape your life?
A: My father, Phillip E. Brande, taught me that a hard day's work earned a good wage and to always do your best even if no one would know, it was your responsibility. He also taught me that a man is only as good as his word and he never lied to me. As a result, I did most of my company's work on a phone call or a handshake. He never offered advice until he was asked. It took me a long time before I realized that no

(continued next page)

Membership Corner

(continued from previous page)

one wants your opinion until they ask for it. I was able to share and thank him for his influence in my life before he died in 1990. He left this world not only as my Father, but also my best friend.

Q: If you weren't involved in pharma/biotech, then what business do you think you'd be in?
A: After more than 30 years in this business of particulate control and measurement, it is hard to imagine doing anything else. I have always thought running a breakfast restaurant in Myrtle Beach was the perfect job, but only because we both like to get up early and you can still play golf in the afternoon.

Q: What is one skill you wish you had that you don't?
A: The ability to be seen and not heard. Everyone who knows me is laughing out loud right now.

Q: Any hobbies? What are they?
A: I'm trying to "master" golf, traveling to see the world while NOT working, and trying to capture some of those moments with photography.

Q: Do you collect anything?
A: Yes I do. I started with Hard Rock Café t-shirts many years ago. The t-shirts represented the cities and towns that I had visited. Soon I realized I would never wear that many t-shirts the rest of my life, so I switched to HRC City pins. I also used to collect logo golf balls from golf courses I have played around the world. After I ran out of space in several display cabinets, I switched over to the golf club's pencils, smaller and free! I do not want to disclose how many I have of either.

Q: Finish this sentence – "I need more…."
A: Time to play golf. Lately my golfing buddies are constantly sending me texts and emails asking where I am and when I am going to play next.

Q: Favorite Food?
A: All my life, hamburgers, the perfect meal! Bread, meat, multiple vegetables are all in one handheld sandwich. I always argued this with my Mother growing up and it continues today with Vickie. Neither has been convinced.

Q: What is something that people would be surprised to learn about you?
A: From 2006 until 2012, I was Chairman of ISO Technical Committee 209 out of Geneva, Switzerland. My committee met in the fall of each year to discuss and evaluate the progress of the 10 sub-committees covering the entire portfolio of standards governing the controlled environment industry worldwide. I had 22 different countries represented on the committee, and many of those representatives were the leading experts in contamination control in their respective countries.

Q: Last movie you saw?
A: I saw *Epic*, only because I couldn't get Vickie to go see F*ast and Furious 6*.

Q: For those in the early stage of their careers, what advice would you give them?
A: Learn how to communicate with people and understand the importance of helping a person to reach their potential. In the end, your success will most likely be measured in how many people you can successfully manage. By the way, this is not taught in school.

Upcoming Events

DATE	DETAILS
August 21, 2013	Durham Bulls Game
August 26-28, 2013	ISPE International Training (Durham, NC), GMP Training
August 27-28, 2013	ISPE International Training (Durham, NC), Biotech Training
September 12, 2013	CaSA Annual Planning Session, Prestonwood Country Club, Cary, NC
October 10, 2013	CaSA ISPE Gala, Umstead Hotel, Cary, NC
November 3-6, 2013	Annual ISPE Meeting, Washington, DC

ISPE-CaSA Summer Social at Durham Bulls Athletic Park

Wednesday, August 21, 2013

Ticket pick-up - 5:30PM-7:30PM | Buffet open - 6:00PM-8:00PM | First Pitch is thrown at 7:05PM

Help the CaSA Chapter cheer on the Durham Bulls against the Charlotte Knights! There will be a variety of food including hamburgers, hot dogs, fried chicken, macaroni and cheese, baked beans, chips and drinks!

Pricing:

■Member $15 ■YP Member $15 ■Student $10 ■Kids (3 and up) $10 ■Non-Member $20

Sponsorship Opportunities Available!
Please visit the event website for more information!

ISPE Connecting a World of Pharmaceutical Knowledge | Carolina-South Atlantic Chapter

Reprinted from PHARMACEUTICAL ENGINEERING®
The Official Magazine of ISPE
September/October 2010, Vol. 30 No. 5
www.ISPE.org

Technical Section

Target Selection and Qualification – The Case of API Manufacturing Facilities

This article proposes an approach for qualification target selection and demonstrates how this can be applied to API manufacturing facilities.

by Masatoshi Takemata, Mitsuyuki Nakajima, Toyohiko Takeda, Tomio Tsurugi, Kimihiro Imamura, Yoshifumi Hara, Norio Yanagisawa, and Naoki Matsumoto

Introduction

Industry associations and regulatory bodies indicate that qualification should be restricted to facilities and equipment that have an impact on product quality. However, the literature[1] does not provide guidelines for identifying facilities or equipment required to be qualified. For the establishment of facilities and equipment for API manufacture, statutory regulations require qualification of those facilities and equipment to be the manufacturer's (i.e., user's) responsibility. In Japan, there are a number of different interpretations of the regulatory requirements based on individual perceptions and understandings. Thus, the targets covered by the requirements and the qualification methods vary in accordance with the users' interpretations, yielding redundant qualification of facilities and equipment. Therefore, an adequate systematic approach for selecting qualification targets and determining qualification methods is necessary.

ICH published Q7: *Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients* (ICH Q7) in November 2000.[1] Although it gives a definition of qualification, it does not explicitly define what must be qualified or how qualification should be performed.

ISPE published the *Baseline® Pharmaceutical Engineering Guide, Volume 5: Commissioning and Qualification (C&Q)*, a practical guide for qualification, in March 2001.[2] The Baseline Guide implies that qualification is required in addition to commissioning in accordance with Good Engineering Practice (GEP).

C&Q also asserts that a system impact assessment for facilities and equipment should be performed to classify the systems on the basis of their impacts on the quality of the product. The systems are classified into three groups: the direct impact systems, those that are critical to the quality of the product; the indirect impact systems, those that only indirectly affect it; and the no impact systems, those that have no impact on it. The components of the direct impact systems are then assessed for criticality and classified as critical components, which have a direct impact on the quality of the product, and noncritical components, which do not have such an impact. Qualification practices in addition to GEP should be applied exclusively to the critical components. Compliance with GEP only is sufficient for the noncritical components, the indirect impact systems, and the no impact systems.

The GMP Committee of the Japan Society of Pharmaceutical Machinery and Engineering (JSPME) has been studying a practical approach for selecting qualification targets and determining qualification methods since 2001. The committee published two case studies, one of a pan coating system in 2003,[3] and the other of blister filling/packaging systems and pillow packaging systems in 2007.[4] In addition, based on these studies, the committee also published a case study of an API manufacturing facility in 2008 as part of its joint research with the GMP Committee of the Japan Bulk Pharmaceutical Manufacturers Association (JBPMA).[5]

Extracting some portion from the case study of the API manufacturing facility, this article proposes a new approach for target selection and execution in qualification practices and also indicates how this approach can be applied to the reactor systems used for the production of intermediates and APIs. The concepts and definitions of qualification activities (DQ, IQ, OQ, and PQ) in this article are based on ICH Q7.

(continued next page)

Technical Section

(continued from previous page)

"In ordinary manufacturing processes, some of the important dynamic and static functions have a direct impact on the quality of the products, while the others have an indirect impact."

Fundamental Concepts of Target Selection and Execution

ICH Q7 states that before starting process validation activities, appropriate qualification of critical equipment and ancillary systems should be completed. The authors propose the following fundamental concepts of qualification of the critical equipment and ancillary systems (hereinafter referred to as facilities and equipment) as to what should be qualified and how the actual qualification activities should be performed.

1. Facilities and equipment for API manufacture have various dynamic functions (work and action) which are performed by the static functions (structure, form, and material) of the facilities and equipment. Manufacturing API products using certain facilities and equipment entails utilizing such dynamic and static functions under prescribed conditions and within ranges of control to produce intended products. In ordinary manufacturing processes, some of the important dynamic and static functions have a direct impact on the quality of the products, while the others have an indirect impact.

   Here, product quality is linked to the ICH Q6A definition "The suitability of either a drug substance or drug product for its intended use. This term includes such attributes as identity, strength, and purity" as described in ICH Q9.[6]

2. Quality risk assessment for those dynamic and static functions, based on the principle of ICH Q9[6], should be performed to classify the functions on the basis of their risks to the quality of the product. The functions are classified into two groups: the direct functions, those that have a risk of a direct impact on the quality of the product; and the indirect functions, those that have a risk of an indirect impact, or no risk of an impact on it.

   Qualification practices in addition to GEP should be applied exclusively to the direct functions. Compliance with GEP only is sufficient for the indirect functions.

3. The suitability and appropriateness of the facilities and equipment, regardless of their impacts on product quality, are verified, documented, and approved with GEP from the standpoint of quality risk at each stage of the engineering activities from design through commissioning.

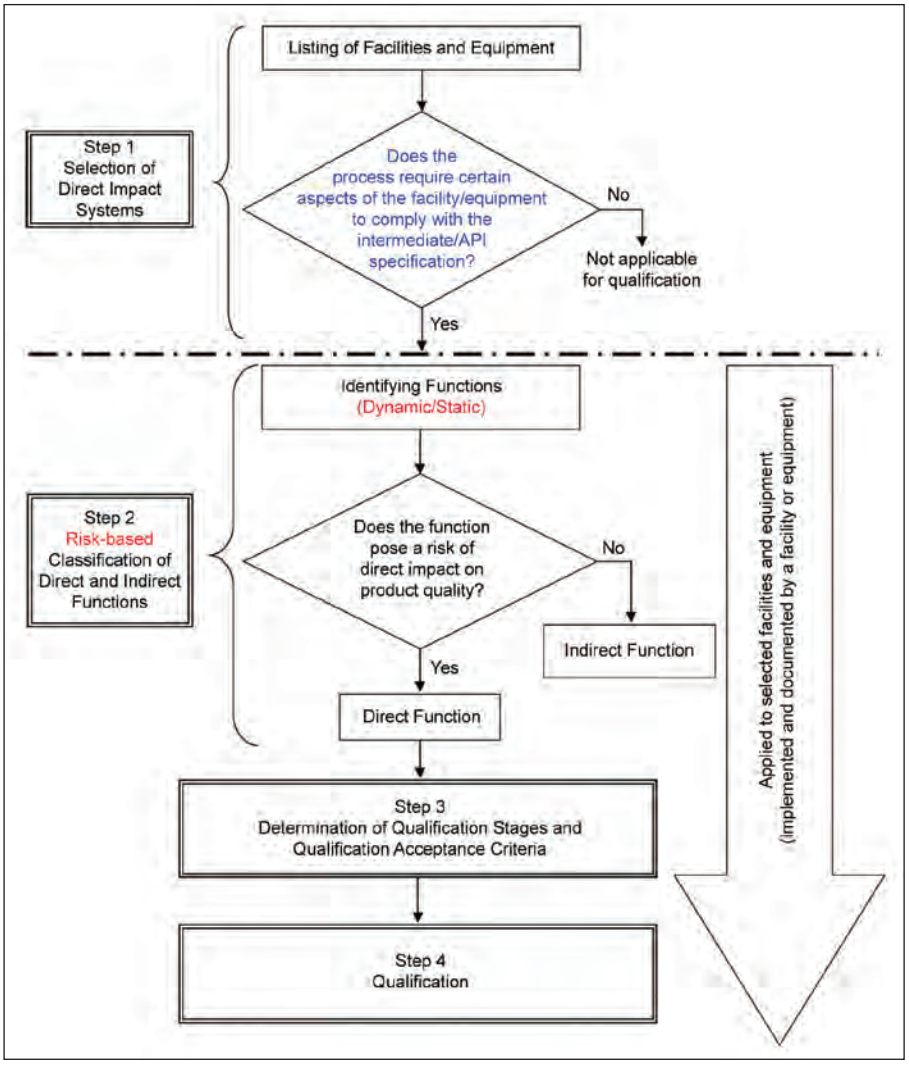


Figure 1. Work flowchart for qualification.

Facilities and Equipment Unit		Selection criterion satisfied?		Reason	Remarks
Name	Area	Yes (direct impact system)	No		
Reactor A System	Area shown in Figure 3	X		Reaction of key intermediates	

Table A. Selection of direct impact systems.

(continued next page)

Technical Section

(continued from previous page)

"Users do not necessarily need to duplicate the verification activities of the items that are already verified with the exception of the high level risk items mentioned later."

Therefore, it is sufficient for users in some qualification activities to confirm that these items are properly verified in the engineering activities. Users do not necessarily need to duplicate the verification activities of the items that are already verified with the exception of the high level risk items mentioned later. However, engineering change control should be applied to ensure that any changes made post verification are adequately addressed in respect to the impact of previously performed and completed verification activities. Qualification can be performed after all the engineering activities are completed, or it can be performed at an appropriate stage of the engineering activities: Design Qualification (DQ) at the design stage, Installation Qualification (IQ) and Operational Qualification (OQ) at the construction and commissioning stages.

	Class	Definition
Severity	5	Direct impact on product quality; reworking or destruction is required.
	4	Direct impact on product quality; reprocessing is required.
	3	No direct impact on product quality; recoverable in subsequent processes under standard manufacturing conditions even when deviations occur.
	2	No direct impact on product quality when manufacturing occurs under standard conditions.
	1	No impact on product quality

Table B. Severity classification (impact on product quality).

		Probability		
		Low	Medium	High
Severity	5	B	A	A
	4	B	B	A
	3	D	C	C
	2	E	D	C
	1	E	E	D

Table C. Level of risk.

Level of Risk	Scope of Qualification	Extent of Qualification
A	Applicable for qualification (Direct function)	Direct verification by user QA approval for documents
B		Supplier-prepared document review by user is permitted. QA approval for documents
C	Not applicable for qualification, verification under engineering practices (Indirect function)	Verification and documentation at engineering stage in accordance with risk level. Approval by head of related section.
D		
E		

Table D. Scope and extent of qualification.

Direct Functions	Qualification Stages			
	DQ	IQ	OQ	PQ
Static Direct Functions	→	→		
Dynamic Direct Functions	→	→	→	
Among Dynamic Direct Functions, Direct Functions Related to Process Control	→	→	→	→

Table E. Direct functions and qualification stages.

4. The direct functions are further classified as static direct functions (e.g., form, material, and surface finish) and dynamic direct functions (e.g. revolutions, temperature, and pressure). Dynamic direct functions can be further classified as either being subject to process control in the Standard Operating Procedure (SOP) or not.

5. If deemed critical, measurement and control devices and computerized control devices are targets of calibration and computerized system validation, and are not discussed in this article.

A New Method for Qualification Practice

Based on the concepts discussed in the previous section, the following explains the required activities and documentation in each stage of qualification using the flowchart in Figure 1.

Step 1: Selection of Direct Impact Systems

Among all the facilities and equipment, the facilities and equipment which have a direct impact on the quality (direct impact systems) are selected based on the selection criterion described below.

Selection criterion: Does the specified manufacturing process require

(continued next page)

Technical Section

(continued from previous page)

certain aspects of this facility/equipment to comply with the intermediate/API specification?

Examples of such manufacturing processes include the agitating processes of multiple ingredients, the phase conversion processes, the isolation processes (concentration or filtration), the temperature and pH sensitive processes, the processes that yield essential molecular components of the products, the intermediate processes in which principal chemical conversions take place, and the final purification processes. The selection is performed using a checklist as exemplified in Table A.

Step 2: Risk-Based Classification of Direct and Indirect Functions

For the direct impact systems selected in Step 1, dynamic and static functions having the potential to affect product quality are identified and classified through quality risk assessment in accordance with ICH Q9.[6,7]

Specifically, the risk-based classification of direct and indirect functions is performed in conformity with the contents of Tables B, C, D, and F. The quality risk assessment consists of risk identification, risk analysis, and risk evaluation as shown in Table F.

At the stage of risk identification, the dynamic functions and static functions are identified and challenged by the question, "What might go wrong?"

At the stage of risk analysis, the consequences are identified and their severity is classified in accordance with Table B. Also, the degree of probability that the unwanted event will occur is determined.

At the stage of risk evaluation, a level of risk is determined in accordance with the criteria shown in Table C. Then, the direct functions and indirect functions are classified using the following classification criterion.

Subsystem	Components	Quality Risk Assessment								Remarks
		Risk Identification		Risk Analysis			Risk Evaluation			
		Functions (Dynamic/Static)	What might go wrong?	What are the consequences?	Severity	Probability	Level of Risk	Direct Functions (Qualification Applied)	Indirect Functions (only GEP applied)	
Reactor System	Reactor Vessel A	Material (contacted process fluid)	Selected material not resistant to process fluid	Has impact on the purity of intermediate and product. Reworking or destruction is required when metal corroded material is mixed in process fluid.	5	L	B	X		
		Capacity	Capacity incorrectly defined	Has impact on productivity, but has no impact on quality of intermediate or of product.	1	L	E		X	
	Agitator	Material (contacted process fluid)	Selected material not resistant to process fluid	Has impact on purity of intermediate and product. Reworking or destruction is required when metal corroded material is mixed in process fluid.	5	L	B	X		
		Agitability	Insufficient study of scale-up	Has impact on impurity profile because of insufficient solid-liquid dispersion for proper reaction. Reprocessing is required when agitation is inadequate.	4	M	B	X		
		Revolution Speed		Individual functions have no direct impact on quality of intermediate and product as various combinations of these functions can achieve proper agitability.	2	M	D		X	
		Blade Shape			2	M	D		X	
		Blade Position			2	M	D		X	
		Motor Output			2	M	D		X	
Temperature Control System	Heat Source Unit, Controller	Reactive liquid temperature (condensation)	Incorrect temperature control range specified	Cause reaction time delay or abnormal reaction. Has impact on impurity profile when abnormal reaction occurs due to improper temperature control. Reworking or destruction is required when temperature is inadequate.	5	M	A	X		
Solvent Supply System	Piping	Material (contacted process fluid)	Selected material not resistant to process fluid	Has impact on purity of intermediate and product. Reworking or destruction is required when metal corroded material is mixed in process fluid.	5	L	B	X		
		Key: Probability L = Low, M = Medium, H = High								

Table F. Excerpt from example of risk-based classification of direct and indirect functions (Reactor A system).

(continued next page)

Technical Section

(continued from previous page)

"Qualification activities (i.e., DQ, IQ, OQ, and PQ) determined in Step 3 are performed and documented in this step. The qualification activities are implemented and reported in accordance with the pre-approved protocol."

Classification criterion: dynamic and static functions that can pose a risk of direct impact on the quality of the product (Severity Class 4 and 5 shown in Table B) are direct functions, while others (Severity Class 1, 2, and 3 shown in Table B) are indirect functions.

The scope and extent of qualification is determined by the level of risk as outlined in Table D.

Step 3: Determination of Qualification Stages and Qualification Acceptance Criteria

In this step, required qualification stages are determined for each direct function obtained in Step 2 in accordance with the criteria shown in Table E.

The acceptance criteria for each direct function in determined qualification stages are also established at this step.

Table G is an excerpt from an example of the determination of qualification stages and qualification acceptance criteria. This table is useful for capturing the entire picture of qualification to facilitate its smooth execution as the table comprehensively shows direct functions (items and contents) as well as required qualification activities and acceptance criteria.

Step 4: Qualification

Qualification activities (i.e., DQ, IQ, OQ, and PQ) determined in Step 3 are performed and documented in this step. The qualification activities are implemented and reported in accordance with the pre-approved protocol. Examples of data sheet formats (part of reports) are shown in Tables H to K.

Outline of API Manufacturing Facilities

This section introduces the outline of API manufacturing facilities and equipment to be studied in applying the new method proposed in Section 2.

The Manufacturing Process of API Intermediate

Compounds A and B, potassium carbonate, and dimethylformamide are agitated at 25°C for 24 hours. Then sodium borohydride, suspended in dimethylformamide, is dropped into the admixture in the presence of N2 gas, keeping the temperature of the reaction solution below 35°C. The admixture is agitated at 25°C for another 24 hours to obtain an intermediate (intermediate C). Figure 2 is a block flow diagram of the manufacturing process.

Components and Functions of the Reactor A System

The major equipment and instruments

Subsystem	Components	Direct Functions		Qualification Stage and Qualification Acceptance Criteria					Remarks
		Level of Risk	Items	Contents	DQ	IQ	OQ	PQ	
Reactor System	Reactor Vessel A	B	Material (contacted process fluid)	Resistance to corrosion in acid and alkali	Glass lining	Glass lining	-	-	
				Chemical resistant gaskets	Fluororesin gasket	Fluororesin gasket	-	-	
	Agitator	B	Material (contacted process fluid)	Resistance to corrosion in acid and alkali	Glass lining	Glass lining	-	-	
				Chemical resistant gaskets	Fluororesin gasket	Fluororesin gasket	-	-	
		B	Agitatability	Solid-liquid dispersion (reagent in DMF)	Designed agitator (motor, sealed axis, blades, controller) operating conditions: (i) Revolution speed (XX ~ YY rpm) (ii) liquid level (min. xx ~ max. yy mm)	Installed agitator (motor, sealed axis, blades, controller) operating conditions: (i) Revolution speed (XX ~ YY rpm) (ii) liquid level (min. xx ~ max. yy mm)	Agitator operating conditions: (i) Revolution speed (XX ~ YY rpm) (ii) liquid level (min. xx ~ max. yy mm)	Potassium carbonate to be dispersed under agitation after charging 6 OL DMF and 11.8 kg potassium carbonate into the Reactor Vessel A	
Below Omitted									

Table G. Excerpt from example of determination of qualification stages and qualification acceptance criteria (Reactor A system).

Subsystem	Components	Direct Functions			DQ Acceptance Criteria	Verified Doc. Name/ No. (Note)	Result	Date	Sign	Remarks
		Level of Risk	Items	Contents						
Reactor System	Reactor Vessel A	B	Material (contacted process fluid)	Resistance to corrosion in acid and alkali	Glass lining		OK/NG			
				Chemical resistant gaskets	Fluororesin gasket		OK/NG			
	Agitator	B	Material (contacted process fluid)	Resistance to corrosion in acid and alkali	Glass lining		OK/NG			
				Chemical resistant gaskets	Fluororesin gasket		OK/NG			
		B	Agitatability	Solid-liquid dispersion (reagent in DMF)	Designed agitator (motor, sealed axis, blades, controller) operating conditions: (i) Revolution speed (XX ~ YY rpm) (ii) liquid level (min. xx ~ max. yy mm)		OK/NG			
Below Omitted										
Note: Refer to attachment for verified documents.										

Table H. Excerpt from example of a DQ report (Reactor A system).

(continued next page)

Technical Section

(continued from previous page)

of the Reactor A system are illustrated in Figure 3. This system is composed of the following six subsystems:

1. Reactor system: performs the chemical reaction of compounds; composed of a Reactor Vessel A, an agitator, and an agitator controller.

2. Temperature control system: controls the temperature of the Reactor Vessel A; composed of a thermometer, a heat source unit, a pump, piping, and a controller.

3. Solvent supply system: supplies solvent to the Reactor Vessel A and the Dropping Vessel A; composed of piping.

4. Dropping system: drops sodium borohydride suspended in dimethylformamide into the Reactor Vessel A; composed of a Dropping Vessel A, a pump and piping.

5. N2 gas supply system: supplies N2 gas to the Reactor Vessel A and the Dropping Vessel A; composed of a flow meter, piping, and a filter, etc.

6. DCS: controls the manufacturing process; subject to computerized system validation.

Subsystem	Components	Direct Functions: Level of Risk	Items	Contents	IQ Acceptance Criteria	Test Method	Verified Doc. Name/No. (Note 2)	Result	Date	Sign	Remarks
Reactor System	Reactor Vessel A	B	Material (contacted process fluid)	Resistance to corrosion in acid and alkali	Glass lining	Visual		OK/NG			
				Chemical resistant gaskets	Fluororesin gasket	Visual		OK/NG			
	Agitator	B	Material (contacted process fluid)	Resistance to corrosion in acid and alkali	Glass lining	Visual		OK/NG			
				Chemical resistant gaskets	Fluororesin gasket	Visual		OK/NG			
		A	Agitatability	Solid-liquid dispersion (reagent in DMF)	Installed agitator (motor, sealed axis, blades, controller) operating conditions: (i) Revolution speed (XX ~ YY rpm) (ii) liquid level (min. xx ~ max. yy mm)	Verify with designed documents checked/ verified in DQ (Note 1)		OK/NG			
Below Omitted											

Note 1: If drawings and specifications are revised after DQ completion, re-DQ must be done for the drawings and specifications prior to IQ start. Change control is required in the case of any change.
Note 2: Refer to attachment for verified documents.

Table I. Excerpt from example of an IQ report (Reactor A system).

Subsystem	Components	Direct Functions: Level of Risk	Items	Contents	OQ Acceptance Criteria	Test Method	Verified Doc. Name/No. (Note 2)	Result	Date	Sign	Remarks
Reactor System	Agitator	B	Agitatability	Solid-liquid dispersion (reagent in DMF)	Agitator operating conditions: (i) Revolution speed (XX ~ YY rpm) (ii) liquid level (min. xx ~ max. yy mm)	Water operation		OK/NG			
Temperature Control System	Heat Source Unit, Controller	A	Reactive liquid temperature (condensation)	Mixture of Compounds A and B, potassium carbonate and DMF to be kept at 25 ±5°C for 24 hours	Temperature control system operating conditions: (i) temperature (XX ~ YY °C) (ii) liquid level (min. xx ~ max. yy mm)	Water operation (Note 1)		OK/NG			
		A	Reactive liquid temperature (reduction)	Reactive liquid to be kept at 25 ±5°C for 24 hours after charging DMF suspension liquid of sodium borohydride							
Below Omitted											

Note 1: The temperature range that cannot be verified by water operation is verified in PQ.
Note 2: Refer to attachment for verified documents.

Table J. Excerpt from example of an OQ report (Reactor A system).

A Case Study of the New Qualification Method

This section describes a case study of the new qualification method applied to the Reactor A system. The description follows the steps shown in Figure 1 except for Step 1 where direct impact systems are selected, referring to Table A.

Step 2: Risk-Based Classification of Direct and Indirect Functions

Table F shows how the components in each subsystem shown in Figure 2 and the direct and indirect functions are classified through the quality risk assessment described in Section 2-2.

Step 3: Determination of Qualification Stages and Qualification Acceptance Criteria

Table G is a list of qualification stages and qualification acceptance criteria for the direct functions selected in Step 2.

Step 4: Qualification

Since the requirements of good documentation practice (version control, etc.) for qualification protocols and reports are widely known throughout the pharmaceutical industry, this article focuses on the content and structure of the documents. The following text describes the content and should be read in parallel with Tables A, B, C, and D, where the Tables provide the structure.

DQ

The DQ protocol describes 1) subsystems, 2) components, 3) direct functions (level of risk, items, and contents), and 4) the DQ acceptance criteria. The DQ report includes the description of the documents checked or verified, the results, etc., as well as 1) to 4) of the DQ protocol. Table H is an excerpt from an example of a DQ report. (It also includes the requirements of the DQ protocol.)

IQ

The IQ protocol describes 1) to 3) of the DQ protocol, the IQ acceptance criteria, and the test method. The IQ

(continued next page)

Technical Section

(continued from previous page)

report includes the description of the documents checked or verified, the results, etc., in addition to all the items in the IQ protocol. Table I is an excerpt from an example of an IQ report. (It also includes the requirements of the IQ protocol.)

OQ

Targets in the OQ are only the dynamic direct functions. The OQ protocol describes the relevant items among 1) to 3) of the DQ protocol. It also should describe the OQ acceptance criteria and the test methods. The OQ report should include the description of the documents checked or verified, the results, etc., in addition to all the items in the OQ protocol. Table J is an excerpt from an example of an OQ report. (It also includes the requirements of the OQ protocol.)

PQ

Targets in the PQ, which is always performed at the user's site, are restricted to the dynamic direct functions that are subject to process control. The PQ protocol should describe the relevant items among 1) to 3) of the DQ protocol. It also should describe the PQ acceptance criteria and the test method. The PQ report should include the description of the documents checked or verified, the results, etc., in addition to all the items in the PQ protocol. Table K is an excerpt from an example of a PQ report. (It also includes the requirements of the PQ protocol.)

Conclusion

The authors propose a new approach for the target selection and execution of qualification practices by quality risk assessment based on the principles of ICH Q9.[6] This new approach is explained for the Reactor A system used in the production of an intermediate, for example. An outline is provided as follows.

Facilities and equipment for API manufacture have various dynamic functions (work and action) which are performed by the static functions (structure, form, and material) of the facilities and equipment. It is necessary to execute such dynamic and static functions under prescribed conditions and within ranges of control to produce the intended products. However, only some of the dynamic and static functions in the critical processes have a direct impact on the quality of the product, while other dynamic and static functions have indirect impact, and others exist in non critical processes.

Quality risk assessment for those dynamic and static functions, based on the principle of ICH Q9,[6] should be performed to classify the functions on the basis of their risks to the quality of the product. Functions are classified into two groups: direct functions, those that have a risk of a direct impact on the quality of the product; and indirect functions, those that have a risk of an indirect impact on or no risk of impact on it.

Qualification practices in addition to GEP should be applied exclusively to the direct functions. Compliance with GEP only is sufficient for the indirect functions.

Qualification execution consists of the following steps:

Subsystem	Components	Direct Functions: Level of Risk	Items	Contents	PQ Acceptance Criteria	Test Method	Verified Doc. Name/No. (Note)	Result	Date	Sign	Remarks
Reactor System	Agitator	B	Agitatability	Solid-liquid dispersion (reagent in DMF)	Potassium carbonate to be dispersed under agitation after charging 60 L DMF and 11.8 kg potassium carbonate into the Reactor Vessel A	Visual		OK/NG			
Temperature Control System	Heat Source Unit, Controller	A	Reactive liquid temperature (condensation)	Mixture of Compounds A and B, potassium carbonate and DMF to be kept at 25±5°C for 24 hours	Temperature to be controlled at 25±5°C for hours after charging the specified amounts of compounds A and B, potassium carbonate and DFM according to the procedure	Record by temperature recorder		OK/NG			
		A	Reactive liquid temperature (reduction)	Reactive liquid to be kept at 25 ±5°C for 24 hours after charging DMF suspension liquid of sodium borohydride	Maximum temperature to be below 35°C during dropping and kept at 25±5°C for 24 hours after dropping under the conditions of specified amount of charge volume of sodium borohydride/DMF	Use thermometer and stopwatch		OK/NG			
Below Omitted											
Note: Refer to attachment for verified documents.											

Table K. Excerpt from example of a PQ report (Reactor A system).

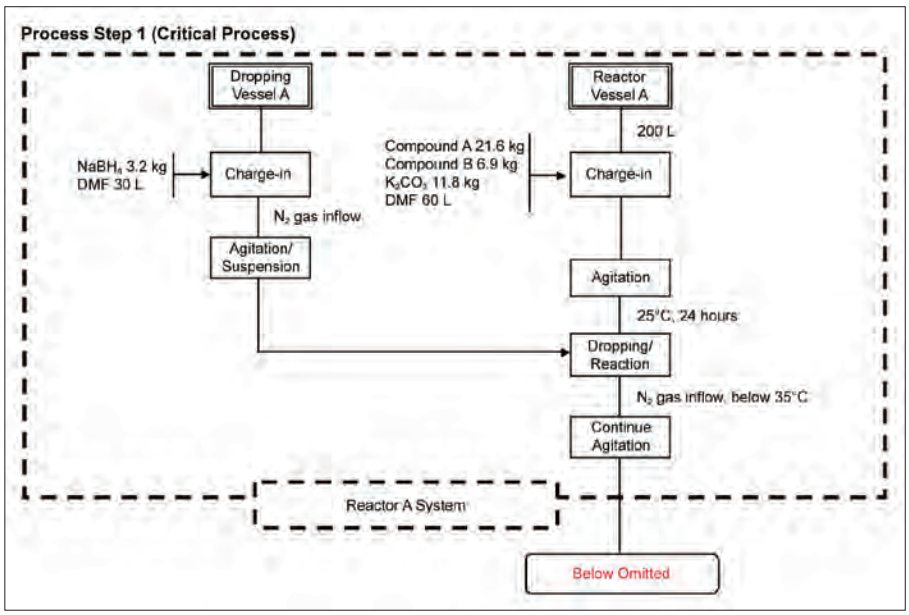


Figure 2. Manufacturing block flow diagram for intermediate products.

(continued next page)

Technical Section

(continued from previous page)

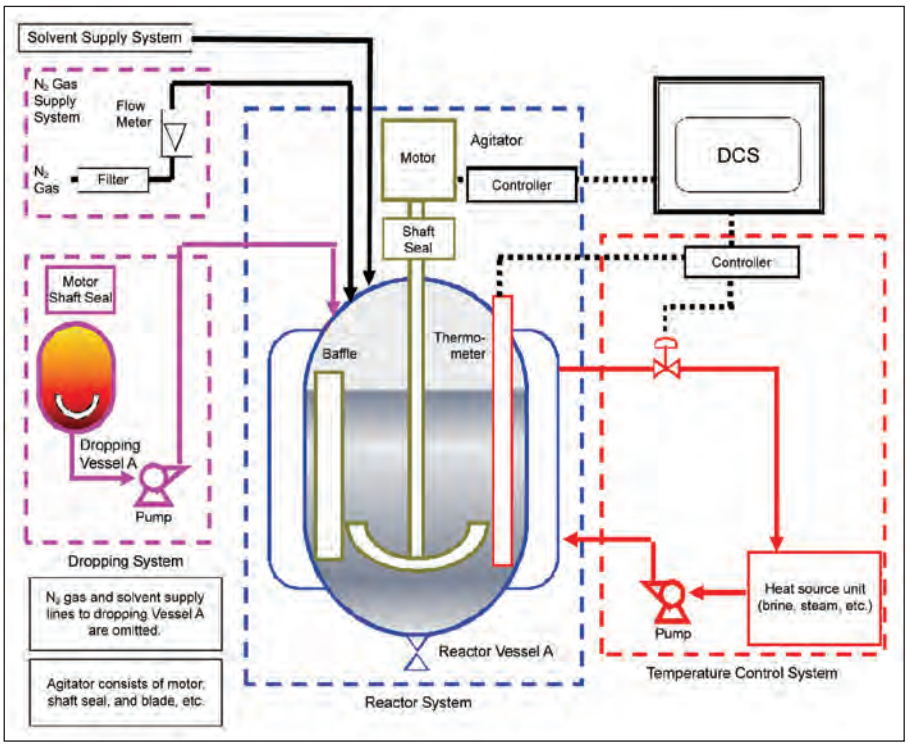


Figure 3. Equipment and instruments of Reactor A system.

1. Select direct impact systems used in critical manufacturing processes.

2. Identify functions (Dynamic/Static) of the direct impact systems and then classify them as either direct or indirect functions in accordance with the level of quality risk determined by risk assessment.

3. Determine qualification stages and qualification acceptance criteria. Static direct functions are to be the targets of DQ and IQ. Dynamic direct functions not subject to process control are to be the targets of DQ through OQ. Dynamic direct functions subject to process control are to be the targets of DQ through PQ.

4. Prepare protocol, implement and prepare a report at each stage of qualification.

References

1. ICH Harmonised Tripartite Guideline, Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Q7, November 2000, www.ich.org.

2. *ISPE Baseline® Pharmaceutical Engineering Guide, Volume 5 – Commissioning and Qualification,* International Society for Pharmaceutical Engineering (ISPE), First Edition, March 2001, www.ispe.org.

3. GMP Committee in Japan Society of Pharmaceutical Machinery and Engineering, Qualification Practices of the Systems for Solid Dosage Forms for Internal Use – The Case of Pan Coating Systems, October 2003.

4. GMP Committee in Japan Society of Pharmaceutical Machinery and Engineering, Qualification Practices of the Systems for Solid Dosage Forms for Internal Use – The Cases of Blister Filling/Packaging Systems and Pillow Packaging Systems, April 2007.

5. GMP Committee in Japan Society of Pharmaceutical Machinery and Engineering and GMP Committee in Japan Bulk Pharmaceutical Manufacturers Association, Qualification of API Manufacturing Facilities: The case of facilities applying to examples of descriptive guidelines on certificate of approval for API manufacturing method, August 2008.

6. ICH Harmonised Tripartite Guideline, Quality Risk Management, Q9, 9 November 2005, www.ich.org.

7. Quality Risk Management ICH Q9, Briefing Pack, July 2006.

About the Authors

GMP Committee, Japan Society of Pharmaceutical Machinery and Engineering (JSPME)

JSPME is a non-profit volunteer society founded in 1991 in order to advance pharmaceutical technology through the exchange of knowledge and experience in a wide range of industries related to pharmaceutical production.

JSPME, Miyoshi Bldg. 3F, 2-7-3 Kandata-cho, Chiyoda-ku, Tokyo 101-0046, Japan, Tel: +81-3-3252-3048.

Masatoshi Takemata is Manager of the Pharmaceutical Service Operations engaged in GMP Compliance Consultancy as well as Commissioning and Qualification (C&Q) work for pharmaceutical and biopharmaceutical projects. He joined JGC in 1981 and has 23 years of experience in GMP technology in various pharmaceutical-related areas, including bio bulk products, sterile products, solid dosage forms, chemical bulk, and medical devices. He has a Bachelor's Degree in mechanical engineering from Chiba University in Japan. He serves on the GMP committee of the Japan Society of Pharmaceutical Machinery and Engineering (JSPME). He has also served as Director of the ISPE Japan Affiliate, as well as a member of the Affiliate's Education Committee and the C&Q COP.

(continued next page)

Technical Section

(continued from previous page)

Mitsuyuki Nakajima, PhD serves as Chief Engineer and Manager, Pharmaceutical and Fine Chemical Engineering Division, IHI Plant Engineering Corporation in Tokyo, Japan.

Toyohiko Takeda is Chief of GMP Inspection Committee of NPO-QA Drug and Food Quality Assurance Support Center. He joined Shionogi in 1959 and has 36 years of experience in development of solid dosage forms, sterile products and quality management. He joined Niigata Engineering in 1995 and then worked for IHI Plant Engineering from 2002 to 2010. He went on to join the Japan Society of Pharmaceutical Machinery and Engineering (JSPME) in 1999-2010 as the Chief of GMP Committee and has 15 years of experience in GMP Technology in API products, sterile products, solid dosage forms and pharmaceutical excipients. He has a PhD in pharmacy from Kyoto University in Japan.

GMP Committee, Japan Bulk Pharmaceutical Manufacturers Association (JBPMA)

JBPMA is a nationwide association comprised of member companies who engage in the manufacture and sales of bulk and intermediate pharmaceuticals. The association was founded in 1975 aiming at the establishment of the Active Pharmaceutical Ingredient (API) GMP and a quality assurance system, etc.

JBPMA, Inagaki Uchikanda Bldg. 5F, 3-17-5 Uchikanda, Chiyoda-ku, Tokyo 101-0047, Japan, Tel: +81-3-3526-5971.

Tomio Tsurugi is Senior Manager of API Manufacturing Section at the Kashima Plant of Eisai Co., Ltd. He joined Eisai Co., Ltd. in 1969 and has 19 years of experience in GMPs for API manufacturing. He is a former member of the GMP Committee of Japan Bulk Pharmaceutical Manufacturers Association, where he served for 12 years, including as Chairman for four years.

Kimihiro Imamura is Manager of the Manufacturing Technology Section the Kurihama Plant of Seikagaku Corporation. He joined Seikagaku Corporation in 1991 and has 18 years of experience in GMP technologies in various pharmaceutical-related areas, including bio bulk products, sterile products, and medical devices. He has a Master's degree in pharmaceuticals. He has served on the GMP Committee of the Japan Bulk Pharmaceutical Manufacturers Association.

Yoshifumi Hara is Senior Manager of the Quality Assurance Unit (QAU) at Otsuka Chemical Co., Ltd. He joined Otsuka Chemical in 1988 and has 17 years of experience in GMPs for API manufacturing. He has a Master's Degree in chemical environmental engineering from Oita University in Japan. He is a former member of the GMP Committee of the Japan Bulk Pharmaceutical Manufacturers Association.

Norio Yanagisawa has served as Manager of Quality Assurance at the Fuji Plant of Kyowa Hakko Kirin Co., Ltd. since February 2009. He joined the Yodogawa Research Institute, Daikin Industries, Ltd. in 1985 and gained six years of experience in conducting research in the manufacturing of perfluoropolyether (research of an optical coupling reaction, research of direct fluorination with fluorine), water-repellence for leather and examining the manufacturing process of high purity HF. He then joined the Yokkaichi Research Laboratories, Kyowa Hakko Kogyo Co., Ltd. in 1991 and accumulated 17 years of experience in conducting research on synthetic method of polylactic acid and industrialization. He has a Bachelor's Degree in pharmacy from the Tokyo University of Pharmacy and Life Sciences. He has been on the GMP Committee of the Japan Bulk Pharmaceutical Manufacturers Association since June 2003 and has edited JPTI (Inovan) since August 2006.

Naoki Matsumoto is Managing Director of Japan Bulk Pharmaceutical Manufacturers Association. He has 15 years of experience in GMPs for API manufacturing at Sogo Pharmaceutical Co., Ltd. He served as Chairman of the GMP Committee of Japan Bulk Pharmaceutical Manufacturers Association for 15 years.

Event Highlights

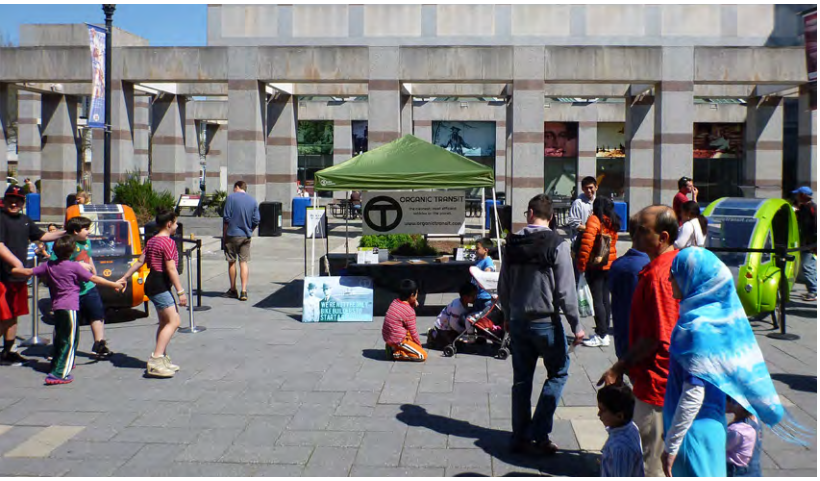
BEST (Biotechnology, Engineering, Science and Technology) Fest

By David Smith, BEST Fest Committee Chair

Celebrating innovation in North Carolina

ISPE partnered with the NC Museum of Natural Sciences and the NC Science Festival to hold the first-ever Triangle BEST (Biotechnology,) Fest! The Triangle BEST Fest expanded upon the huge success of last year's Biotechnology Day by highlighting Engineering, Science and Technology in addition to the field of biotechnology. The mission of the event was to showcase the amazing work scientists, researchers, engineers, students, universities and local companies are engaged in throughout the state, and allow the general public to experience first-hand how these people and organizations are advancing science technology through interactive exhibits and presentations.

ISPE and the NC Biotechnology Center (NCBC) partnered to facilitate a scavenger hunt to help guide families to learn about why these fields are important to their daily lives and be inspired to pursue further information about them. Scavenger hunt participants were entered into four drawings that occurred throughout the day, and the winners received a Nook tablet which was a big hit. The ISPE and NCBC volunteers had a wonderful time talking and guiding families as they toured the festival, and we served our industry by highlighting the great work our Member organizations were showcasing at the event. We also had the opportunity to share about benefits of ISPE to industry professionals and highlight some of the upcoming events CaSA will be facilitating.



BEST Fest

Held April 6, 2013 at Raleigh's Museum of Natural Sciences

Highlights of the Event:

- **Over 6700 attendees visited the museum during the course of the day**
- **Well over 200 volunteers participated with about 50 exhibit areas**
- **11 highlighted presentations and panels throughout the day**

We heard from most of the exhibitors and several attendees that the event was a smashing success. We also had a number of attendees that said that they appreciated the great work ISPE did for helping to put on such a wonderful opportunity for their families to experience science and technology in such a fun way. Additionally, a few organizations expressed their commitment to participate in next year's event.

Next year's event promises to be even more exciting. The CaSA ISPE Chapter will be partnering with the museum to put together an event showcasing the science and technology behind healthcare. The event is tentatively scheduled for **April 5, 2014**, and we are already preparing for it!

(continued next page)

Event Highlights

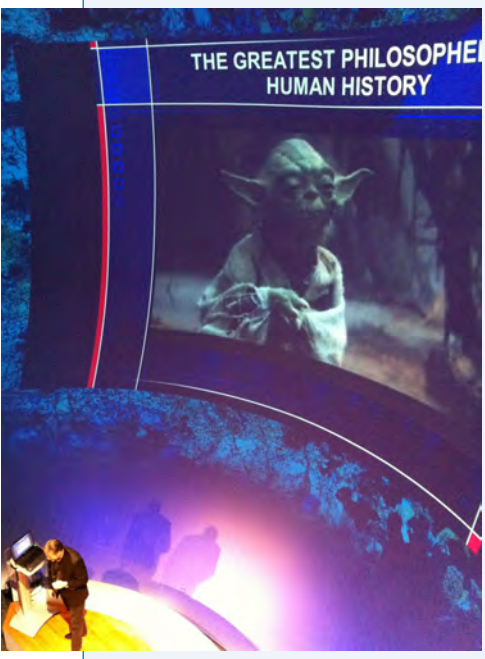
(continued from previous page)

Presentation Highlights:

Materials for Medical Devices

Roger Narayan, Professor, UNC/NCSU Joint Department of Biomedical Engineering

This talk provided a historical review of how materials for medical devices were initially developed. Some modern examples of medical devices were also discussed mentioned.



MEOR Spells MORE Oil

Sidney J. Nelson, President/CEO and Phillip Launt, COO of RAM Biochemicals, Inc.

SCIENCE SATURDAY! Primary and secondary oil recovery methods leave as much as 60% of the oil unproduced and stranded in the reservoir. Microbial enhanced oil recovery [MEOR] is a biologically based technology that utilizes the unique ability of biological factories (microbes) to recover significant volumes of stranded oil.

USDA Animal Care: Ensuring the Welfare of Research Animals (and other animals, too!)

Nicolette Petervary, VMD, Regional Animal Care Specialist, USDA Animal and Plant Health Inspection Service, Animal Care, Eastern Region

This presentation provided an overview of the Animal Welfare Act and how it relates to research animals.

What's IN R FOOD?

Keval Mehta, InRFood Inc.

Food has become more chemistry than biology. Remember, you are what you eat. This talk provided a snapshot of what's in our food today.

Proteins, the Meat of the Story and Beyond

Bradley Hintze, Duke University

This talk described many aspects of proteins including scale (size), function, and structure. Examples used were related to aspects that everybody can comprehend.

How the NIEHS Manages Conflicts of Interest for its Scientists and Managers

Bruce A. Androphy, Esq., Director, NIEHS Ethics Program, National Institutes of Environmental Health Sciences

The federal government has strict rules governing conflicts of interests for its scientists and managers. This presentation discussed such items as financial disclosure, protocol review, improper gifts, outside activities and other issues relating to conflict of interest.

Panel Discussion: Ethics and Corporate Responsibility in the Biotech Industry

Richard Kouri, PhD, Director, BioSciences Management Initiative, Professor of Practice, Poole College of Management, NCSU

David Kroll, PhD, Director of Science Communications and Investigator, Genomics and Microbiology Research Laboratory, NC Museum of Natural Sciences

Cedric Pearce, PhD, Founder and CEO, Mycosynthetix, Inc.

Using genetic engineering to produce foods, industrial products, and medicines has great benefit to society. But some view these advances with concerns about safety, pricing and patents. How do agricultural and pharmaceutical bioscience companies operate ethically while remaining innovative in a competitive global marketplace?

Life GPS: Make It Happen

Paul McKellips, Executive Vice President, Foundation for Biomedical Research

All too often we tell our children that they can become anything they want in life but we don't tell them how to do it. Life GPS is a high-energy, inspiring and motivational multimedia presentation that provides young people the "how to" road map that transforms dreams into reality, especially in the fields of biomedical research and life sciences.

Regenerative Medicine-A New Frontier in Medical Science: Where Are We?

Dr. R. Edward Branson, Wake Forest Institute for Regenerative Medicine

Regenerative Medicine deals with repairing or replacing tissues and organs by using advanced materials and methodologies such as cloning and has been around for decades starting with the first kidney transplant in 1954. Since then,

(continued next page)

Event Highlights

(continued from previous page)

numerous advances have been made in repairing the human body from bone marrow transplants to the construction of replacement organs and the treatment of metabolic disorders. Regenerative medicine consists of multiple technologies, including cell therapy, tissue replacement, organ replacement and gene therapy. With the ability to repair or replace many of the body's non or poorly functioning parts, regenerative medicine offers the promise of a healthier and more fulfilling life for mankind.

Genes, Genetics and Gene Therapy, The Incredible Journey

Dr. Jude Samulski, University of NC at Chapel Hill

This talk provided illustrations and examples of how genes go awry. Diseases are an inevitable outcome and our ability to reverse these back to normal function and healthy beings.

Ethics of Genetically Modified Organisms

David B. Resnik, JD, PhD, Bioethicist, National Institute of Environmental Health

This presentation discussed the ethical issues surrounding genetically modified organisms (GMOs), considering both the benefits and risks of GMOs.

Exhibitor List:

- North Carolina Science Festival
- ECU Pirates: Walking the Plank of Science — Brody School of Medicine Graduate Student Association
- STEM Bus — NC BioNetwork/WTCC
- Green Chemistry and Toxicology — U.S. Environmental Protection Agency
- Solar Fuels at the UNC Energy Frontier Research Center — UNC Energy Frontier Research Center
- BTEC at NCSU - Biomanufacturing Training and Education Center; Come hear about and learn about how medicines are made…right here in NC! — BTEC-Biomanufacturing Training and Education Center at NCSU
- State of Matter: Dry Ice Storm and Playing with Polymers — Mad Science
- Future BRITE Scientists — BRITE-NCCU
- Novartis Vaccines and Diagnostics
- A Day in the Life of Biotechnology Manufacturing — Pfizer

- How Muscles Do Work: The Sarcomere — University of North Carolina at Chapel Hill Laboratory of Monte S. Willis, MD, PhD
- Biotechnology: Making Everyday Products Better Every Day. — Novozymes
- Gila Monsters and Medicine: Lizard Spit in Your Drugs! — NC Museum of Natural Sciences
- Come Fly with the Science House — The Science House
- Chemistry's Rainbow — ISPE, UNC-CH Chapter
- Modeling the DNA Molecule — Ronald Monti
- ISPE/NC Biotechnology Center — ISPE
- Better Crops for a Better Future — BASF Plant Science
- Biotechnology in GSK RTP — GlaxoSmithKline
- Biotech Buttons! — NC Museum of Natural Sciences
- Applications of Biotechnology to Enhance Crop Productivity — Monsanto Company
- North Carolina FFA — North Carolina FFA Association
- Biomedical Engineering at East Carolina University — East Carolina University, Department of Engineering
- Antibodies: Nature's Secret Weapon — ImmunoReagents, Inc.
- SEE Your Speech! — Business Speech Improvement
- Unique Metals — Duke University
- Biotechnology/Biomanufacturing — Biogen Idec
- Kelly Scientific Resources — Kelly Scientific Resources
- Advancing Agriculture — North Carolina State University Plant Pathology Department
- Robots! — NC FIRST Robotics
- Use of Animals in Biomedical Research: Understanding the Issues — Charles River Laboratories
- Animals of Biotechnology — NC Museum of Natural Sciences
- SoundBytes — NC Museum of Life and Science
- Make Your Own Space Mud! — High Touch High Tech of RDU

(continued next page)

Event Highlights

(continued from previous page)

- Separation in Science — Campbell University College of Pharmacy & Health Sciences Department of Pharmaceutical Sciences
- Wearable Robotic Exoskeletons — Human PoWeR Lab, UnC Chapel Hill/NCSU Joint Dept. of Biomedical Engineering
- INRFOOD: You Are What You Eat — INRFOOD
- Plant Biology for Kids — North Carolina State University
- SEM of Ants — NCSU Dept. of Materials Science and Engineering
- School of Ants — Your Wild Life Team, NC State
- Learn to Solder with Maker Faire North Carolina — Volunteers with Maker Faire North Carolina will teach you the essential skill for making electronics: soldering! Volunteers educate visitors on proper soldering technique and safety (ages 5 and up).

SAVE THE DATE!

Annual CaSA ISPE

BEST Fest

at the

Raleigh Museum of Natural Sciences

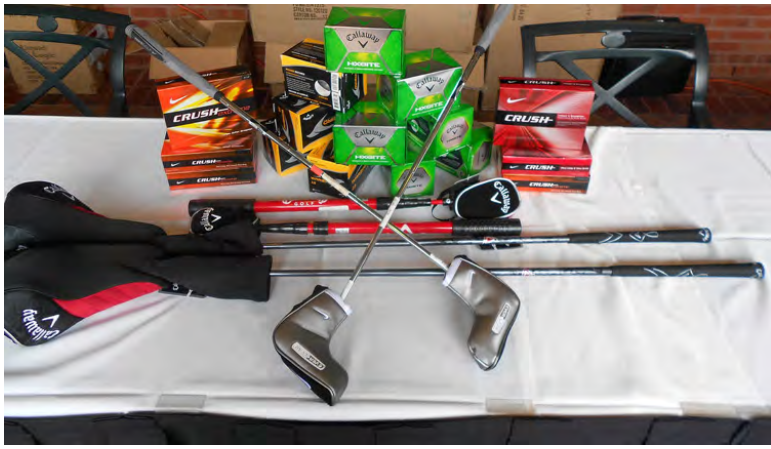
April 5, 2014

Event Highlights

2013 ISPE CaSA Summer Golf Tournament

By : Jim McGlade, Golf Event Organizer and John Marr, Golf Event Organizer & CaSA ISPE Networking Chair

Neither rain, nor snow, nor sleet, nor gloom of night stays these golfers from their rounds! Certainly snow, sleet, and nightfall will stop some golfers; however it was proven rain will not stop ISPE CaSA golfers! (But lightning is a whole other story). One hundred and sixty golfers showed up in their best rain gear for the 19th Annual ISPE CaSA Golf Tournament at Prestonwood Country Club in Cary, NC on Monday, May 6, 2013.



After several light rain showers, play was concluded due to lightning and torrential rain after 12 holes. Despite the weather, which many recalled as the only time this event has experienced rain, everyone enjoyed the extended networking time the rain out provided. The event included a Raffle for a bounty of golfing items and ten lucky players won cash and prizes totaling over $2,800, including a $500 grand prize. Each player was a winner despite their luck in the raffle as door gifts included a party cooler, courtesy of CRB, and a metal can coozie courtesy of Burkert Fluid Control Systems.

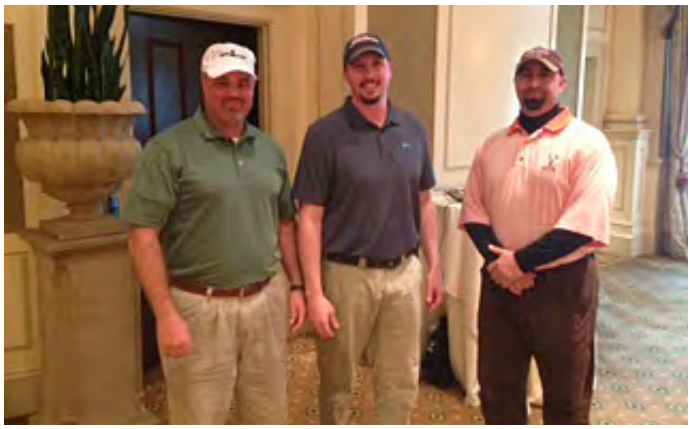
Prizes!

On-course games included the chance to win a Harley Davidson motorcycle with a hole-in-one, sponsored by RGD. Additional hole-in-one prizes included the chance to win an Apple ipad and iphone, set of Callaway clubs, and a $750 Visa card. Regrettably, no golfer was able to make the first ace in the tournament's history. Maybe next year the curse will be broken.

(continued next page)

Event Highlights

(continued from previous page)



We love our sponsors

Additional sponsors included Hydro Service and Supplies, Inc. and Triangle Process Equipment providing the beverage carts, Avid Solutions, Inc. sponsoring the Scoreboard and Rules Sheet, and the following hole sponsors: Applied Calibration Service, Inc., Advent Biotech, Clark Nexsen Architecture and Engineering, PCI, Propharma Group, Pharmasys, CAI and Sequence Validation.

Awards

First and second place prizes were awarded for each of the two courses played. The abbreviated event concluded with an awards ceremony and the ever-popular BBQ meal including fried chicken, BBQ pork, hushpuppies, and all the fixins.

Thank you!

ISPE CaSA sincerely thanks all of this year's players and sponsors for braving the weather. We hope to see you all back next year on a sunny day in early May.

(continued next page)

Event Highlights

(continued from previous page)

ISPE CaSA Young Professional Committee Evening Discussion on Leadership

By Jon Doyle, CaSA ISPE Young Professionals Committee Chair

On June 3 the ISPE CaSA Young Professional Committee held an evening discussion on leadership to provide valuable information on developing the "Emerging" leader found within each of us. Ken Ewan, an industry veteran turned Leadership Coach, gave an electric talk followed up with action plans, reference materials and personal advice on how to move onward and upward. Ken provides coaching to all corporate levels across many disciplines throughout the industry. Visit his LinkedIn profile for more information (www.linkedin.com/pub/ken-ewan/10/a08/669).

The event was held in Rocky Mount to highlight Hospira's Technical Professional Development Program (TPDP) that was initiated in 2012. Hospira alone signed up over 40 Young Professionals! Allison Vessels, of the Hospira Human Resources department, was instrumental in finding the meeting location and gathering the Hospira attendees for this event. Thanks Allison!

During the interactive discussion, Ken spoke of the importance of taking your career development into your own hands. The earlier you start the better. Take the Hospira TPDPs and the other YPs that attended this event for example. You should expect to cross paths with these bright, motivated individuals at some point in the near future!

More information

Keep a lookout for more Young Professional events through the ISPE CaSA information eblasts. If you would like more information about the Young Professionals group please contact Jon Doyle at casayoungprofessionals@gmail.com.

Event Highlights

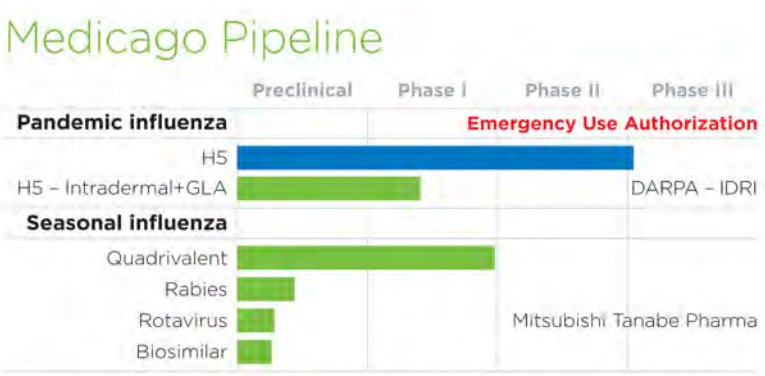
ISPE CaSA Medicago Tour

By Chip Chapell, Medicago Tour Organizer, and Amy Lineberry, CPIP Medicago Tour Organizer and former CaSA Education Chair

The ISPE CaSA Chapter recently held a tour of Medicago's new facility in Research Triangle Park, NC. This sold out event was attended by 60 Members representing 36 various companies from our Chapter. Thanks to all who attended and a very gracious thank you to Medicago for having us out!

Our tour of this facility opened with Medicago representatives orienting groups of Members and introducing us to the goals and capabilities of the facility. Presentations were given about Virus Like Particles (VLPs) and how Medicago is using this emerging vaccine technology to generate effective and long lasting protection against influenza, rabies, rotavirus and others. The advantage is that VLPs activate key aspects of the immune response to achieve potent immune stimulation which fosters immunological memory. This is a result of the cells lacking their core genetic material rendering them unable to replicate yet they are rapidly recognized by the immune system.

Groups were then taken down to the production floor where each step of the process was explained as we progressed though the facility. The step-by-step process is demonstrated by the graph below.



Thanks to Clark-Nexsen

We would like to thank Clark-Nexsen for sponsoring this event! Their sponsorship allowed CaSA Members to expand both their knowledge and business network within our region's biotech sector.

ISPE CaSA Chapter E-Newsletter Ads

Newsletter Ads Work for Your Business!

Our Chapter produces six e-newsletters per year, and we depend on the support of our advertisers. We send out the newsletters via e-mail and via web link to all of our Chapter Members throughout the Southeastern U.S.

That means you get targeted access to top-notch pharma, biotech, and bio-science professionals and managers. These newsletters are also posted on our **website** so your ad can be accessed by interested visitors to our site.

Best of all, the cost is only $650 for your full color, business-card-sized ad for six insertions. That's only $650 for targeted advertising in full color for an entire year!

Ask About HOT LINKS!!

Would you like to have targeted customers simply click on your ad and get right to your website?

A hot-link can be added to your ad, connecting readers directly to your company website for an additional $500.00 for a whole year.

If you are interested in advertising with the ISPE CaSA e-newsletter, please contact our Chapter headquarters at:

ISPE-CaSA
1500 Sunday Drive
Suite 102
Raleigh, NC 27607
919-573-5442
info@ispeCaSA.org

You will be notified via e-mail or telephone when your advertisement has been accepted by the ISPE CaSA Communications Committee and asked to submit your advertisement digitally.

Full-color business card-sized ads (3.5" x 2") may contain your logo or other artwork. Artwork should be sent directly to pdepas@firstpointresources.com.

We ask that your text be no smaller than 12 pt so that the text is easily readable in the electronic format. PDF, JPEG or TIF formats are easiest for us to work with. Space is limited, sign up today!

ISPE Carolina-South Atlantic Chapter Newsletter

1500 Sunday Drive, Suite 102
Raleigh, NC 27607
Tel: 1-919/861-4531 • Fax: 1-919/787-4916
whaines@manganinc.com

EDITORIAL POLICY

Articles should be written for technical professionals in the pharmaceutical, biotechnology, and medical device industries. The author is responsible for the accuracy and correctness of all statements contained in the manuscript (ISPE Carolina-South Atlantic Chapter assumes no liability.) Manuscripts should be forwarded to a Member of the Communications Committee at whaines@manganinc.com for review 30 days prior to publication. A brief three to four sentence synopsis of the article, as well as a brief biographical statement about the author that includes educational background, title and job affiliation, job responsibilities and major areas of accomplishment must accompany the article.

Got News?

Send it to:
whaines@manganinc.com

Entries should be brief and be of general interest to the readership. Entries must include a name and telephone number for verification purposes. We reserve the right to edit and select entries.

A word to the ISPE CaSA Newsletter advertisers:

Thank you all for your continued support. Without it we could not have the wonderful support staff to get our ISPE CaSA Members the news in such a timely and professional fashion. If you have updates to your advertisements or find any other error, please contact us so that we can serve you better.