People • Science • Regulation

PDA Letter

Volume XLVIII • Issue 8 www.pda.org/pdaletter September 2012

Job Aids Slowly Evolve from Paper to Electronic, Move From Shop Floor to Office Suites 30

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

PDA®
Parenteral Drug Association

The Parenteral Drug Association presents...

2012 PDA/EMA Joint Conference

Compliance: A Prerequisite for Availability of Medicinal Products

- Falsified medicines regulation and it's impact to regulators and industry
- Ensure availability and quality of drugs in a challenging environment
- Risk management to control product shortage due to manufacturing quality problems; business continuity plans
- New trends in manufacturing and controls
- Closing plenary: The regulatory and industry environment 2020

Four Interest Group Meetings:

EU Inspection Trends
Stephan Rönninger, *F. Hoffmann-La Roche*
EU Regulatory
Barbara Jentges, *PhACT*
Quality Systems
Lothar Hartmann, *Crucell*
GMP Link to Pharmacovigilance
John Ayres, *Eli Lilly*

PDA-PIC/S Training: GMP for APIs (ICH Q7)

4-7 December 2012

Hotel Cascais Miragem
Lisbon (Cascais) | Portugal

CONFERENCE 4-5 DEC | **EXHIBITION** 4-5 DEC | **TWO-DAY TRAINING COURSE** 6-7 DEC

https://europe.pda.org/PDAEMA2012

The Parenteral Drug Association presents the...

PDA Biennial Training Conference

From Training to Learning – Improving Performance in a Regulated Environment

October 8-9, 2012

Hyatt Regency Bethesda | Bethesda, Maryland

Following the networking reception on Monday, PDA will be hosting an open house at the TRI facility. Come and see where TRI training takes place!

Taking a systemic view to training is vital to your organizations as a result of generational changing of the guards, the evolution of technology at a more rapid rate than ever before and evolving global regulatory expectations.

Come to the *PDA Biennial Training Conference* and hear about:

- Regulatory Training Expectations, **Umit Kartoglu**, MD, PhD, Scientist, *World Health Organization*
- Why Should Supervisory Training be Different? **James Vesper**, President, *LearningPlus*
- The Globalization of Quality Training: Identifying, Assigning, Tracking and Reporting, **Nadine Rozowsky**, Global Training System Manager, *Baxter Healthcare*
- Evidence-Based Competency: More Than an Observation! **Jill Drummond**, Director, Training and Education, *Blood Systems* and **Jan Gray**, Instructional Design Manager, *Blood Systems*
- Human Error, **Ann McGee**, Managing Director and Principal Consultant, *McGee Pharma International*
- The Open Courseware Initiative at Johns Hopkins University, **Sukon Kanchanaraksa**, PhD, Director, Center for Teaching and Learning, *Johns Hopkins Bloomberg School of Public Health*

"The *2010 PDA Biennial Training Conference* was one of the best events I have attended."

Jacquelyn Scarsella, *ONY*

PDA's Training and Research Institute will be hosting three training courses following the *PDA Biennial Training Conference* on October 10-11.

Visit **www.pda.org/biennial2012** for more information and to register

Exhibition: October 8-9 | Courses: October 10-11

PDA Letter

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Cover Art Illustrated by Katja Yount

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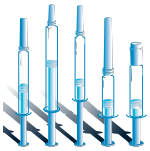


In Memoriam: Former PDA President Nathan "Nat" Kirsch

Robert Myers, Beacon Point Group (former PDA Director, Chair and President)

[PDA is sad to announce the passing of Nathan C. Kirsch, who died on June 23, 2012. He built a distinguished career in 42 years at Schering-Plough, retiring in 1983 as a vice president. "Nat" was a committed leader at PDA. He is a past president and received the first Distinguished Service Award. He was the eleventh member to receive Honorary Membership.]

I was sad to hear of Nat Kirsch's passing this summer, and it caused me to reflect on his positive impact on my life and his similar positive impact on PDA, an organization he loved.

I met Nat in 1974 at Schering-Plough when he was Director of Manufacturing for our Union, N.J. site, and I was an entry level chemist in sterile manufacturing. He was a powerful influence on the site and went on to lead our quality organization in the late '70's and early '80's. He remained my mentor for my entire industry career, including my many years in the PDA organization.

During the '60's and '70's Nat was active in PDA, serving as both a Board Member and Chairman of the Board, and he made significant contributions to the modernization of the parenteral industry. One of his most important improvements was bringing a scientific approach to the new concept of pharmaceutical sterilization and process validation. In the mi-70's, the FDA oversight group lead by Bud Loftus and Ted Byers required that we, the product manufacturers, prove scientifically that our systems and processes do what they were supposed to do. Nat had the insight to bring thought leaders from the food industry, such as Irving Pflug, PhD, from the University of Minnesota Food Science Department, to the parenteral drug industry to educate both the manufacturers and the FDA in the proper way to conduct validations. This basic scientific approach that was introduced to our industry through the PDA at that time has now been adopted at a global level.

Nat remained interested in PDA activities long after he retired. During our dedication of the new TRI in Bethesda in 2007, he expressed to me that he was amazed to see that PDA is so well recognized here in the United States and internationally, both by industry and regulators. I think he viewed our success with tremendous pride since he cared so much about PDA and had invested so much of his time and energy. He set a great example for all of us and will be sorely missed.

[Editor's Note: In 2006, Bob Myers interviewed Nat for the *PDA Letter.* The following is an excerpt. The complete interview is in the January 2006 *PDA Letter,* available in the members only archive at www.pda.org/pdaletter**.]**

Myers: What do you see as PDA's largest contribution to the industry?

Kirsch: That's almost like asking which of my kids I like best. PDA has made many contributions to the industry in the area of better pharmaceutical science, especially in the area of sterility assurance. In the 50's and 60's, the pharmaceutical industry was using techniques for sterilization that just didn't work. One technique was called tindallization, which called for raising the temperature of a solution to 50-60°C for one hour and then cooling it. This was repeated three times, and the material was supposed to be sterilized. This, of course, does not sterilize.

This brings me to my most significant contribution to the industry. This was to get Irving Pflug [University of Minnesota] to put the sterilization course together. I told him that the industry needed a progressive sterilization program with a good validation approach. That goes back 30 years, and believe it or not, the PDA Board at the time was not 100% behind the idea, since some of the members thought we already knew enough about sterilization....PDA has used his material ever since.…It is a good lesson for PDA—focus on the need of the industry, not what people want to talk about.

Myers: What direction do you see PDA going in the future?

Kirsch: One of the most important aspects of PDA is the Association's interest in trying to get people to talk in meetings about issues. The ability to ask speakers questions at meetings has been one of the great things about PDA… Those discussions were generally better than the presentations.

Nathan Kirsch, his wife Ida pose with then PDA President Bob Myers at the opening of the new TRI facility in 2007

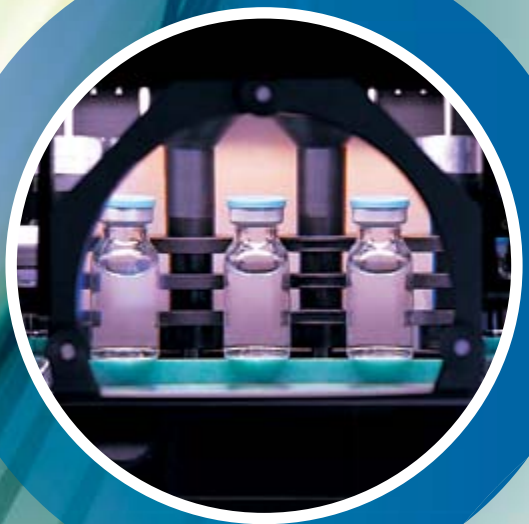
The Parenteral Drug Association presents...

2012 PDA Visual Inspection Forum

See the Highlights:

- **Recent compendial and regulatory activities**
  - Regulatory inspection trends
  - What's new from the pharmacopoe and health authorities
- **New inspection technologies**
  - Particles
  - Protein aggregates
  - Freeze dried products
  - Automated integrity and leak testing
- **Special considerations for the inspection of biopharmaceuticals**
  - Monoclonal antibodies
  - Freeze dried products and liquids in pre-filled syringes
- **Preparation and use of standards and defect sets**
- **Classification of defects and preparation of defect libraries**
- **Qualification of manual and validation of automated inspection systems**

Training Course An Introduction on Visual Inspection - Make sure your seat!



You will have a plenty of case studies, networking and discussion opportunities. Don't miss the two-day hands-on training course!

25-28 September 2012

RAMADA Hotel Berlin-Alexanderplatz
Berlin | Germany

CONFERENCE 25-26 Sep | **EXHIBITION** 25-26 Sep | **TRAINING COURSE** 27-28 Sep

https://europe.pda.org/VisInsp2012

Volunteer

Jonathan Morse, Principal Consultant, Complya Consulting Group

Areas of Volunteerism: New England Chapter: Board (Secretary), Event Planning Committee, and Middlesex Community College Scholarship Committee

PDA Join Date: 2009

Interesting fact about yourself: I am an avid traveler. I dream about starting a business in a developing country in the future.

Why did you join PDA? The PDA New England Chapter is made up of a wonderful group of professionals and served as my initial exposure to PDA. The camaraderie and community here lured me in, and I've never looked back!

Of your PDA volunteer experiences, which have you enjoyed the most? In 2011, I volunteered to review Middlesex Community College Scholarship applications (the Chapter provides scholarships to deserving students). I had the privilege to read several outstanding applications and inspiring essays from the students, and I was reminded of the real reason we are in this industry.

How has volunteering in PDA benefited you professionally? PDA provides a space for like-minded professionals to meet and share stories, technical information and friendship. Networking within PDA has introduced me to some fantastic new colleagues and reconnected me with long-lost former coworkers.

Which PDA conference/training course is your favorite? *The PDA/FDA Joint Regulatory Conference* is my all-time favorite. This conference provides an outstanding opportunity to ask the FDA, and industry leaders, first-hand about whatever is on your mind. In a few cases, we've been able to provide clients with 'real-time' feedback from conference by asking the FDA anonymous questions on their behalf.

What would you say to somebody considering volunteering with PDA? Go for it! PDA volunteers are the backbone of this great organization.

2010 Honor Awards Recipients

The PDA Honor Awards are bestowed on members who provide exceptional leadership and service to the Association and have been awarded at the Annual Meeting since 1958. The 2010 award winners were announced at the *2011 Annual Meeting* in April, and they will be highlighted in each *PDA Letter* until next year's event. This month we present the Frederick D. Simon Award winners.

Frederick D. Simon Award

This award is presented annually for the best paper published in the *PDA Journal of Pharmaceutical Science and Technology.* This award is named in honor of the late Frederick D. Simon, a previous PDA Director of Scientific Affairs.

The paper, *Risk Analysis of Sterile Production Plants: A New and Simple, Workable Approach* was chosen by the Fred Simon Award Committee. It was published in the May/June 2011 issue of the *PDA Journal.*

Guenther Gapp, PhD

Peter Holzknecht

Your "Secret Weapon" in the battle for compliance

USE YOUR "SECRET WEAPON" TO LEARN:

- How to avoid criminal 'Park Doctrine' liability if your company cuts corners on quality
- How to make sure recalls don't cause shortages of your drug products
- How to win FDA approval for big changes like single-use systems
- How to protect your supply chain from high rollers in procurement
- AND MUCH MORE!

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are eligible for specially
discounted rates*
for new/individual subscriptions.

For more information, contact: **Ida Stepinac**,
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PDA Italy Chapter Meets Italian Medicines Agency

PDA headquarters is not the only part of the Association driving the connection with regulators. On May 8, 2012, the PDA Italy Chapter had the pleasant opportunity to present its activities to the new General Director of the Agenxia Italiana del Farmaco (AIFA, the Italian Medicines Agency). Professor **Luca Pani** met with Chapter leaders at the AIFA headquarters in Rome.

Italy Chapter President **Dr. Walter De Matteo**, Past President **Dr. Stefano Macciò,** CTP, and Chapter Steering Committee member and PDA Director **Dr. Gabriele Gori** met with Dr. Pani and other employees and inspectors of different AIFA offices.

The meeting began at about 14.30 with an introduction by Dr. Macciò and a discussion of PDA and the Italy Chapter by Dr. De Matteo. The latter presentation covered the Vision and Mission of PDA and highlighted various technical publications issued by PDA.

The PDA Italy Chapter, founded in 2000, aims to apply the goals and mission of PDA, though tailored to meet the specific needs of members in Italy, without losing sight of the international standards. The objective of the Italian Chapter is to establish an avenue of dialogue between AIFA and industry, in order to facilitate understanding of the applicability of the regulations.

Dr. Gori said this initiative will allow both industry and the Agency to access and share a heritage of great scientific and technical knowledge—the result of activities and collaboration between PDA and many scientific and regulatory institutions around the world. Together, the PDA Italy Chapter and AIFA can adapt and develop this information according to specific needs of the Italian market and open a way to further the contribution of Italian experts to the advancement of pharmaceutical science.

Dr. Pani showed much interest in the training/information activities carried out by the PDA Italy Chapter. He recommended that these initiatives be implemented in Rome, thereby minimizing the costs of travel of inspectors. He then outlined the new rules and limitations for requesting participation of inspectors from the Italian health agency to events organized by professional associations. For these purposes, the PDA Italy Chapter proposed to AIFA the active participation of AIFA representatives in planning conferences and workshops, in PDA task forces and other activities.

Dr. Pani confirmed the interest in a partnership between PDA and AIFA, provided the following criteria are met:

- PDA will ask the Agency's formal consent whenever the Italian Agency is referenced in PDA Chapter material
- The Agency shall have the right to veto any document or PDA Italy Chapter activities involving the Agency which is not considered appropriate by the Agency itself.
- AIFA personnel who will collaborate from time to time with the Association will be chosen by the Agency.

The PDA Italy Chapter offered three free annual PDA memberships for AIFA personnel, to be selected by Prof. Pani and communicated by AIFA: This will allow them to receive free Technical Reports and Association documents.

The meeting ended with mutual satisfaction of both parties.

This initiative will allow both industry and the Agency to access and share a heritage of great scientific and technical knowledge

PDA Who's Who

Luca Pani, General Director, AIFA

Walter De Matteo, IBSA

Stefano Macciò, CTP

Gabriele Gori, Novartis Vaccines & Diagnostics

The Parenteral Drug Association presents...

The Universe of Pre-filled Syringes and Injection Devices

Integrating the Unmet Market Needs: Bringing it All Together for Tomorrow's Success

October 15-17, 2012

Red Rock Resort and Spa | Las Vegas, Nevada

Visit over 80 exhibitors and suppliers at this year's meeting!

It has long been acknowledged that pre-filled syringes offer significant benefits to both the user and drug manufacturer. Regulatory requirements, industry experience and evolving market trends are critical considerations to ensure a complete understanding of the application of pre-filled syringes and injection devices to drug delivery.

The Universe of Pre-filled Syringes & Injection Devices conference is an excellent opportunity to interact with peers and industry experts in this growing field. Whether you are new to the field or an industry veteran, you will take away practical knowledge to put immediately into use as well as meet new colleagues and contacts.

If you have an interest in drug delivery devices, pharmaceutical/biopharmaceutical manufacturing with drug delivery devices, relevant regulatory requirements or want to see what's new, then join us today!

Device Professionals:
- Session A1: Device Development – Lessons Learned
- Session B2: Case Studies in Human Factors
- Session P5: Human Factors

Manufacturing Professionals:
- Session B1: Brief Technical Updates from PDA
- Session B2: Formulation and Development of Pre-filled Syringes
- Session B3: New Development in Filling a Pre-filled Syringe
- Session B4: Tools and Measurements

Regulatory Professionals:
- Session A1: The Fundamentals of a Pre-filled Syringe and Combination Products
- Session A2: Case Studies in Pre-filled Syringe QbD
- Session B1: Safer Injection Design and Practices
- Session P2: Compliance/Adoption
- Session P3: Regulatory Trends
- Session P4: Combination Products
- Session P6: Emerging Market Assessments and Panel Discussion

What's New:
- Session P1: Keynote Address – A Patient Needs
- Session A2: New Technologies – Technologies of the Future
- Session A3: New Development of Glass Syringes
- Session A4: New Development of Polymer Syringe

"There was a wealth of information available"
Lisa Gebbia, *Pfizer*

Immediately following the conference, PDA's Training and Research Institute (PDA TRI) will host three courses from October 18-19, 2012.

Visit **www.pda.org/prefilled2012** for more information and to register.

Exhibition: October 15-16 | Courses: October 18-19

Please Welcome the Following Industry

Karla Aberle, Sigma Tau Pharmasource

John Abt, Teva

Yuki Akiyama, Nippon Kayaku

Takashi Amano, Astellas Pharma Inc.

Nicola Ambler, Pharma IQ

Anthony Andrews, Pharmeng Technology

Marika Antunes, BEBEVIDA SA

Midori Anzai, BD Medical

Jennifer Archer, Gilead Sciences Inc.

Ofra Axelrod, Israeli Ministry of Health

Masanobu Azekawa, Nihon Pharmaceutical Company Inc.

Rose AzzaroBass, Acceleration Laboratory Services Inc.

Gitte Bach-Breitling, Danish Health and Medicines Authority

Patrick Bailey, Merck

Meade Baker, DME Alliance

Julie Barbeau, GlaxoSmithKline Vaccines

Gudrun Bauer, Baxter SA

Jennifer Bayer

Heather Beard, NHS Blood and Transplant

Barbara Behle, Miltenyi Biotec GmbH

Rim Benmaamar, Novartis Pharmaceuticals

Irene Berner, Worcester Polytechnic Institute

Fabrice Berthaud, GlaxoSmithKline Vaccines

Thierry Bilbault, Galderma

Anna Bjerg Jessen, William Cook

Enrique Blanco, Teva Pharmaceuticals

Emma Blasi, VCN Biosciences

Diane Blinn, Millennium

Lesley Bobiak, Merck

Lisa Boswell, GlobeImmune, Inc

Lamine Bouakaz, Novartis Pharmaceuticals

Mathias Braun, Optima Group Pharma

Mitchell Brockey, Kremers Urban Pharmaceuticals Inc.

Amy Brown, Upsher-Smith Laboratories Inc.

Sonja Broyles, Genzyme

Emily Buck, Amgen

Robert Buhlmann, Amgen

Andrey Bulimov, Novartis Vaccines & Diagnostics

Zaklina Buljovcic, PharmaLex GmbH

Naomi Burgos, MSD

Thomas Burns, Genentech

Zsuzsanna Buzas, National Institute of Pharmacy (NIP)

Lucio Cabral, UFRJ

Roslyn Cameron, BioReliance

Cliff Campbell, Cliff Campbell Consulting Ltd.

Samantha Cantrell, Novartis Animal Health

Nicolás Caputi Adium Pharma

Arturo Carrion-Portela, Amgen

Sofia Caruso, SANDOZ

William Cashin, Alexion

Thea Catalig, Onyx Phamaceuticals

Natacha Cendrier, Altran

Larry Chan, ProPharma Group, Inc.

Dipen Chemburkar, Millennium

Trisha Chetty, National Bioproducts Institute

Britt Christensen, Bavarian Nordic

Amy Chu, Onyx Pharmaceuticals

Rawle Collins, Hospira

Claudio Correa, F. Hoffmann-La Roche Ltd.

Cheryl Crain, Regeneron Pharmaceuticals Inc.

Damaris Cruz, Sartorius Stedim Biotech

Richard Czarnecky, Biopharmaceuticals

Michael Daferner, Bayer Healthcare AG

Yoshihiro Daito, FujiFilm

Miguel Dalmau, Amgen

Shannon Daly, Onyx Phamaceuticals

Terumi Daly, Biogen Idec

Neil D'Angelo, Onconova

Maged Ahmed Darwish, F. Hoffmann-La Roche Ltd.

Arun Das, Aurobindo Pharma Limited

Claire Davies, Coldstream Laboratories Inc.

Christopher Day, Bristol-Myers Squibb

Matthew Deacon, Eli Lilly

Francois Delval, GlaxoSmithKline Biologicals

Kristin Demyan, Genentech

Isidro DeSantiago, Fresenius-Kabi

Prasad Deshmukh, Baxter Healthcare

Abraham Diaz-Debien, Bristol-Myers Squibb

Tracey Dickens, Pfizer

Alexandra Dilis, Bayer HealthCare

Evelyn DiMarco, Genentech

Klaus Diry, Abbott

Brittany Doyle, Hospira

Beverly Drever, Genentech, Inc..

Dianne Dreyer, Consultant

Michelle Duber, Ben Venue Laboratories

Anna Ducka, Polpharma S.A.

Egidio Durante, Novartis Animal Health

Jason Durkin, Nypro Inc.

Tod Eberle, Amcor Rigid Plastics

Gunilla Edman, Medical Product Agency Sweden

Nasir Egal, Sanofi U.S.

Robin Emrick, Merck

Jochen Farrenkopf, Abbott

Chase Fischer, CSL Behring

James Flament, AMRI

Karin Frausing Basse, William Cook Europe ApS

Crystal Fujihara, OSO Bio Pharmaceuticals

Yutaka Fukazawa, Daikyo Seiko, Ltd.

Brian Fuller, Baxter Healthcare

Michael Garcia

Kiee Garland, OPK Biotech LLC

Scott Gaskins, Eli Lilly

Rene Geyeregger, St. Anna Children´s Cancer Research Institute

Aarti Gidh, GlaxoSmithKline Biologicals

James Gilbert, Biogen Idec

Christophe Gimberg, F. Hoffmann-La Roche Ltd.

Megan Gladfelter, Fresenius Kabi / APP Pharmaceuticals

David Goldschmidt

Manuela Gottschall, F. Hoffmann-La Roche Ltd.

Deborah Gross, Merck

Anthony Grzib, Wedgewood Pharmacy

Roland Guenther, Boehringer Ingelheim

Jens Peter Gundorf, Novo Nordisk AS

Sharad Gupta, Merck, Sharp, and Dohme

Stephen Hadley, CMC Biologics

Rob Hamilton, Sigma Tau Pharmasource

Tomoyuki Hanazawa, Mikasa Seiyaku

Marlene Hansen, Novo Nordisk

Shinichi Harada, Maruho Corporation

Leaders to the PDA Community

K. Nicole Harter, Eli Lilly

Jeff Hartman, medimmune

Jason Hartman, Genzyme

Thomas Haselwander, Novartis

Ryosuke Hashimoto, Toyama Chemical

Takao Hayakawa, Kinki University

Toni Hedge, Morphotek

Nacer Hedroug, Hospira

Hasse Herlevsen, Leo Pharma A/S

Michelle Herrick, Lantheus Medical Imaging

Liat Hershkovitz, ADRES Advanced Regulatory Services Ltd.

Hans-Jörg Hesselbarth, Ellab GmbH

Leanne Hickman, Eli Lilly

Brenda Hildebrand, BioReliance

Toshinobu Hirayama, BD Medical

Galia Hochstadt, Sanofi-Aventis Israel ltd.

Andras Holczinger, Gyemszi-Ogyi - National Institute fo Pharmacy (NIP)

James Horger, Covidien

Jeremy Howell, Hospira

Boriana Hristova, Charles River Laboratories

Benjamin Hsieh, ProPharma Group, Inc.

Brian Hubka, Pegasus Pharmaceutical Inc.

Harry Ingersol, Cambrex Charles City, Inc

Wataru Ishii, Tokyodylec Corporation

Haruki Iwamoto, Rohto Pharmaceutical

Signe Jakobsen, Novo Nordisk

Hanne Jensen, Nycomed

Barrington Johnson, Therapeutic Proteins International, LLC

David Johnson, BioPharm Consult LLC

Timothy Johnson, Johnson & Johnson

Brian Johnson, Pfizer

Nigel Johnson, Tissue Therapies Ltd.

Peter Jones, OxfordBioMedica

Tanja Kaartinen, Finnish Red Cross Blood Service

Masayuki Kadosawa, Japan BCG Laboratory

Masashi Kagihiro, Dainippon Sumitomo Pharma

Chiemi Kamakura, NextDocs Corporation

Martin Kane, Sangart, Inc.

Jennifer Kay, Seattle Genetics, Inc.

Alexander Khaw, ICQ Consultants

Daniel Kim, Hospira

Kaoru Kimura, BD Medical

Satoshi Kiyose, Kyowa Pharmaceutical Inc.

Lacey Klungseth, Biothera

Kathrin Knauf, Novartis

Jonathan Knight, Avanti Polar Lipids

Patricia Knoblauch, Abbott Laboratories

Motoi Kobayashi, Mikasa Seiyaku

Takayuki Kondo, OZU Corporation

Shinichiro Konishi, TSUMURA & Company

Mark Kontny, Patheon Inc.

Ines Kraemer, Roche Diagnostics GmbH

Patricia Krainski, American Stelmi Corporation

Isao Kudo, Ube Industries,Ltd.

Andrey Kuharenko, THC

Todd Kuhn, West Pharmaceutical Services

Ajith Kumar, SCHOTT KAISHA PVT Ltd.

Christopher Kump, Merck

Sadashi Kusuki, Nipro Pharma

Michael Landwehr, BIVI

Gary LaRowe, Genentech

Steven Laurenz, Abbott Laboratories

Elena Learner, Otsuka America Pharmaceutical

Seonyoung Lee, Hanmi Pharm.

Thomas Leitch, Merck

Lilian Liew, GSK Biologicals

Allan Lin, Daiichi Sankyo Co Ltd.

Ming Der Lin, Purzer Pharmaceutical

Jorge Lockwood, Baxter

Tony LoCurcio, W.L. Gore and Associates

Yi-Yin Lu, Taiwan Parenteral Drug Association

Audrey Luecke, Kremers Urban Pharmaceuticals Inc.

Ronald Mack, Hospira

Klaus Madsen, Bavarian Nordic A/S

Wencke Maeder-Wotruba, CSL Behring GmbH

Scott Magalengo, Merck Sharp & Dohme

Elizabeth Mahoney, Baxter SA

Kirit Majumdar, Pfizer Pharmaceutical India Pvt. Ltd.

LaDonna Marquette, Celgene

Henry Martinez, Genentech

Felix Martinez, General Electric

Gil Martinez-Betancourt, Valence Group

Tomoko Matsubara, TEIKOKU SEIYAKU

Yukari Matsumoto, RaQualia Pharma Inc.

Christian Mayer, AGES PharmMed

Danelda McCullagh, BioReliance

Claire McCarthy, Amgen

Timothy McCoy, Genzyme

James McFarland, Gerresheimer

Donna McMutrie, BioReliance Ltd.

M. Gail Meadows, PnuVax SL Biotherapeutics

Hedie Meka, Tissue Therapies Ltd.

Jonathan Menard, Genzyme

Pedro Mendez, ALPHA TECH USA, L.L.C.

Julie Meno, Ben Venue Laboratories

Kunihiko Metsugi, Rohto Pharmaceutical

Ellen Milano, Milano Regulatory Solutions

Jeffrey Miles, Hospira

Corinne Miller, EMD Millipore

Raymond Miller, Sanofi U.S.

Paul Miller, Merck Sharp & Dohme Corp.

Samuel Minno, Bio-Concept Laboratories, Inc.

Hiroshi Miyachi, FujiFilm KYOWA KIRIN BIOLOGICS

Setsuko Miyanari, Cosmo Seiwa Agriculture

Yutaka Miyazaki, Mochida Pharmaceutical

Michael Moran

Patrick Morris, Eli Lilly

Britta Mortensen, Novo Nordisk

Elizabeth Moser, bioMerieux, Inc

Michael Moshman, Lachman Consultants

Juli Moticka, Regeneron Pharmaceuticals

John Motzi, Janssen Research & Development

Cheryl Munday, Prometheus Laboratories

Juan Munoz, Microbiology & Quality Associates Inc.

José Muradian, Pall

Toru Murakumo, Mitsubishi Tanabe Pharma Corporation

Koichi Muramoto, BD Medical

Charles Mutchiga, Johnson & Johnson

Please Welcome the Following Industry Leaders to the PDA Community

Scott Myers, Ben Venue Laboratories

Koh Nakagawa, Nagase Medicals

Katsuya Nakazawa, BD Medical

Venkata Nanduri, Bristol-Myers Squibb

Fumihide Nishio, Asahi Kasei Pharma

James Norton, Ben Venue Laboratories

Tetsuhiro Ogino, Dainippon Sumitomo Pharma

Hidenori Ohki, Towa Pharmaceutical

Augustus Okhamafe, BioMarin

Niall O'Leary, Regeneron Pharmaceuticals Inc.

Pedro Oliveira, Trb Pharma

Laurie Oliver, Hospira

Haruki Oota, Futaba Pharmacy

Duncan Pack, Genentech

Ravi Paladugu, Baxter Healthcare

Sarah Parker, IDRI – Infectious Disease Research Institute

Allyson Parris, SANDOZ

Gayle Pasik, Bausch & Lomb Inc

Raj Patel, 888 Consulting

Clive Patience, Biogen Idec

Warren Perry, QUMAS

James Petzel, Abbott Laboratories

Jens Philipp, Optima Group Pharma

Christopher Phillion, Pfizer

Scott Piro, Merck Sharp & Dohme Corp

Jonathan Platt, Amgen

Kristen Potuck, Merck Company

Eliud Poventud, CryoLife

Priti Prasad, Slade Health

Malcolm Pratt, Grifols

Anja Preissmann, Boehringer Ingelheim Pharma

Robert Quesinberry, JHP Pharmaceuticals

Karen Quigley, European Medicines Agency (EMA)

Andrew Quinn, GlaxoSmithKline

Hina Qureshi, Abbott Laboratories

Jonathan Rado, Lehigh University

James Ranlet, Hyde Engineering & Consulting

Andrew Ratz, Eli Lilly

Janet Rea, Protein Sciences

Michaela Rehberg, Spezialgeräte

Laura Reid, Duke Clinical Research Institute

Leticia Reyes, Azaya Therapeutics Inc.

Martha Riddle, Nantworks

Timothy Riggie, Cangene bioPharma

JeanFrancois Rioux, GSK Vaccines

Skye Rivera, Avid BioServices

Joel Rivera Gandia, Amgen

Keanicia Rodgers, Hospira

Steven Roese, Marken LLP

Arthur Romo, Baxter SA

Brid Rooney, Genzyme

Agnes Roque, Gilead Sciences Inc.

Deborah Rose, Hospira

Simona Rovetta, MolMed

Josee Roy, Medtronic

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Alicia Sardar, ImClone Systems / Eli Lilly

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Tadashi Seto, Rohto Pharmaceutical

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Lisa Shaner, Pfizer

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Ashley Velez, JHP Pharmaceuticals

Jaana Vesterinen, Finnish Medicines Agency

Philip Villari, Merck Sharp & Dohme Corp.

Jennifer Vo, Becton Dickinson

Loc Vo, biomarin

Robert Vonder Reith, Sangart

Nicole Wagner, Roche

Rebekah Wagurak, Gateway Analytical

Atsuo Waki, National Institute of Radiological Science

Stan Walczynski, Kymanox

Der-Yuan Wang, Taiwan FDA

Kazuichi Watanabe, Kitasato Daiichi Sankyo Vaccine., Ltd

Takeshi Watanabe, Guerbet Japan K.K.

Hitoshi Watanabe, BD Medical

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Tung Hei Yong, Dept of Health and Human Services

Satoshi Yoshida, Mikasa Seiyaku

Mika Yoshimatsu, Daiichi Sankyo

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PDA/FDA Pharmaceutical Supply Chain Conference

Global Supply Chain Integrity – A Shared Responsibility

November 13-14, 2012

Bethesda North Marriott Hotel | Bethesda, Maryland

PDA has secured regulatory speakers from diverse groups like: *CDER Compliance, Office of Drug Security, Integrity and Recalls; Forensic Chemistry Center; Office of Criminal Investigations; CDER Drug Shortage Program & Inspection Enforcement and Standards Division, MHRA*

Building on earlier PDA-cosponsored conferences and workshops, the 2012 PDA/FDA Pharmaceutical Supply Chain Conference will provide a forum for presentations by industry experts as well as group discussions that will foster the implementation of innovative ideas that will enhance supply chain integrity to protect patients from potentially unsafe or ineffective medicines.

- **Lieutenant Commander Eleni Anagnostiadis,** Acting Deputy Director, Division of Supply Chain Integrity, Office of Drug Security, Integrity and Recalls, *CDER, FDA*
- **Ilisa Bernstein,** PharmD, JD, Acting Director, Office of Compliance, *CDER, FDA*
- **Frederick Fricke, Jr.,** Director, Forensic Chemistry Center, *ORA, FDA*
- **Gregg Goneconto,** Special Agent, Office of Criminal Investigations, *FDA*
- **Gerald Heddell,** Director, Inspection Enforcement & Standards Division, *MHRA*
- **Captain Valerie Jensen,** Associate Director, Drug Shortage Program, *CDER, FDA*
- **Commander Connie Jung,** PhD, Acting Associate Director for Policy and Communications, Office of Drug Security, Integrity and Recalls, *FDA*
- **Nancy Kennedy,** Special Agent, Senior Operations Manager – Drug Investigations, Office of Criminal Investigations, *FDA*
- **Steven Wolfgang,** PhD, Acting Associate Director, Risk Science, Intelligence and Prioritization, *CDER, FDA*

Immediately before the conference, the PDA Training and Research Institute (PDA TRI) will be hosting a one day course, Developing a Robust Supplier Management Process on November 12th.

Visit **www.pda.org/supplychain2012** for more information and to register.

Exhibition: November 13-14 | Course: November 12

PDA Interest Groups & Leaders

PDA Interest Groups are divided into five sections by subject matter. Any PDA member can join one or more Interest Group by updating their member profile (www.pda.org/volunteer). Please go to www.pda.org/interestgroups for more information.

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- Trends in Manufacturing
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Wolfgang Epple, *Cilag*
Günther Gapp, *Sandoz*
Paolo Golfetto, *Nuova Ompi*
Roland Guinet, *RGmp Compliance, Former AFSSAPS*
Friedrich Haefele, *Boehringer Ingelheim Pharma*
Jackie Horridge, *Azbil BioVigilant*
Torsten Müller, *Cilag*
Jim Nadlonek, *Bausch + Ströbel*
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The following are PDA's Chapters, organized by the regions of the world in which they are located. For more information on the Chapters, including their leaders and upcoming events, go to their websites which are listed below.

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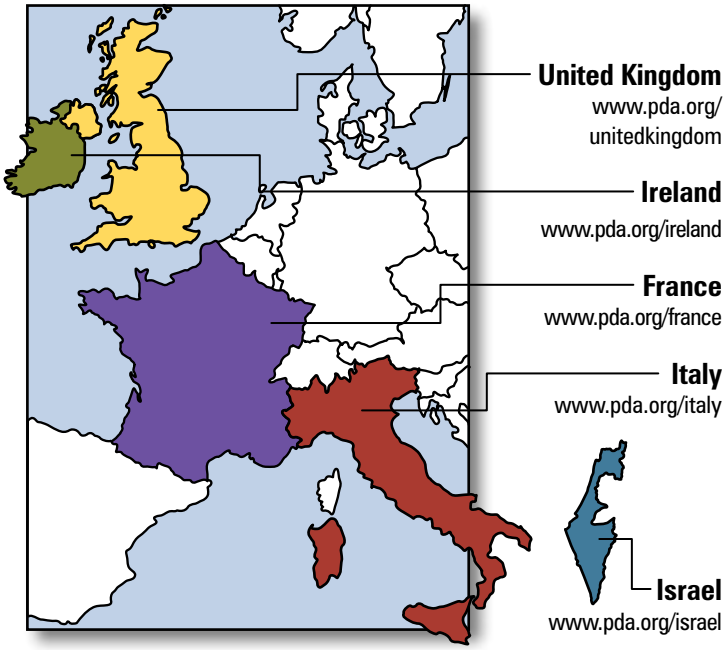
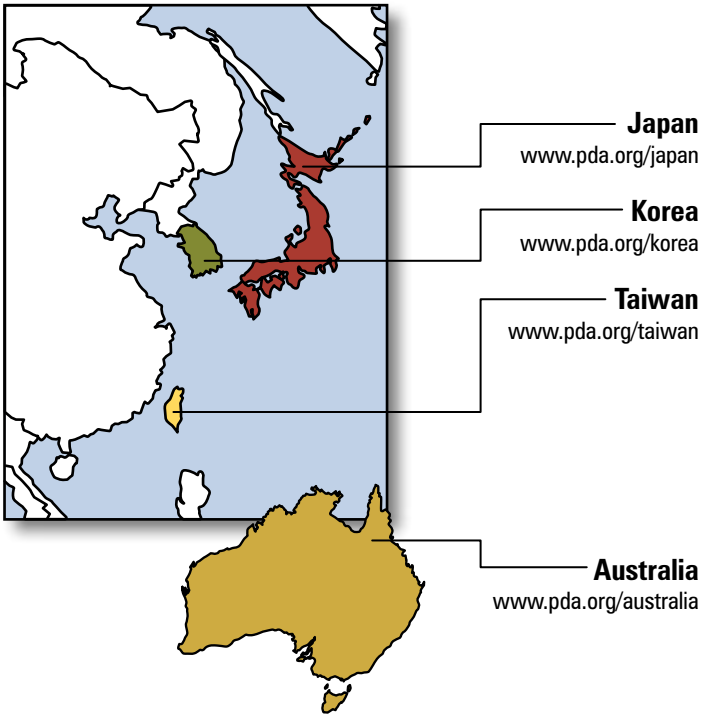
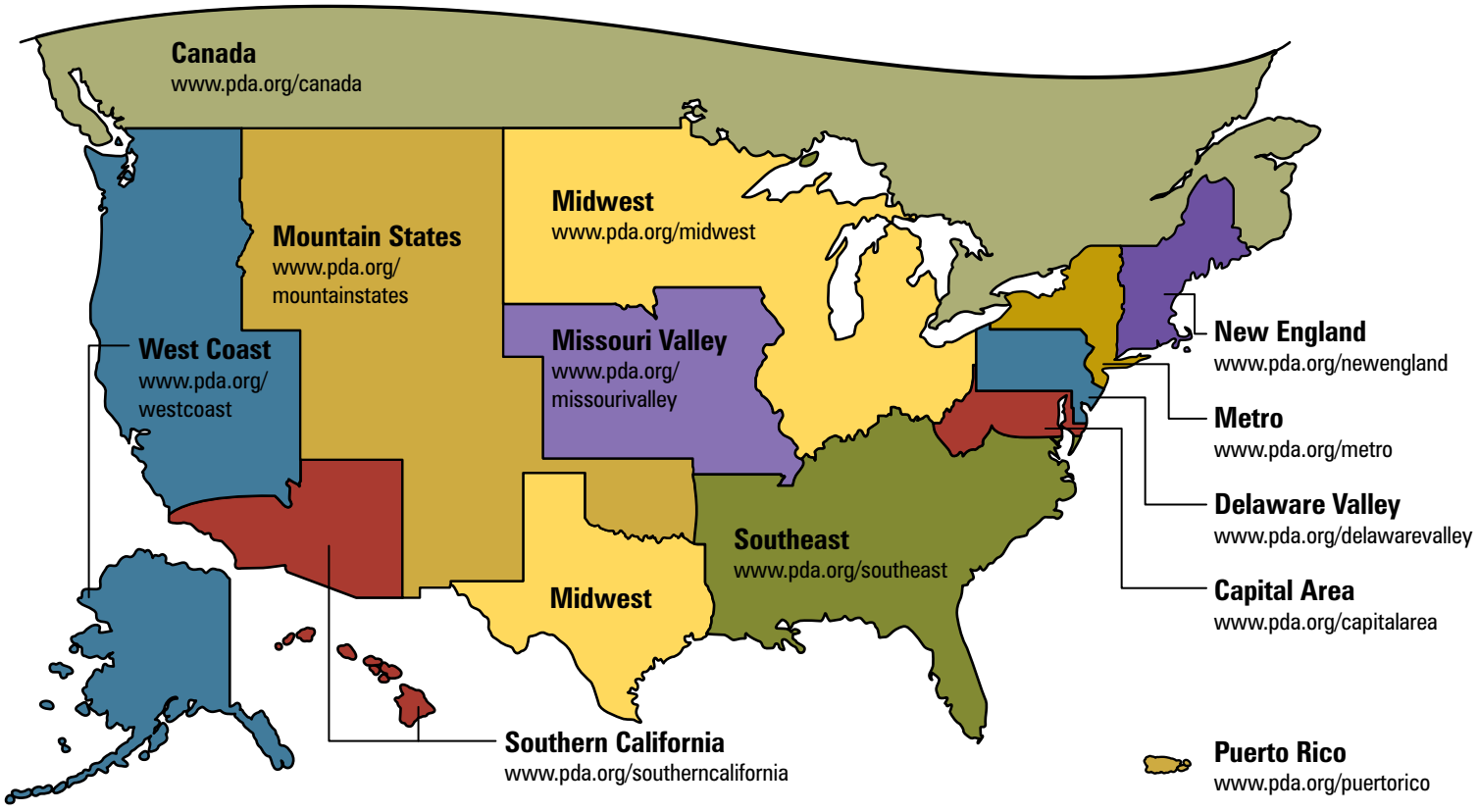


ASIA-PACIFIC



NORTH AMERICA



snapshot

In *Print*

Strategize Enterprise System Testing

The following is excerpted from the chapter "Test Strategies," which appears in the PDA/DHI book, Validating Enterprise Systems: A Practical Guide, *by David Stokes. The book can be purchased at the PDA Bookstore, pda.org/bookstore.*

Testing is a fundamental requirement for the successful validation of an enterprise system. For a system that has been significantly configured or customized, it is final user acceptance testing (UAT) that provides the necessary documented evidence that the system is fit for purpose and meets the regulated company's requirements.

In the case of an enterprise system with minimal ability to reconfigure, it may be possible for the regulated company's users to confirm that the system meets their needs by way of a documented assessment against defined requirements. If this approach is taken, it is also necessary for the regulated company to ensure that the software has been appropriately tested by the software vendor.

In a nonregulated industry, the testing of an enterprise system may well be limited to such UAT, and this may be the only formal testing that will be conducted (and this is done as much for contractual reasons as for quality assurance purposes).

The successful validation of an enterprise system requires testing to be conducted for other reasons (i.e., to provide evidence that the system fulfills the regulated company's requirements and is therefore fit-for-purpose) and the scope and nature of the testing usually exceeds that seen in other industries.

Chapter 16 describes how testing should be conducted, but, before this can start, it is important to define the appropriate scope and nature of the testing to be conducted. It is therefore useful to develop a test strategy to not only describe the approach to testing, but to justify such an approach in the context of risk-based validation (see chapter 14).

Whereas smaller systems or nonvalidated enterprise system will usually have a test plan, a test strategy is a separate stand-alone document (or it can be combined with other validation deliverables), and defines the strategic approach to testing. Where a test plan will focus on defining the "what" and "how" of testing for each test cycle, the test strategy may define common testing practices (including test documentation standards and test deviation processes). It most importantly defines how a risk-based approach to testing will be taken and how the different test cycles are related to one another.

Depending on the size of the program and the regulated company's usual approach to validation documentation, the test strategy can be included as part of the validation plan or can usually can be combined with the risk management plan (since testing will largely be risk-based, and testing is one of the primary methods of risk mitigation). However, in many cases, not all of the testing approach will be fully understood at the time the validation plan is written. So deferment of the development of the test strategy to a later stage in the program provides time to investigate the necessary issues and develop an efficient and effective approach to testing.

Before thinking about the content of a test strategy, it is worth considering the different types of testing that play a useful part in the implementation of an enterprise system.

Testing and Other Forms of Verification

As explained earlier, testing is just one of the forms of verification that has a role in the validation of an enterprise system. Other forms may include requirements review, manual inspection of physical items and configuration settings, review of supplier documentation, review of training material, and so on.

While there is no widely accepted agreement on the difference between testing and other forms of verification, testing can be considered to be a proactiv process, where a defined, proactively applied input condition (or conditions) produces a predefined output condition (expected outcome).

Verification can be considered as a review of an existing item comparing a preexisting input to the resultant output. Example of this are an independent comparison of the requirements against the actual package configuration settings (to verify the CRP activities) or reviewing the server build process by comparing the hardware design specification against the actual hardware item during installation qualification.

The test strategy may focus solely on testing activities, but it can also be extended to include the approach to other forms of verification. As a minimum, the scope of the document should be clear with an explicit acknowledgement that not every requirement can be confirmed by testing and that other forms of verification will be used.

As discussed in chapter 8, some activities can be considered either as testing or may be described as another form of verification (e.g., design qualification or prototyping). It is very important that everyone on the program understand that testing is only one form of verification and that test and verification terminology are used in a consistent manner. The development of a test strategy

Continued at bottom of page 22

Journal *POV*

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Govind Rao, PhD, Editor

Evidently you do. I base this on the fact that that you (not you individually—don't worry!) are downloading (and hopefully reading!) the content in our journal. Article sales are also impressively up. These metrics are great—our editorial team works hard to ensure that the highest quality science is published in this journal. Our rejection rates have gone up significantly over the past two years—we spend a great deal of time up front to filter publications.

However, our submissions are down. We need you readers to tell people around you that you like what you are seeing in the *PDA Journal of Pharmaceutical Science and Technology* and to encourage your colleagues and co-workers who may be hard at work in various roles in your organization to publish their work. Our role is to disseminate knowledge and advance the field of regulatory sciences, and all objective measures tell us that we are achieving that goal. However, people do need to make the effort to collate the knowledge they have and send it in so that the collective wisdom that we all share continues to advance.

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So, please invest in your journal and help it to grow and thrive.

Have a great and productive summer (and work on that submission)!

[Editor's Note: Dr. Rao's latest editorial was published in the July/August 2012 issue.**]**

Journal *Preview*

September/October 2012 Lineup

Associate Editor Anurag Rathore tackles the complex issue of biosimilars in India in an editorial. Having returned to India several years ago, Dr. Rhatore provides unique insight on the topic. Commentary articles have been provided, one on filtration and one on auditing.

Editorial

Anurag Rathore, "Guidelines on Similar Biologics: Regulatory Requirements for Marketing Authorization in India"

Commentary

Karen Bartel, et al., "Pre-use/Post-sterilization Integrity Testing of Sterilizing Grade Filters"

Stephan Rönninger, et al., "Considerations on Auditing and GxP Requirements along the Product Lifecycle"

Research

Seung-yil Yoon, et al., "Mass Extraction Container Closure Integrity Physical Testing Method Development for Parenteral Container Closure Systems"

George Miesegaes, et al., "A Survey of Quality Attributes of Virus Spike Preparations Used in Clearance Studies"

Hirotaka Sudo, et al., "Development of A Nondestructive Leak Testing Method Utilizing the Head Space Analyzer for Ampoule Products Containing Ethanol-Based Solutions"

Technology/Application

Praful K. Bhusari, et al., "Application of Flow Cytometry for Rapid Bioburden Screening in Vaccine Virus Production"

Brigitte Zuleger, et al., "Container/Closure Integrity Testing and the Identification of a Suitable Vial/Stopper Combination for Low-Temperature Storage at –80 °C"

Review

Shinkar Dattatraya Manohar, et al., "Drug Delivery from the Oral Cavity: A Focus on Mucoadhesive Buccal Drug Delivery Systems"

You can view the Journal at journal.pda.org/

In Print continued from page 20

can considerably aid in the development of this understanding. The test strategy should be considered as mandatory reading for the whole program team, not just those directly involved in testing.

To Test Or Not To Test

One of the objectives of risk-based validation is to focus validation resources on the areas of the system that pose the greatest risk to product quality and patient safety. In some areas of the system, this will mean that the nature of the testing will be more comprehensive than others.

However, if this is not to have an adverse impact on overall validation resources, it means that some areas of the system may not be tested at all. These are typically those areas with low-risk priority (or which have no GxP criticality) or may include functionality that has previously been tested by the software vendor or the system integrator or the regulated company on a previous project.

While it may be acceptable not to test parts of the system, there are some important considerations that need to be considered.

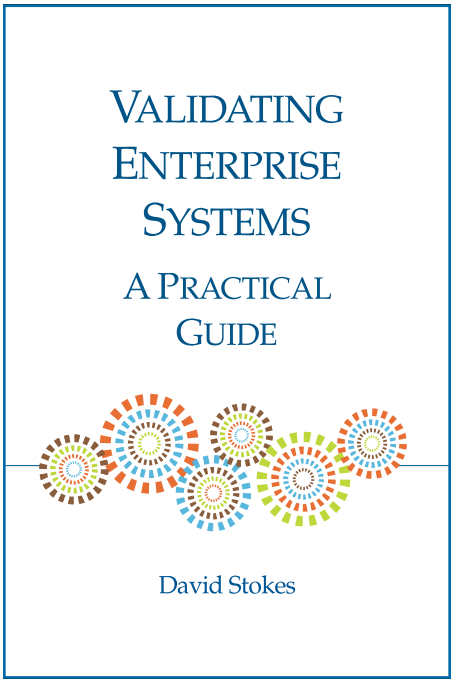
- As an industry, the life sciences sector tends to be risk adverse; this often results in an attitude of "better be safe than sorry." This means that there has been a tendency to test everything, even when there is no pragmatic reason to do so.
- There may be contractual reasons to test every function in the system. In some cases significant stage payments may be linked to the successful testing of the system; this may require testing to be conducted even when there is no risk-based rationale to do so.
- In large complex systems such as an enterprise system, there is often a high degree of interaction between many functions. While regulatory guidance suggests that there is no need to test unused functions, the same guidance also states that it is necessary to prove that the unused functions have no impact on the correct functioning of the desired features.

Bearing all of these points in mind, this frequently leads to a pragmatic situation where:

- Unused functions will be "locked down" (under change control and configuration management), but will not be tested. Since all of the used functions will be tested at some point, this is justified on the basis that there is no undesirable impact.
- All used functions within the system are tested to a minimum extent. This minimum extent will typically be end-to-end positive case business process testing, conducted as UAT and confirming that contractual obligations have been met. Where there is appropriate evidence of testing by the software vendor or the system integrator, this does not have to be tested again by the regulated company.

Note, however, that many software vendors and even system integrators are reluctant to share the results of their own testing—there is an impression that any test defects that are revealed will reflect badly. However, the key issue is not that there were test defects, but that they were fixed before the software was released. The willingness of the software vendor and system integrator to share the results of their previous testing should be part of the supplier assessment.

Finally, consideration needs to be given to the testing of the GxP critical functions when compared to non-GxP critical functions. While it is possible to segregate the two areas, the most pragmatic approach is to extend the risk assessment of the system to include business risks (including financial compliance, e.g., Sarbanes-Oxley controls) and to develop a test strategy that can be applied to both the GxP critical and noncritical functions. This is because appropriate testing is a fundamental part of good quality assurance, regardless of the GxP critical nature of the software. Appropriate testing has value in terms of reducing overall implementation, maintenance and support costs and it makes sense to develop a single test strategy to consider all of the necessary testing.



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Advanced Delivery Systems are Popular, but Pose Challenges for Biotech Injectables

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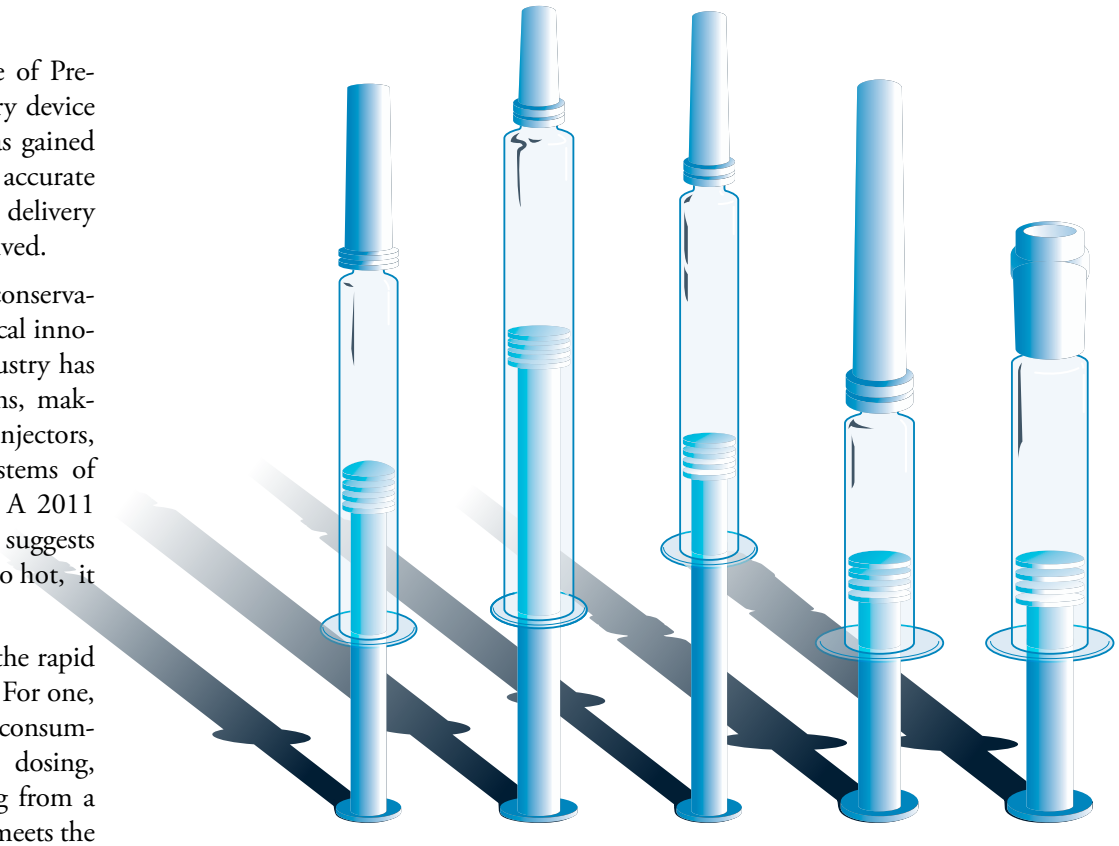

Momentum behind the use of Prefilled Syringes as a delivery device for injectable drug products has gained so much steam, it is no longer accurate to describe them as "emerging" delivery systems. For sure, they have arrived.

For an industry oft-labeled "conservative" with respect to technological innovation, the pharmaceutical industry has embraced these delivery systems, making prefilled syringes and auto injectors, to name two, the delivery systems of choice for injectable products. A 2011 industry report by Visiongain suggests the market for these systems is so hot, it will grow 50% by 2015 ***(1).***

It is easy to see the reasons for the rapid proliferation of this technology. For one, it provides enormous benefits to consumers and practitioners (accurate dosing, elimination of transferring drug from a vial to syringe, etc.). Second, it meets the needs of a changing healthcare marketplace caused both by new therapies and shifting economics (self-administration of drugs, new therapeutic areas). Third, it offers manufacturers benefits (improved safety, increased assurance of sterility, reduced drug overfill).

Part of the explosive growth in the usage of prefilled syringe and auto-injection devices can be explained by the equally explosive growth in the quantity and types of biopharmaceutical products—most of which are sterile injectable products. New therapeutic classes aimed at chronic conditions like arthritis, multiple sclerosis, osteoporosis, to name a few, are also driving growth.

Prefillable Syringes Desirable, Challenging for Vaccines

Adoption of prefilled syringes and auto injectors has not come without challenges, however, particularly with biologics products. The complexity of biologics, and vaccines in particular, requires drug manufacturers to carefully examine delivery system options in order to ensure compatibility. Prefilled syringes and auto injectors must be studied both as delivery devices and storage devices. Placing drug product into one of these devices means exposing the product to, in many cases, at least three different materials, including silicone, which can have deleterious effects on the product. Drug adsorption is another concern.

In development, the appropriate syringe configuration needs to be determined and a complex combination of formulation parameters needs to be understood. This challenge is very acute for vaccine manufacturers. According to **Kingman Ng,** PhD, Head, Pharmaceutical Sciences, Novartis Vaccines & Diagnostics, there are many unique qualities to vaccines that make advanced delivery systems difficult to employ, although such systems are desirable in the marketplace. "First, vaccines products are prophylactic as opposed to therapeutic. Not to mention more often than not, the target population is children and pregnant women, so the regulatory standard is very high," said Ng. "Second, the product types are diverse, such as recombinant proteins, glycoconjugates, virus-like particles, attenuated viruses, and live viruses. On top of that, the doses are usually very small, and we want to combine multi-antigens in one shot. Furthermore, sometimes we need to dose with adjuvants to boost the immune response. You can see the complexity."

Nevertheless, Ng noted, there are many reasons for using prefilled syringes or auto injectors for vaccines. "Unlike other biologics, vaccines are only administered by healthcare professionals; there is no self-administration. Think of a vaccination clinic setting—there is a large number of doses to be given and ➤

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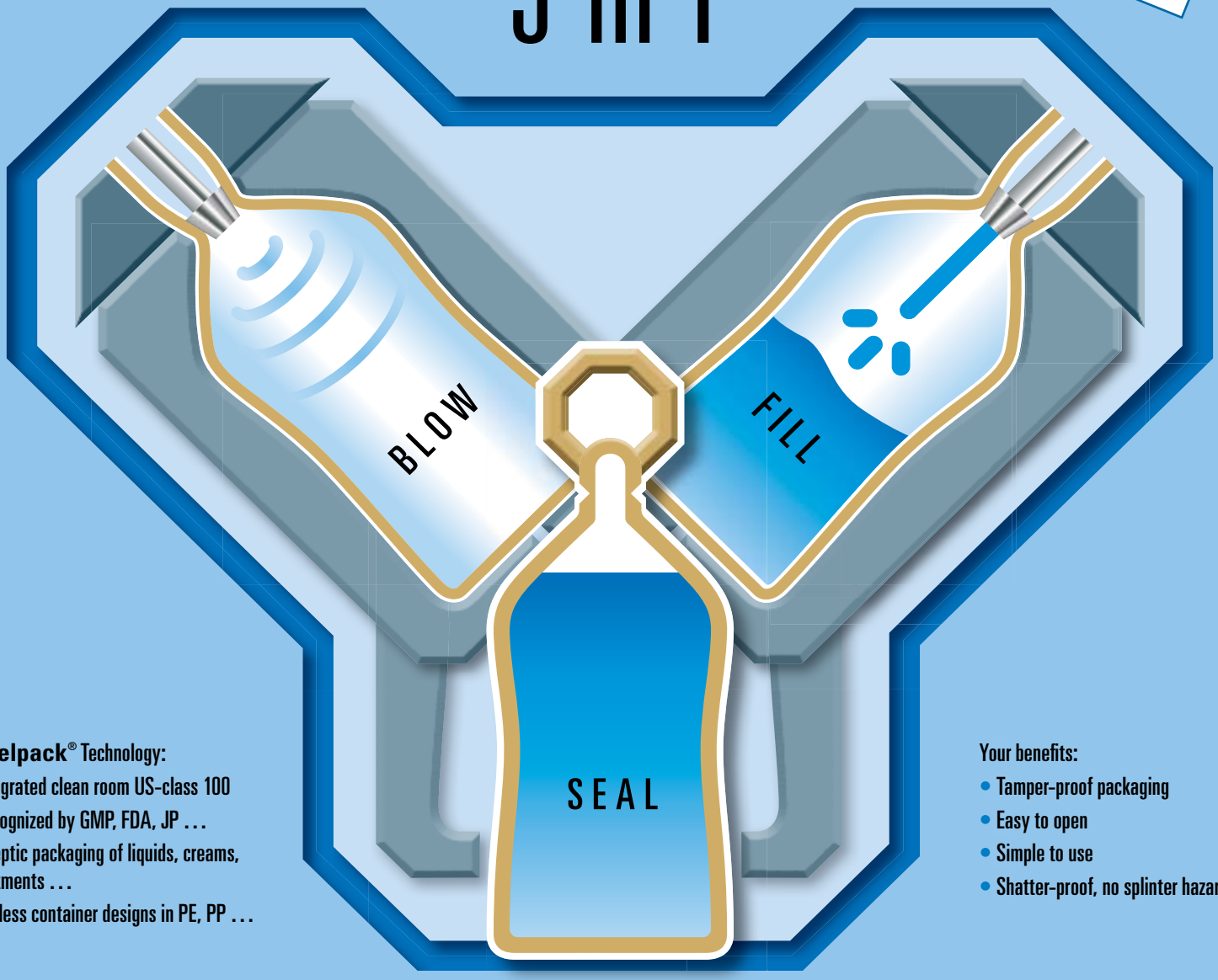

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A challenge in prefilled syringe design is to minimize the amount of lubricant used, typically medical-grade silicone

there is some time pressure. So ease of use without complicated steps plus free of dosing error is critical. You can conclude there is a clear need and driver for prefilled syringes."

Potential incompatibility issues are difficult to overcome, particularly because of the different economies in vaccine production versus other biologics product types. The question is, Ng said, "can we afford new technologies for vaccines due to the very different economics?"

Ng intends to address this issue at the upcoming PDA *Universe of Prefilled Syringes and Injection Devices Conference*. His talk, "Prefillable Syringes for Vaccines," is the first in a session that includes a talk by **Bruce Eu,** PhD, Principal Engineer, Amgen, called, "Formulation Development Work Using Polymer (CZ) Syringe – The Collaboration between West and Amgen."

Solving the Silicone Problem

Requirements for prefilled syringes have significantly increased in accordance with rise of drug delivery devices. The more sophisticated the delivery device becomes, the more stringent the requirements and the design space of the container in regards to performance and defect control.

A challenge in prefilled syringe design is to minimize the amount of lubricant used, typically medical-grade silicone.

According to MedImmune Principal Scientist **Mariana Dimitrova,** "Silicone oil is commonly used as a lubricant coating in prefilled syringes and is becoming one of the most highly discussed syringe attributes posing potential interface incompatibility challenges in the development of sensitive protein therapeutics. Undesirable protein-silicone oil interactions, often resulting in the formation of subvisible and visible particles, have been reported in multiple publications which triggered the need to develop alternative coating offerings."

Dimitrova spoke to the *PDA Letter* about a new BD product her firm is looking at to solve the problem. She will discuss the product more at the upcoming Universe of Prefiled Syringes Conference. "This talk will introduce cross-linked silicone oil coating technology for prefillable syringes, minimizing the container origin subvisible (SbVP) particles while keeping the appropriate syringeability." Her case study will highlight the advantages of the novel coating technology, with a focus on "the evaluation of the compatibility of BD's ➤

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XSi syringe with two monoclonal antibodies that are sensitive to silicone oil. Results will be presented first considering the advantages of the XSi syringes and second demonstrating no adverse impact on the protein therapeutics critical quality attributes, while improving the integrity of lubricant coating and significantly reducing SbVP following fill-finish operations, real life transportation and long term stability."

BD's **Sebastien Jouffray,** Worldwide Program Manager/Research and Development, will discuss the new coating alongside Dimitrova at the conference. He addressed some of the challenges in developing the coating his firm, one of the largest suppliers of prefilled syringe devices (and an advertiser in the *PDA Letter* and sponsor of the upcoming conference), faced in developing it.

Finding a solution is difficult, as it is a "trade-off between the contradictory goals of good lubrication performance and minimal SbVP formation."

Syringes have improved in the past 10 years, said Jouffray. "The first level of control comes from simply decreasing the quantity of silicone oil applied to the barrel while tightly controlling its distribution. To achieve this in the last decade, we first modified the method by which silicone oil is deposited during manufacturing." Robust processes with sprayed or baked silicone results in the need for less lubricant.

BD has developed "a breakthrough innovation" that the firms calls "advanced XSi coating," which achieves both, the required lubrication and prevents SbVP formation from the container, according to Jouffray. It delivers and maintains the best mechanical performance over the full shelf life of the drug while reducing SbVP formation to a minimum.

Together, Dimitrova and Jouffray will present "New Prefilled Syringe Technology: Cross-linked Silicone Coating Reducing Sub-visible Particles (SbVP) and Improving Compatibility with Biologics."

For more on the *2012 Universe of Pre-Filled Syringes & Injections Devices* see the article below.

Continued at bottom of page 42

Vegas Offers Answers to Your Burning Questions

The Universe of Pre-filled Syringes/Injection Devices • Oct. 15-17 • Las Vegas • www.pda.org/prefilled2012

Conference Co-Chair Thomas Schoenknecht, SCHOTT Pharmaceutical Packaging

Time is flying and the 9th PDA *Universe of Pre-filled Syringes and Injection Devices* is just around the corner. This year's conference, in Las Vegas, brings together the drug delivery marketplace under the theme: "*Integrating the Unmet Market Needs: Bringing it All together for Tomorrow's Success*".

As in previous years, the conference brings together industry and regulatory experts to share their experiences, new developments, regulatory considerations, challenges and industry trends in this exciting area. The topics will benefit those looking for a basic understanding of these delivery systems, as well as those looking for a more in-depth presentation of current challenges and developments. This is a must-attend event for all industry professionals involved in the development, manufacturing, marketing or use of pre-filled syringes and injection devices.

No other drug delivery container type has seen such substantial improvements and changes in expectations than the prefilled syringe over the last ten years. With the combination of the container to devices such as injectors or safety systems, the regulatory landscape evolved significantly. The container industry was able to find answers in addressing those needs by using state of the art technology and by teaming up with their partners in the pharmaceutical industry. Find out how by interacting with your colleagues from around the world who have already met the complexities challenging their innovation, imagination and tenacity. Their achievements are novel and many. Collectively they have helped move our industry forward to a new level of previously unmet market needs, while continuing to work on developments that will ensure the future successes of tomorrow and ensure patient safety as most valuable goal.

The challenges of new product introduction and support of existing products require that companies be aware of new developments. A variety of case histories, plenary and poster sessions, exhibitions, combined with ample, valuable face time to interact with old and new colleagues will be your ticket to helping foresee the future of our industry. Consider just a few of the many sessions to be held over this exciting conference:

- The keynote will provide attendees with unfiltered insights of the patients perception struggling from a chronic disease on drug delivery offerings and how using these tools have greatly affected the quality of their life.
- A number of compelling revelations of new methods and techniques from the "front lines" which will show you how to increase patient compliance and safety in difficult to treat patients.
- How a novel integrated approach to prefilled syringes and injection devices helps to meet market needs of compliance, safety, costs, and dose accuracy

Continued at bottom of page 34

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PTI Inspection Systems, Nikka Densok USA and Lighthouse Instruments will exhibit at the PDA Universe of Pre-Filled Syringe and Injection Device Conference, October 15-17, 2012 at the Red Rock Resort and Spa, Las Vegas, Nevada. **Visit us in booth 105 to Learn about the latest developments in CONTAINER CLOSURE INTEGRITY TESTING.**

Job Aids Slowly Evolve from Paper to Electronic, Move From Shop Floor to Office Suites

Walter Morris, PDA

For ICU doctors and nurses, the simple and elegant checklist is a valuable, though not common job aid—and not always a welcomed one. Over the last decade, however, checklists for routine ICU procedures have improved medical practitioner performance, saved lives and reduced costs.

Surgeon and author **Atul Gawande,** MD, wrote about this in a 2010 article in the *New Yorker* magazine ***(1).*** According to Gawande, Johns Hopkins Hospital critical-care specialist **Peter Provonost,** MD, PhD, developed a checklist for use in administering central lines, which, if not done properly, can cause deadly infections (a familiar battle fought by sterile drug manufacturers). The checklist was all of five steps. In what Gawande described as "revolutionary," Provonost convinced hospital administration to empower nurses to stop doctors who were not using the checklist.

After just ten days, Provonost noted a reduction in the line-infection rate from 11% to 0%. Over the next fifteen months, Hopkins determined that "the checklist had prevented 43 infections and eight deaths, and saved two million dollars in costs," Gawande wrote. A job aid did this. A five-step checklist.

The users of this checklist are highly trained and highly educated. They know what to do. Yet, even they made errors, and the insight and inventiveness of one of their own has made their jobs easier. No need for retraining, conferences, lectures, emergency meetings. Just use the checklist. Gawande is quite enamored with this type of job aid. He published a *New York Times* Bestseller on the topic ***(2).***

The ICU checklists soon multiplied at Hopkins: checklists were developed to help nurses appropriately monitor patients for pain and to ensure mechanical ventilation was set up properly. Most innovative was the encouragement of doctors and nurses to develop their own checklists based on what they felt was needed. Results, as reported by Gawande, were staggering. Soon Provonost was spreading his "revolutionary" ideas to the Michigan Health and Hospital Association, which approached him in order to adopt his checklists. Following great success in Michigan, Provonost was involved in spreading his ideas in Rhode Island, New Jersey and even in Spain.

The PDA Letter sat down with four professional trainers to discuss the future of job aids and the pharmaceutical industry

In the 2010 article, Gawande gets to the heart of why this is so "revolutionary." Using checklists both in the ICU and in the cockpit, as it turns out, goes against the image of the "Right Stuff" type people who perform these jobs. A checklist just does not mesh with the image of a high-risk individual relying solely on their brains, guts and guile. But, as Gawande puts it, "If someone found a new drug that could wipe out infections with anything remotely like the effectiveness of Provonost's lists, there would be television ads…extolling its virtues, detail men offering free lunches to get doctors to make it part of their practice, government programs to research it, and competitors to jump in and to make new, better versions."

Common Pharmaceutical Job Aids are Shop Floor Tools

But job aids in the pharmaceutical industry go well beyond checklists. SOPs are a common (and cGMP required) job aid, and many more exist, like flow charts, drawings, etc.

The *PDA Letter* sat down with four professional trainers to discuss the future of job aids and the pharmaceutical industry: **Joanna Gallant,** Joanna Gallant Training; **Tim Gillum,** PhD, Sr. Manager Training, Baxter Healthcare; **Richard Sands,** Project Manager, RTS Training Services; and **James Vesper,** President, LearningPlus. The four experts, along with **Joyce Winters,** J. Winters Consulting, will facilitate roundtable discussions about job aids at the *PDA Biennial Training Conference,* Oct. 8-9 in Bethesda, Md.

Job aids are simple tools that are usually used at the shop-floor level. At this time, most job aids are printed materials, maybe laminated. According to Richard Sands, "A lot of people are using SOPs or some kind of derivative of an SOP that may be a condensed version on a laminated piece of paper….something that they can use to kind of jog their memory."

Multimedia and computers are being employed as job aids in some cases. Tim Gillum noted that his firm has developed a series of videos to help employees use the latest version of the enterprise system. Currently, 48 video vignettes have been developed as "just in time reinforcement" of the more transactional pieces of the enterprise system. Instead of expecting users to page through a complicated computer system manual, the videos allow them to quickly determine which fields need to be clicked into.

Joanna Gallant works with a client that is preparing a visual aid for using a documentation program. The intended audience is entry-level employees who do not have experience with the documentation software. "They are basically building a point and click on how to use the system, so they do not have to put the information into an SOP," she explains. The goal is to avoid "bogging down the SOP with a hundred-page point-and-

Article At a Glance

- Most pharmaceutical job aids need to be linked to procedures and version controlled
- Larger companies are exploring multimedia job aids, including videos, large-screen monitors and IPADs
- Job aids can help management perform standard work functions
- Join the experts for a roundtable discussion of job aids at the 2012 *PDA Biennial Training Conference*

It is important to link job aids tightly to procedures when they are derivatives of a larger procedures

click document that only certain people are going to use." In this case, the job aid utilizes a series of screen shots that system users can view as they enter information. They can follow along this document, which tells them "what to put where in the computer."

PDA members will be most familiar with a common job aid found in gowning rooms, James Vesper said. "A lot of companies will have pictures of what are the step-by-step things you have to do as you are moving through" the gowning process. "So you have illustrations, and those are all keyed to the procedure."

Vesper has seen other job aids in the medical device industry that shows what the completed device should look like. "Also, I've seen it as an illustration or graphic or photo for doing line clearance. You have a piece of packaging equipment and you have a graphic on the wall—these are the places you need to go, and you do that, and then you document what you did either in your packaging record or another type of log book."

Vespers says it is important to link job aids tightly to procedures when they are derivatives of a larger procedures. "You can't just have it standing there by itself. You have to have it version-controlled. If your procedure changes you, have to change your job aid.

Vespers noted that the change-control aspect was specifically discussed at the 2010 *PDA Biennial Training Conference* during a presentation by **Rebecca Rodriguez,** National Drug Expert, U.S. FDA. When asked about job aids, she said the Agency won't tell companies what tools to use or not use, but any type of job aid should integrated into a change control program and not restrict possible responses in an emergency or while troubleshooting.

Job aids are relatively simple, but they provide powerful tools to employees by offering easy access to information at the point of work.

Need Now, Learn Now

"You are embedding that information where you are doing the work," explained Vesper. One way of looking at them, he said, is they allow you to take "knowledge from the mind" and place it "in the world." He referred to Allison Rossett, PhD, Professor of Educational Technology, San Diego State University, who has written about job aids ***(3).*** "You are putting information where people need it, when people need it; you are making it available to them. You are trying to de-clutter the mind and say, 'you don't need to remember all of this stuff, but here it is right when you need it.' It is just in time."

Gillum said his company coined the phrase "need now, learn now" as it works to improve processes and enhance systems.

As regulatory pressure mounts on companies to improve quality and manufacturing, new kinds of job aids are surfacing to help employees handle new challenges. Amgen announced the use of a photo library that personnel can reference to ensure the authenticity of incoming materials. The library contains images of barrels, packaging, labels, etc., for the incoming materials (see "Industry Repairing Links in the Supply Chain," Mach 2010 *PDA Letter,* cover story).

Not every useful tool is a job aid. For instance, PDA's Technical Reports and the U.S. Pharmacopeia are not job aids, as they serve as reference documents that help employees figure out how to perform tasks. "No one is going to use a technical report every time they do a job," Sands said. "But maybe you could develop a job aid out of one, depending on what it is. But I cannot see it as a job aid."

Effective job aids are "more like extracts from a procedure," said Vesper. "These are the critical functions." Job aids provide the 'how to,' not the 'what to,' and they are "very specific to particular operation."

Gallant added, "It is a job aid if it helps them actually accomplish the task. Most job aids are going to be very specific to the task that is being performed at the company."

"Besides checklists, there are flow charts. They can be a job aid. This is the sequence of how we do it with the 'yes' and 'no's,'" Sands added.

Job aids do not have to be specific to shop floors and non-managerial functions. Gillum mentioned his firm's effort to develop aids for "leader standard work" as part of a larger effort to apply Lean Principles around all standard work within the operation.

"The discussion we just had was very technical, shop floor, yes/no, right/wrong, for the operators and the quality folks and folks making some specific tactical action," Gillum said. On the other side, his firm is looking at "less formalized" job aids that will help its leaders "proceed with their standard work for things like shift exchange and then apply some of the lean principles."

For the example given, the firm has developed and deployed a checklist for front line supervisors to use for standard work functions associated with shift exchange. The company does not need to be as concerned with version control for this checklist, "because they are not actually manufacturing the product or they are not approving or rejecting things at the time," Gillum said. Management is embracing the job aids, particularly around the lean standard work. Gillum looks forward to the round table discussion at the Biennial Training Conference to discuss job aids for management and see if other companies are using them.

E-Job Aids? I-Job Aids?

While the experts provided some examples of new technologies being used, Gallant said some companies she works with hesitate on this front. "Partially because they are very small and they do not have the money to implement new technology," she said. Small firms "are not going to be looking to outfit the manufacturing folks with smartphones and iPADs, or anything like that."

Besides cost, Gallant said, "you have to worry about when you bring this technology into the manufacturing area, how do you manage it?" She also believes it is not a high priority for larger companies, either, not only because of the cost and control issues, but also because of the perceived value.

Gillum noted that even at his firm, there are still plenty of laminated job aids on the manufacturing floor, though some are now in color, he quipped. But at the newly designed facilities, technology is being put in place to help workers. For instance, 52" LED screens are used to show where they are in the manufacturing process.

The firm is also equipping its leadership with iPADs. "So that leader standard work that we talked about is very much alive and well on that technology." In the middle ground, the company is using the video vignettes for the enterprise data system. So for those instances, the firm is "using technology to teach technology."

Gillum feels the use of technology in these ways is growing more important with the next generation of workers. A middle ground must be found, he said, for how job aids can meet the hierarchal, version controlled needs of Knowledge Management while engaging the new generation ("need it now, need to comment on it now").

Vesper noted that he has seen companies utilize touchscreen notebooks before the iPAD existed to help employees use manuals for e-batch record systems. He also discussed the idea of using QR codes on equipment for maintenance folks. The idea is they can scan the equipment to access on their smart device the procedures and other information regarding the machinery. But some firms resist allowing smart devices on the shop floor. The fear of photographs and the desire to know who is doing it already can quell momentum, said Vesper.

In wrapping up the discussion, Vesper said he encourages the pharmaceutical industry to look more broadly at how other industries use job aids.

Sands advises firms to support the use of job aids more broadly as the complexity and sophistication of drug products change. Job aids need to help employees with critical thinking skills, he said.

Gallant observes that training in general is still treated as a check-the-box function. She notes, however, that there needs to be a lot more thinking involved.

Gillum believes it is important to shift the focus of job aids from being a comfort tool for the SOP to a tool that suits the user.

As one can see, there is a lot going on in the world of job aids, and the upcoming roundtable discussion at the *2012 PDA Biennial Training Conference* offers the perfect opportunity to learn more about this topic. The *PDA Letter* thanks the four experts for their time.

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About the Experts

Joanna Gallant is owns Joanna Gallant Training Associates, LLC. Prior to consulting,

she spent 20 years in the pharmaceutical, biotech, and medical device industries. She spent eleven years in QA, performing and managing the function that designs, develops, and delivers training programs in CGMP and technical training, supporting all related functions at her sites. She now provides a range of training services to her clients, including design and delivery of training, packaged training materials, and training system audits and remediation. Joanna regularly speaks at industry meetings on interactive training, OJT, investigations and root cause analysis.

Tim Gillum, PhD, has worked both in academic and business environments for more than 15 years focusing on learning and change management within regulated environments. Tim has designed and implemented end-to-end training systems for start-up facilities in both the U.S. and Europe and rebuilt training systems for organizations under Consent Decree with the U.S. FDA. His area of expertise centers on aligning learning organizations to the company's overall strategy. In his current role at Baxter, Tim is responsible for the Global Quality Training Process/System.

Dick Sands retired from Merck & Co., Inc. in 1999, after almost 39 years. During that time, Dick held a variety of line and staff positions within Merck's Manufacturing Division. Prior to his retirement, Dick was charged with establishing a divisional level group to provide regulatory and job skills training for over 13,000 employees worldwide through internal partnering, external joint venture initiatives and leveraging existing resources. Dick is currently a consultant for the industry, specializing in regulatory and job skills training and assessments, working with a number of major pharmaceutical and chemical manufacturers.

James Vesper established LearningPlus, Inc. in 1991, and he and his firm have worked with pharma/biopharma, device, and blood products organizations around the world consulting on performance solutions and custom learning events. James is frequently asked to present training courses and workshops on a variety of topics. He has 30 years experience in the pharmaceutical industry, and worked 11 years at Eli Lilly and Company, where he established the department and mission for GMP education and instruction. He is an accomplished author, and has written a PDA/DHI book. He is a recipient of the PDA Agallico Award for Teaching Excellence. Currently, Mr. Vesper is a consultant to World Health Organization's Vaccine Quality Network – Global Learning Opportunities, working in China, Turkey, and Switzerland.

Discuss Job Aids at the 2012 PDA Biennial Training Conference

Bethesda, Md. • Oct. 8-9 • www.pda.org/biennial2012

Training organizations are experiencing the need to balance the validity of knowledge Management with the evolution of social learning within their businesses. This "need now, learn now" requirement is placing an increased level of attention on the effective use job aids.

This facilitated round table session will provide participants with the opportunity to share their experiences, methods, tools and challenges with other learning professionals. The session will center on five key topics:

- What is the risk of using job aids?
- How do organizations leverage mobile technology for job aids?
- Where do job aids currently reside within your Quality System?
- What are the best methods and tools to ensure success in utilizing job aids?
- How do we gain management understanding and support?
- Participants will have the opportunity to rotate through the topics in this extremely interactive session.

Vegas Offers Answers to Your Burning Questions continued from page 28

- Discussions and new advances in material construction, manufacturing processes, and other improvements that ensure a dynamic future for the drug delivery arena in the future.
- Country-specific discussions on how combination products are being used differently in Europe versus the United States and what is being done to manage these differences.
- A series of presentations on new and challenging guidelines from the varies regulatory agencies that continue to challenge and demand new approaches from manufacturers.
- What challenges, needs and trends emerging markets have on prefillable containers.

Immediately following *The Universe of Pre-filled Syringes and Injection Devices,* PDA's Training and Research Institute will be host three courses on October 18-19.

So please mark your calendar now! You should not miss this exciting event, where you certainly will leave with the latest information and a long list of new contacts. Please, let me invite you to participate and be part of this fascinating community. I hope to see you in Vegas!

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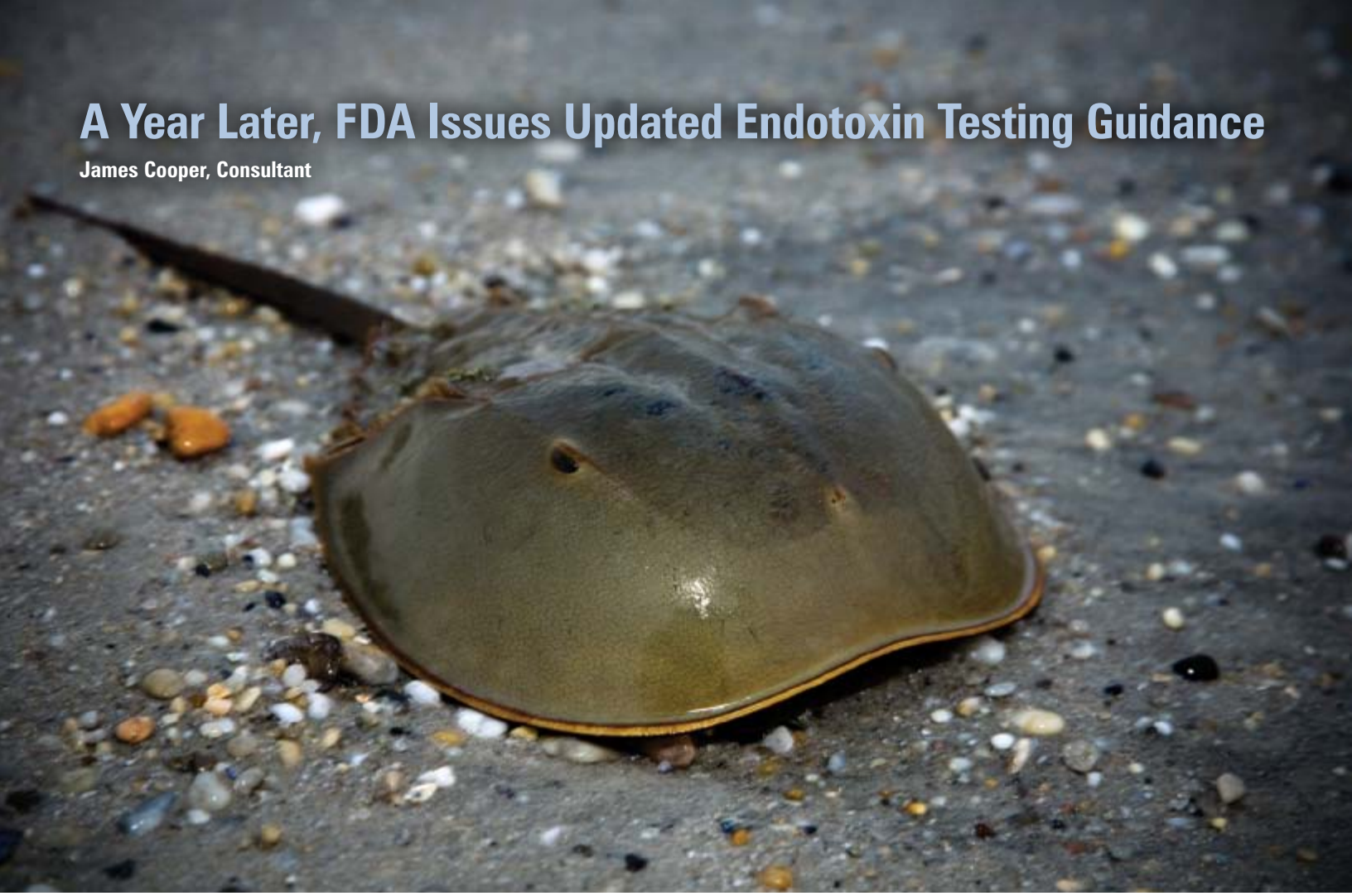
A Year Later, FDA Issues Updated Endotoxin Testing Guidance

James Cooper, Consultant



The U.S. FDA's new recommendations for pyrogen and endotoxin testing do not replace a more comprehensive 1987 Agency guideline, but they include useful guidance not found elsewhere.

In 2011, the FDA retired the 1987 *Guideline on Validation of the Limulus Amebocyte Lysate Test as an End-Product Endotoxin Test for Human and Animal Parenteral Drugs, Biological Products, and Medical Devices* because it no longer addressed all of the FDA's concerns for endotoxin nor was it relevant to industry needs. The LAL guideline was critical to our industry because it provided the regulatory framework for replacing the problematic rabbit pyrogen test with the more effective bacterial endotoxins test (BET) and LAL reagent ***(1).*** Essential items in the LAL guideline included:

1. The concept of an endotoxin limit that enabled the creation of dose-related limits for parenteral drugs and devices
2. Standardized LAL test methods with procedures for method validation. During the past decade, however, all important features of the 1987 LAL guideline were incorporated in other standards, specifically, the USP <85> Bacterial Endotoxins Test and the AAMI ST72 endotoxin standard ***(2).***

In June 2012, the FDA released a new guidance regarding endotoxins ***(3).*** The new guide recognizes that the USP and AAMI endotoxin standards contain more contemporary and comprehensive information for BET test methods and have a mechanism for update and review by healthcare and industry experts. Therefore, the new endotoxin guidance was not designed as a replacement for the 1987 LAL guideline; rather, it addresses endotoxin issues of concern to the FDA that are not necessarily expressed elsewhere. Speaking for the FDA about the guide, **Robert Mello**, PhD, Sr. Review Microbiologist (and former PDA Director/employee) also specified endotoxin test data that the FDA expected in the CMC (chemistry, manufacturing and controls) section of new drug applications ***(4).***

The new guide is in a question-and-answer (Q&A) format that addresses thirteen issues:

- Parenteral drug firms should develop a comprehensive sampling plan for new products that identifies the risk of endotoxin contamination throughout the manufacturing process, including in-process and finished product samples.
- Investigations and retests of out of specification (OOS) results should follow the intent and spirit of the FDA guidance for OOS investigations even though it is not intended for biological assays, such as the BET. Retest provisions in the 1987 LAL are no longer relevant.
- Firms should establish procedures to

assure that BET sample storage allows for "stability of assayable endotoxins content."

- BET samples of pharmaceuticals, except suspensions, may be pooled for a BET provided that the maximum valid dilution (MVD) is adjusted to account for the number of pooled samples. The pool should be aliquots taken from containers.
- Firms may use alternative endotoxin and pyrogen assays, such as recombinant Factor C assay and the monocyte activation test, if they are validated by USP <1225> and shown to be equivalent.
- A firm may transition to an alternative endotoxin/pyrogen method (identified above) after FDA acceptance of a prior approval supplement.
- Calculation methods described in the USP and AAMI standards should be used to establish endotoxin limits because monograph limits for drugs may not account for current dosage regimes.
- Quality by Design concepts should address production process areas and processes that are at risk of endotoxin contamination. In this regard, quantitative testing may be preferable to limit testing to facilitate data trending.
- The rabbit pyrogen test is required for certain biological-origin products, but BET methods may be substituted for some products if they are shown to be equivalent.
- The endotoxin limit for veterinary products should consider the variety of species, age and maximum product dose. Man and rabbit respond similarly to endotoxin. However, Sheldon Wolff and coworkers studied pyrogenic response of many species at the National Institutes of Health during the 1960s and found that some were more resistant than rabbits to endotoxin ***(5).***
- The endotoxin limit and extraction procedures for medical devices are adequately addressed in USP <161> and AAMI ST72 standards.

The greatest effect of the endotoxin Q&A guidance will be on developers of new drugs

- Recognizing that BET procedures are susceptible to interfering conditions, firms should determine the lowest product dilution that avoids interference. Firms should report these findings and fully describe their BET methods in applications for new therapeutic drug products. The impact of this requirement on established test procedures is uncertain.
- The USP dropped its description of the calibration of secondary endotoxin standards when <85> BET was harmonized in 2001. To fill this gap, FDA encourages the use of control standard endotoxins (CSEs) that are suitably calibrated to the international endotoxin standard; this is current practice in the industry.

Impact of New Endotoxin Guidance

What is the expected impact of the new endotoxin guidance on the parenteral drug industry? The greatest effect of the endotoxin Q&A guidance will be on developers of new drugs and, perhaps, certain combination products. In the past, new drug submissions were generally acceptable if they contained certification that compendial BET methods would be validated and used for endotoxin detection. As presented by Dr. Mello ***(4),*** the FDA expects greater detail about the BET in the CMC section of new drug applications:

- Rationale for endotoxin limit of new drug
- Detailed description of sampling plan plus storage and handling procedures
- Detailed presentation of BET validation data, including calculations, non-inhibitory concentration and lab qualification.
- Conservative endotoxin limits for pediatric dosage forms.

The new guide may not impact significantly on established, routine BET tests for approved drugs and devices because it generally reconfirms support for critical elements in the 1987 LAL guideline. Many of the recommended practices are current procedures in our industry, such as pooling of routine test samples and use of CSEs. Recommendations for testing at a fraction of the MVD may be an exception.

The AAMI ST72 document, extensively revised and published earlier this year, is endorsed as the principal resource for applying the BET to medical devices ***(3).*** ST72 is the most current and comprehensive source of procedures for all BET methods. Annexes to the standard provide helpful information on sample preparation and test methods.

New Endotoxin Interests at the FDA

The introduction indicates that the new guide describes current FDA thinking and clarifies issues that are subject to misinterpretation or are inadequately covered elsewhere. Some issues deserve more scrutiny.

Several points address the BET sampling plan. The plan should address the complete spectrum of in-process and finished product samples associated with a new product. Overkill testing may be reduced and reported as confidence in the process is met.

The new guide perpetuates the notion of testing a uniform batch of drugs with as few as three samples taken from be-

Article At a Glance

- Firms should fully explore the endotoxin risks associated with new drugs through comprehensive sampling of raw materials, in-process materials and finished product
- Applications for new drugs should contain complete information on endotoxin limit calculations, test interference characteristics and endotoxin sampling plans
- Quantitative endotoxin test methods are encouraged to enable trending of data

ginning, middle and end of batch; these samples may be pooled into a composite sample. However, the MVD for pooled samples should be adjusted by dividing by three (1/3 MVD) to avoid diluting out excessive endotoxin contributed by one of the samples. A new requirement directs pooling aliquots of drug samples so that the original container is available for investigation if endotoxin is detected. The guide doesn't mention the MVC (minimum valid concentration), which may be a more useful tool for an active pharmaceutical ingredient (API) or raw materials.

age regimen was a factor in the pyrogenic outbreak caused by gentamicin in 1998-99, when divided doses were changed to once daily, which increased the volume administered in an hour. However, the principal cause of the outbreak was failure to recognize the magnitude of endotoxin contamination that was out of trend in the API ***(7).***

Implementation of quality by design concepts implies that quantitative testing is a more prudent way to evaluate relative endotoxin risk and quality trending of in-process tests. Photometric BET methods generate trending data by quantitative testing with microplate, tube or cartridge readers with endotoxin specific software.

Further, the new guidance suggests that hold times for endotoxin-test samples should be studied for stability using various endotoxin standards

Further, the new guidance suggests that hold times for endotoxin-test samples should be studied for stability using various endotoxin standards. Although such stability studies are uncommon, Bowers and Tran described the use of a naturally occurring endotoxin preparation for hold-time stability studies ***(6).*** Hopefully, products that are made in the absence of bioburden or are inherently non-pyrogenic could be exempted from such experiments.

The new guidance warns that current endotoxin limits in monographs may not reflect current dosage forms and schedules. Failure to recognize new dos-

The quality unit should study the new guidance and determine the impact of the new FDA concerns on existing BET procedures.

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About the Author

James Cooper, PharmD, is an innovator of the bacterial endotoxins test for parenteral products. His publications span the history of LAL technology. He founded Endosafe Inc. in 1987, an LAL production unit, which is now part of Charles River Laboratories. Following retirement in 2001, he consults on depyrogenation, BET methods, endotoxin issues and root-cause investigations. He teaches the endotoxin component for PDA and U.S. FDA courses.

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Reports from the 2012 PDA/FDA

PDA Glass Survey Results Spark Fruitful Day 1

Thomas Schoenknecht, SCHOTT Pharmaceutical Packaging

More than 500 people participated in the scientific sessions of the conference and discussed market trends in glass quality improvement over the whole drug product lifecycle, June 4-5 in Washington, D.C. The on-site exhibition offered an excellent platform for attendees to further exchange opinions about required improvements in glass quality and to see the latest technologies.

PDA President **Richard Johnson** opened the conference by presenting the results of the recent glass container quality and glass supplier survey PDA conducted over the previous few months. This was a follow up to a survey conducted in 2011, so Johnson also compared the results of each survey.

The 2012 survey had 109 respondents; 80% represented multinationals and out of those, 59% traditional pharma and 25% biologics. A significant increase in tubular glass defects compared to moulded glass defects was reported; yet, generally, respondents indicated that glass quality in total has improved. Remarkably, when ranking glass suppliers by the quality of their product, there was no change from the prior survey; the same suppliers received the highest quality ratings in 2012 as in 2011 and so on.

About 88% of the survey respondents test their incoming lots and about 63% still allow pre-delivery, or tailgate, samples, which represents a small reduction compared to 2011 results; but the process is still dominant.

The principles and processes as described in PDA Technical Report No. 43 ***(1)*** are dominant, with 77% of the responding companies citing usage of the document, an increase by 10% from 2011. 98% of the respondents do full inspections of filled goods, where manual inspection is decreasing. A significant improvement of the quality was reported, as two thirds of the respondents have seen less than one lot of glass fail inspection prior to filling. The processes applied to failed glass lots, for example, re-inspection of the lot, stayed unchanged.

The survey results show the complaint rates for critical glass defects, such a broken vials or syringes, have been reduced, which is reflected in a decline of glass-related recalls over the last three years. However, the rate is still too high.

Possibly due to the rate of glass defects, the survey showed a corresponding uptick in plastic container qualification programs, from 14% in 2011 to 21%. However, glass is still the dominant container material.

Finally, the survey confirmed a trend of improving cooperation with respect to quality between industry and suppliers; where now 88.5% of the respondents reports the existence of a quality agreement and also states annual supplier auditing is now applied by 37 %; both double the rate compared to the results of the 2011 survey.

U.S. FDA Delineates Expectations

The next speaker, **Steven Wolfgang,** PhD, Acting Associate Director, Risk Science, CDER, outlined the Agency's quality expectations and lessons learned on glass quality over the last 12 months. He pointed to advances in technology that can be used to test drug product vials for delamination, and noted that FDA's expectation is for quality to be built into the product.

Since glass is not inert for all formulations, application of quality by design principles can help control delamination/corrosion, because the available toolbox of analytics allows for the characterization of the interaction between the drug solution and the container material, Wolfgang explained. Further, communication and early engagement of glass suppliers for drug product specific container development and adaptation was recommended to ensure patient safety.

Greater Understanding of Delamination

The next session addressed work done over the last twelve months to further understand the root cause of delamination and how the glass converting processes may affect the tendency of delamination/corrosion of a glass container after drug filling.

Speakers shared explicit insights into what technologies could be used to identify changes in the glass morphology and how these changes in the glass itself might promote delamination in specific buffer solutions. In addition, presentations were given on existing products and services and new products in development that can help avoid or minimize delamination.

The first day also included insightful updates from the PDA Glass Handling Task Force, the PDA Visual Inspection Interest Group, and the American Glass Research.

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1. PDA *Technical Report No. 43: Identification and Classification of Nonconformities in Molded and Tubular Glass Containers for Pharmaceutical Manufacturing.* PDA: 2007. www.pda.org/bookstore

Glass Quality Conference

Making Glass Work the Focus of Day 2

Diane Paskiet, West Pharmaceutical Services Inc.

Glass is here to stay, but risks associated with the complexity of products, compatibility, manufacturing flows, distribution networks, and product lifecycle may result in implementing mitigation strategies or selecting an alternative material.

During the second day of the PDA Glass Quality Conference, speakers demonstrated that glass containers can meet the requirements of most parenteral applications, as long as the container closure system, process and equipment requirements are well defined and controls linked to patient safety. Still, regulators emphasized that the potential exists for millions of patients to be exposed to risks associated with glass when of millions of the vials in distribution have been recalled: in addition it would be prudent to look at some products already on the market to gain better insight on potential for risks.

Evidence that the container closure system is fit for use with the dosage form should consider delivery to the patient across the supply chain. Integration of patient safety with the science of glass, parenteral product development, the drug manufacturing process and distribution is vital to demonstrating glass suitability. The overall supply chain was explored from the point of glass manufacture to the last mile of delivery to the patient. Problems and potential solutions for handling glass and reducing risk for breakage were conveyed with respect to:

- Filling and Sterilization
- Quality Control
- Secondary Packing and Transport
- Storage and Shipping
- Wholesale Distribution
- Patient Administration

The most common customer complaint category for a vaccine manufacturing site was reported to be cracked and broken vials, as compared to other complaint categories. A process was demonstrated for identifying areas of improvement and mitigating risks. Another case study was presented that showed how to investigate cause for glass breakage working from patient handling back through manufacture. Processes to improve handling of glass were evaluated by identifying the areas of breakage occurrence and rate of defects for critical processes. Washing processes, heat tunnels and filling lines showed higher defect rates which were observed more on vials compared to syringes; main defects were scratches, scarves and cracks. The study concluded that breakage of glass can be mitigated through identification of manufacturing areas where breakage can typically occur and institution of defect codes for process and incoming that can be correlated to weaknesses which signal alerts and appropriate action.

Glass breakage was well recognized as issue for all parties of the supply chain. Multiple stakeholders cannot work in a vacuum to solve problems and machine manufactures can optimize equipment with feedback from drug manufacturers. Friction problems arising from glass-to-glass contact contributes to breakage throughout the manufacturing processes, reduction of breakage and complications associated with broken glass can be minimized by use of individual transport systems. Total solution can be very sophisticated and a big investment to be balanced depending on types of product, speed of filling line and complexity.

Risk assessment case studies have shown that a critical step in the process is after secondary packaging and beyond. There are distinct opportunities for suppliers, pharmaceutical, distribution and transportation companies to work together for the benefit of all. Dynamic and environmental conditions during shipping and handling were considered. Shock, vibration, compression, temperature, humidity

The June PDA/FDA Glass Conference

Speakers demonstrated how fractured specimens and components were characterized to show where and why the glass broke

and pressure can all have a harmful impact on drug products. Measurement and continuous monitoring of distribution and handling environment is the only way to confidently understand what the product and packaging system can tolerate.

Although there are ways to mitigate hazards associated with glass, it is important to be able to identify and understand the defects associated with breakage and other issues of glass suitability to enable preventative measures. The science of fractography was presented. Speakers demonstrated how fractured specimens and components were characterized to show where and why the glass broke.

Root cause investigations of particulates is another aspect of glass quality. Sources of particles in drug products can result from glass chips, delamination, interaction products or foreign contaminates; appropriate isolation and identification of particles is necessary to diagnose problems and implement corrective actions. Forensic analysis of particles and glass breakage can lead to discovery of root cause and development of control strategies. Current compendia methods can type glass, but more guidance is needed to qualify glass containers for intended use. The USP published for comment in *Pharmaceutical Forum* 38 a new General Chapter <1660> Evaluation of the Inner Surface Durability of Glass Containers. Examples of elements that leached into drug products were also cited.

Assuring product quality control points is opportunity for failure, but ownership takes place in multiple places in the supply chain: The wholesale distributors and specialty pharmacies all have a vested interest in product quality (reducing returns) but do not all have the resources or expertise. Pharmaceutical companies should develop guidelines of best practices for proper cold chain and glass handling/packing and communicate with distributors on risks and consequences.

Nearly 10 million vials in distribution were recalled for lack of sterility assurance and over 118 million vials in distribution were recalled for presence of particulate matter, according to FDA.

Pharmaceutical companies and glass container manufacturers should work together to establish a final product quality specification that is based on patient safety and product requirements.

Overall, presentations illustrated that lessons have been learned based on the mechanical aspects of manufacturing with potential to damage or create weaknesses in glass. Multiple root causes were identified; examples include: misalignment-stress during filling, labeling metal contact-component-flaws supplier controls, glass forming, glass to glass contact and supplier variability. In addition, root causes for particulate matter included shattered vials during sterilization/depyrogenation; delamination and product interaction. A strong message was conveyed that communication through-out the supply chain is key to solve challenges to benefit all stakeholders to enable delivery of quality medicines to patients.

Advanced Delivery Systems are Popular, but Pose Challenges for Biotech Injectables continued from page 28

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About the Experts

Mariana N. Dimitrova, PhD, is a group leader in the Formulation Sciences Department at MedImmune. Her current responsibilities include technical leadership in the formulation and fill/finish operations of biologics, with a special emphasis on development of prefilled syringe presentations for subcutaneous administration. Prior to MedImmune, Dr. Dimitrova was a member of the Drug Product and Device Development Department at Amgen Inc. where she assumed increasing responsibilities in the biophysical characterization of protein structure, stability, and degradation pathways. Between 1999 and 2003 Dr. Dimitrova was a postdoctoral research fellow at the U.S. National Institute of Health (NIH, NHLBI) in Bethesda, Maryland.

Sebastien Jouffray is a Program Manager, R&D Advanced Product Development for BD Medical-Pharmaceutical Systems, where he has worked since 2001 in the R&D organization. He began there in the sustaining engineering team, responsible for customer projects development and as well supporting customer technical demands. Most recently, in the Advanced Product Development group, he managed the team responsible for the Advanced Coating program.

Kingman Ng received a doctorate in biophysical sciences from University of Minnesota. Dr. Ng had more than 15 years of biologics formulation development experience with Eli Lilly and Company prior to joining Novartis Vaccines and Diagnostics as Head of Pharmaceutical Sciences in Jul 2011, where he is leading and setting up the department of pharmaceutical sciences responsible for vaccine formulation and analytical development in the United Staes. In addition, Dr. Ng is also building a center of excellence for primary packaging development with special focus on prefilled syringe.

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snapshot

Health Authority *Special Report*

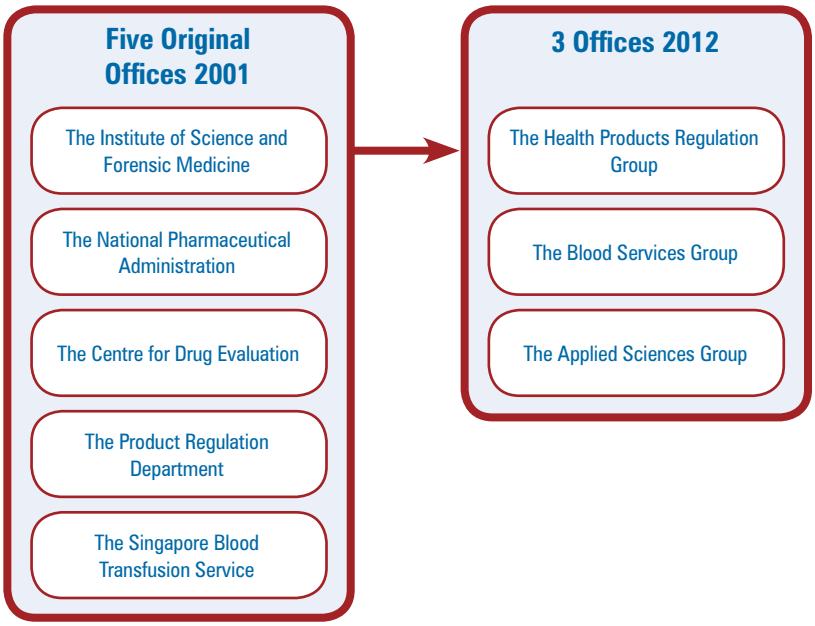
Singapore's HSA Partners with International Regulators

Sannie Chong, and David Woo, Health Sciences Authority

The Health Sciences Authority (HSA) was established on April 1, 2001, following the integration of five separate agencies under the Ministry of Health, Singapore. Following several reorganizations, HSA is now comprised of three professional groups to redefine our wide scope of scientific expertise and activities (see **Figure 1).**

The scale and scope of HSA's work spans a wide spectrum of scientific and professional functions. Drawing on the synergies from this diversity and adopting an inter-disciplinary approach in managing our responsibilities has not only enabled us to harness limited resources in the most efficient and effective way, but also strengthened our scientific and operational capacity.

Figure 1 Transformation of HSA 2001 and 2012



The Health Products Regulation Group

The Health Products Regulation Group (HPRG) ensures that the quality, safety and/or efficacy of all health products in Singapore meet internationally benchmarked standards throughout the product lifecycle. It implements a robust and risk-based framework that takes into account pre- and post-market and manufacturing and distribution precautionary measures for a broad range of health products, including advanced therapies, medical devices, cosmetic products, traditional medicines and Chinese proprietary medicines.

The group is made up of three divisions and the Group Director Office (see **Figure 2).** The Pre-Marketing Division oversees areas such as product evaluation and registration prior to market entry, while the Vigilance, Compliance & Enforcement Division focuses on post-marketing activities, such as adverse event monitoring, compliance monitoring, surveillance and enforcement. The Audit & Licensing Division is responsible for monitoring GMP/GDP (Good Distribution Practice) compliance. It also issues licenses for dealers to market health products in Singapore. The Tobacco Regulation Branch is a unique part of HPRG in that it focuses on administering and enforcing existing legislation on the control of tobacco in Singapore with the objective of reducing the prevalence of smoking. In addition to the above responsibilities, the Pre-Marketing division also ensures that clinical drug trials in Singapore are carried out in accordance to international ethical and scientific quality standards. Overseeing all three divisions is the Group Director Office which not only provides guidance for the three divisions and administrative support for the entire group but also is also involved in international collaborations with HSA›s regulatory partners.

The Blood Services Group

The Blood Services Group (BSG) plays an integral part of Singapore's healthcare system with its responsibility to provide blood and blood components of the highest possible standards of safety and quality to all hospitals. This group works closely with clinicians to maintain stringent standards of blood transfusion safety and clinical transfusion medicine practice. BSG's expertise in the other fields of transfusion medicine has broadened over the years. It provides immunohaematology and tissue typing services to local and regional healthcare institutions. As the boundaries of knowledge continue to expand in transfusion medicine, it has expanded its experience and expertise in the new and exciting arena of cell therapy with the Cell Therapy Facility, which collaborates with clinicians to explore the therapeutic applications of cells like natural killer cells and haematopoietic stem cells.

The Applied Sciences Group

The Applied Sciences Group (ASG) provides national forensic and analytical science testing capabilities to enforcement agencies and the judiciary. Laboratories housed within the group provide specialized scientific and investigative services to government agencies, healthcare institutions and private companies. These cover forensic medical consultancy services in support of death investigations that take place in Singapore; forensic science services such as criminalistics and DNA profiling in support of criminal investigations and illicit drugs control; toxicological services to hospitals; analytical testing in support of pharmaceutical and cosmetic regulation; cigarette and tobacco product control; and water testing and food safety regulation. Since 2008, it has taken on a new ➤

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responsibility as the designated institute for Chemical Metrology in the medical and pharmaceutical fields, as well as in the areas of food, healthcare and forensics.

The three Professional Groups work closely with our Corporate Headquarters, which provides strategic direction and corporate support to advance the mission of our organization as a champion and protector of national health and safety.

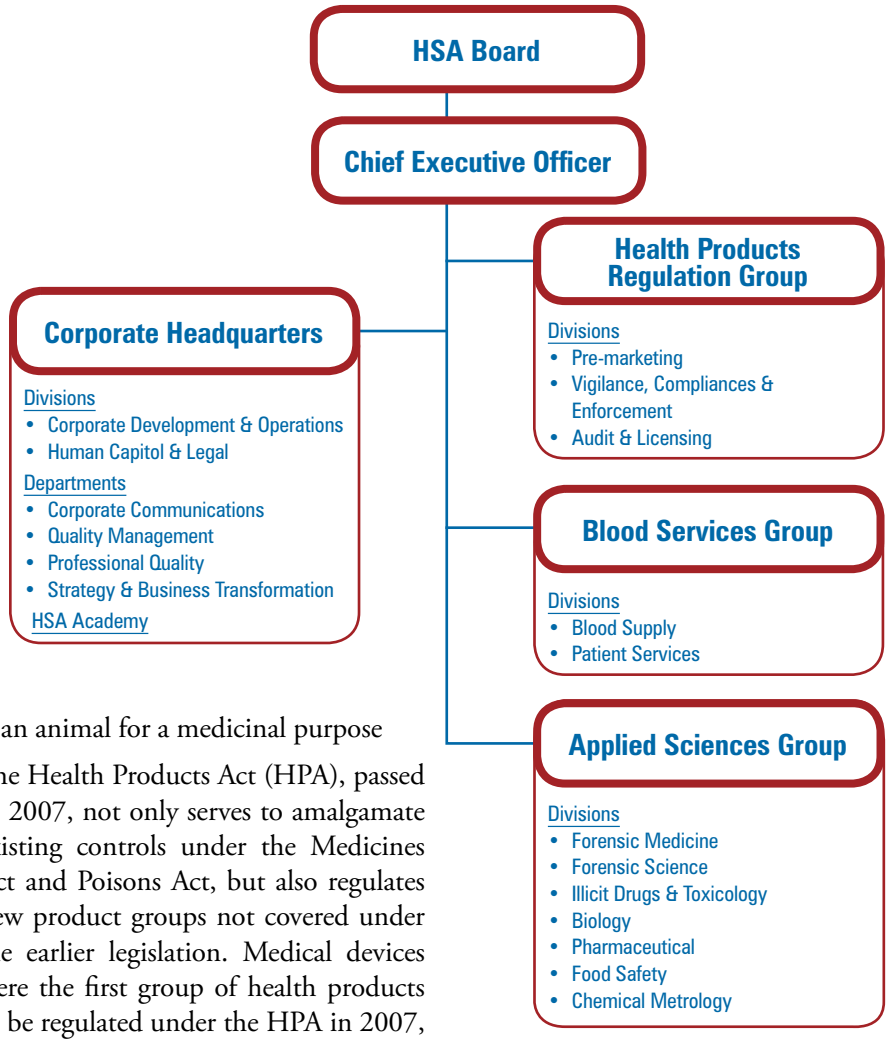
Towards Smarter Regulation

Health products regulation has become more challenging. Factors like the advent of new technologies, changing lifestyles and disease patterns, demographic shifts, increasing public expectations and cost pressure, to say the least, have contributed to making the regulatory environment a dynamic landscape. But, HSA's principal regulatory role in safeguarding public health and safety by ensuring that health products that are approved for market meet rigorous standards of quality, safety and/or efficacy remains unchanged. This is why, in line with our priority to be a "smart" regulator, our health products regulatory framework has been constantly fine-tuned to stay relevant to emerging scientific and public health concerns. We constantly fine-tune our framework s to ensure that regulatory practices do not present bureaucratic obstacles to research & development of new health products while ensuring that patients in Singapore continue to have access to safe, efficacious and good quality health products.

Health products today are regulated under different pieces of legislation in Singapore, one of which is the Medicines Act, a core piece of legislation applicable for regulating medicinal products. Under the Medicines Act, a "medicinal product" refers to any substance or article (not being an instrument, apparatus or appliance) which is manufactured, sold, supplied, imported or exported for use wholly or mainly in the following ways:

- Used by being administered to a human being or an animal for a medicinal purpose
- Used as an ingredient in the preparation of a substance or article that is to be administered to a human being or an animal for a medicinal purpose

Figure 2 HSA Organization Chart



The Health Products Act (HPA), passed in 2007, not only serves to amalgamate existing controls under the Medicines Act and Poisons Act, but also regulates new product groups not covered under the earlier legislation. Medical devices were the first group of health products to be regulated under the HPA in 2007, followed by cosmetic products with the implementation of the ASEAN Cosmetic Directive in 2008.

A Valued Partner

HSA has witnessed a productive decade under unprecedented challenges and change since its formation. In a span of ten years, HSA's reputation in its various fields of expertise has grown, both at home and abroad.

We are grateful to be closely affiliated with and accredited by some of the world's leading institutions. We enjoy the unique distinction of housing four World Health Organization Collaborating Centers (Transfusion Medicine, Drug Quality Assurance, Food Contamination Monitoring and Tobacco Testing & Research) and one WHO Pre-qualified Quality Control Laboratory. Our system of multiple pre-market authorization routes for evaluating new drug applications has often been cited by WHO as an innovative model for expediting regulatory decisions without compromising scientific robustness and safety. As the first national blood service in Asia to be accredited by the AABB (formerly known as the American Association of Blood Banks), we have had the privilege of supporting and helping to establish other blood banks and contributing expertise to enhance their infrastructures and systems. Our Tissue Typing Laboratory, which now offers critical support to clinicians to provide transplant patients with new life-saving treatments, has also achieved accreditation by the American Society for Histocompatability and Immunogenetics. HSA was also the first agency outside of North America to be accredited by the US-based National Association of Medical Examiners.

We value every opportunity that al-

lows us to collaborate and learn from our overseas partners as we recognize that the challenges we face today are best addressed through joint efforts. We have signed Memoranda of Understanding (MOUs) with many of our global regulatory counterparts. These MOUs strengthen our strategic alliances, deepening our collective understanding of the most pressing issues impacting world health and safety and transforming the way we manage them.

As we enter our second decade, we look forward to contributing in greater ways in the international scientific, biomedical and forensic communities.

The HSA Academy was established in 2010 to further develop our thought leadership and research capabilities and also to be a key enabler in transforming the organization as we continue to push the boundaries of scientific and professional excellence. Building on existing scientific expertise, the Academy aims to foster synergy across the different professional groups internally to develop innovative approaches to health products regulation, transfusion medicine and the relevant applied sciences. It supports the professional groups to drive training, research and collaborative efforts with both local and international agencies.

Though still in a nascent stage, the Academy has been involved in various important initiatives. This includes an engagement with the Massachusetts Institute of Technology's New Drug Development Paradigms consortium comprising academia, industry and regulatory bodies. This project explores progressive authorization and the progressive market entry of a product as clinical outcome evidence is generated under real-world use to better define the benefit risk profile at the time of full market authorization. Another engagement included the co-organization of the 14th WHO International Conference of Drug Regulatory Authorities with the WHO in Singapore in November 2010.

Through these collaborations, we hope to add to the richness of the discussions, inject more creative thought, and translate more ideas into practical innovations that will shape and inspire global developments in health products regulation, blood-banking and transfusion medicine, forensics and the analytical sciences.

About the Author

Dr. **Sannie Chong** is the Director of the Generics & Biosimilars Branch, Pre-Marketing Division, Health Products Regulation Group.

Mr. **David Woo** is a Regulatory Consultant in the Generics & Biosimilars Branch, Pre-Marketing Division, Health Products Regulation Group.

This is the first article in a series featuring the work of the Health Sciences Authority (HSA), Singapore. We will continue to share with you about HSA's medicinal product approval and registration processes in future articles.

Regulatory Briefs

Regulatory briefs are compiled by PDA member volunteers and staff directly from official government/compendial releases. Links to additional information and documentation are available at www.pda.org/regulatorynews.

North America

U.S. FDA Reports Another Glass Vial-related Recall

FDA's MedWatch included a report on Aug. 16 of Hospira's reall of three lots of Propofol injectable emulsion because of visible particles embedded in the glass. The concern is that product could contact the particles, dislodging one or more of them, thus endangering patients.

eCTD Support Docs Available — Will Accept eCTD in 2013

The FDA has announced that documents that support electronic regulatory submissions using the electronic Common Technical Document (eCTD) specifications are available. Supporting technical files will also be made available on the Agency website. FDA estimates it will be able to receive electronic submissions by September 2013.

For more information, go to: tinyurl.com/electronic-Common-Tech-Doc.

Europe

EMA Opens Up

The EMA's latest step to be a more transparent public health authority announced in July that it will publish agendas and minutes of Agency scientific committees. The initiative began the week of July 15 with the publication of minutes from the Paediatric Committee meeting, followed with the publication of the Pharmacovigilance Risk Assessment Committee's inaugural meeting minutes. The plan is to have all agendas and minutes published for all seven EMA committees by the end of 2013.

Links to the minutes/agendas already available can be found here: tinyurl.com/EMA-minutes.

EMA Revised Biosimilar Guideline Available

An EMA revised guideline on the quality of biosimilar medicines explains the requirements for the manufacture and comparability testing for biological medicines claiming to be similar to another medicine already on the market.

Comments are being accepted until November 30. tinyurl.com/EMA-biosimilar-comments.

Transgenic Animal Systems Guidelines Under Consultation

The EMA has posted a guideline that has adapted existing quality guidance for other recombinant production systems to transgenic animal systems.

The guideline is open for consultation until November 30 at tinyurl.com/EMA-transgenic-animal-systems.

International Inspections

Sterile Processing Violations Impact Vaccine, Cancer Therapies

Allegations of sub-standard practices in the processing of sterile products were made by both the U.S. FDA and the EMA in recent inspections.

FDA issued a warning letter to Sanofi Pasteur S.A. following March and April inspections of two facilities in Canada. The lengthy letter outlines in much detail problems with many critical sterile processing functions, like environmental monitoring, equipment cleaning and disinfection, sterility test method validation, aseptic processing validation, and investigations into failing pyrogen testing results. The company asserts it is working with the Agency to remediate problems. So far, there are no reports of shortages of the vaccines manufactured at the two plants. The warning letter is available at FDA's website: tinyurl.com/FDA-warning-letter.

That is not the case for the cancer therapy DepoCyte, which is the product manufactured at Pacira Pharmaceuticals San Diego plant. The site was inspected in July by the UK and French medicines agencies. Inspectors found numerous GMP violations undermining the firm's sterility assurance efforts. The firm suspended production and release of the product, following the inspection. On August 24, 2012, the EMA issued a "questions and answers" regarding the ongoing shortage of the cancer therapy, which is available at: tinyurl.com/EMA-medicine-q-a.

Key Regulatory Dates

Comments Due:

November 30 — EMA Revised Biosimilar Guideline Available

Transgenic Animal Systems Guidelines Under Consultation

Register by **October 15th** and save up to $200

The Parenteral Drug Association presents the...

2012 Pharmaceutical Cold Chain & Good Distribution Practice Conference

Temperature Controlled Supply Chain – A Global Partnership

November 15-16, 2012

Bethesda North Marriott Hotel | Bethesda, Maryland

Brochure Now Available! Download at www.pda.org/coldchain2012

The current regulatory environment is as rapidly changing as it has ever been. Countries worldwide have begun to realize the critical impact of temperature control logistics on the health and welfare of their citizens and are moving aggressively to ensure that logistics activities are as well-controlled as manufacturing has become.

At the *2012 Pharmaceutical Cold Chain & Good Distribution Practice Conference:*

Learn about updates on the new strategic direction for USP Supply Chain Chapters from:

- **Chris Chandler**, Pharmacist, *US Department of Veteran Affairs*
- **Desmond Hunt**, Scientific Liaison, General Chapters Department of Standards Development, *United States Pharmacopeia*

Hear from Pharmaceutical Cold Chain Interest Group Members about the following PDA Technical Reports:

- PDA *Technical Report 39, (TR 39) Cold Chain Guidance for Medicinal Products: Maintaining the Quality of Temperature-Sensitive Medicinal Products Through the Transportation Environment*
- PDA *Technical Report 46, (TR 46) Last Mile: Guidance for Good Distribution Practices for Pharmaceutical Products to the End User*
- PDA *Technical Report 52, (TR 52) Guidance for Good Distribution Practices (GDPs) for the Pharmaceutical Supply Chain*
- PDA *Technical Report 53, (TR 53) Guidance for Industry: Stability Testing to Support Distribution of New Drug Products*

Explore supply chain integrity and security issues with:

- **Charles Forsaith**, Director of Supply Chain Security, *Purdue Pharma*
- **Mark Seitz**, Advisor, Global Supply Chain Logistics, *Eli Lilly and Company*

Visit **www.pda.org/coldchain2012** for more information and to register

Exhibition: November 15-16

Real Improvements in Temperature Control Distribution

Pharmaceutical Cold Chain & GDP Conference • Bethesda • Nov. 15-16 • www.pda.org/gdp2012

Karl Kussow, FedEx Custom Critical

This year's *2012 Pharmaceutical Cold Chain & Good Distribution Practice Conference* is back to back with the PDA-FDA Supply Chain Conference for a reason: Both conferences are moved to the fall when the heat of summer with its challenges to the cold chain is finally over and still fresh in everyone's mind. The cold of winter is just around the corner with its own significant challenges to temperature control logistics.

Now is just the right time to meet to review the data, share solutions, and discuss how our companies can best meet the challenges of Good Distribution Practice expectations, no matter where our shipments are traveling to or from.

The agenda of this year's conference is ambitious, as it needs to be in order for all of us to consider strategies to achieve complete integration of temperature control, Security, and Supply Chain efficiency. Whether your activity is regulated directly by the U.S. FDA or you are a solution provider, there are few conferences that are more impactful to our ability to create impactful improvements in our business practices.

The current regulatory environment is as rapidly changing. Countries worldwide have begun to realize the critical impact of temperature control logistics on the health and welfare of their citizens and are moving aggressively to ensure that logistics activities are as well-controlled as manufacturing has become. Good Distribution Practices are at the forefront of new regulation and guidance.

At this year's conference we will discover efficient ways to apply new guidance from the USP updates to their general chapters <1079>, <1118>, <1083>, and learn in advance what is coming next in time to be prepared. We will compare global regulations and discuss the quality systems and supply chain solutions needed to comply in ways that are also cost efficient. Participants will contribute to the continuous improvement of industry best practices, including the guidance recently published in PDA Technical Reports 39, 46, 52, 53, and share real data and practical applications for room temperature logistics, as well as the traditional cold chain.

Stability data is critical to enabling management of logistics to ensure product safety

Stability data is critical to enabling management of logistics to ensure product safety. In order to continue to enhance our ability to accurately understand the impact on medicinal products from the supply chain environment, we will consider the issues of collecting and interpreting the right data from shock, vibration, pressure, and humidity as well as temperature and using it to improve the safety of the supply and distribution chains.

As if all that were not enough, security continues to be a challenge as thieves and counterfeiters react to increased supply chain protections with improved methods of their own. This is particularly important in light of their expansion into all areas of the supply and distribution chain, from raw material to finished products. The industry must continue to innovate in our response to security threats and do so in a way that enhances supply chain efficiency and sustainability.

The PDA and the Pharmaceutical Cold Chain Interest Group are dedicated to increasing the body of knowledge and the development of best practice that enhances public health and cost efficient solutions. By joining this conference you become a part of this important and influential voice to the industry and to the global regulatory community.

I invite you to join me and the PCCIG in this effort. With the challenges we face in the economy, the regulatory environment, and from threats to security, can you afford not to participate? I look forward to seeing you there.

For more details on the conference and to register online, please visit www.pda.org/gdp2012.

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Discuss Special Biotech Issues

PDA Parenterals 2012 • Bacelona • Nov. 6-7 • europe.pda.org/Parenterals2012

Conference Co-Chair Friedrich Haefele, PhD, Boehringer Ingelheim Pharma

Following up on our successful PDA Parenterals conference held two years ago in Berlin/Germany, the community of manufacturers, technology and service providers and international regulatory authorities will meet again this year in Barcelona, Spain. The focus topic of this upcoming PDA *Parenterals 2012* symposium is biopharmaceutical products.

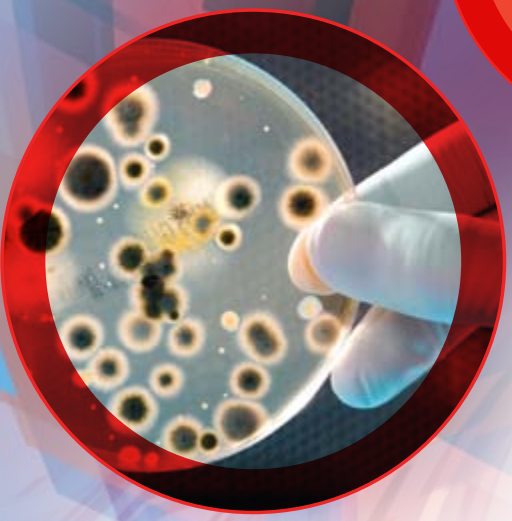
For more than 20 years now, biotech products have entered the global pharmaceutical market and, since then, have changed for better the lives of millions of patients in a growing number of indications. With a steady business growth rate, biotech companies are clearly outpacing traditional research based pharmaceutical companies. Biosimilar, or biobetter, drug products will allow an even larger population to take advantage of these innovative therapeutic entities and there is a growing demand for high quality biopharmaceuticals for yet unmet medical needs in the light of budget constraints in public healthcare. Biopharmaceuticals have special challenges deriving from their manufacturing process, which involves aseptic cell culture and related extraction and purification steps. Their physicochemical nature as large molecular weight proteins or glycoproteins needs specialized analytical methods and tools to characterize and assure reproducible quality.

The parenteral route of administration of these sensitive drugs requires aseptic filling technologies and, increasingly, injection aids or devices that allow patient self administration. This may shift the regulatory scope from pharmaceutical to combination products. New guidelines on process validation and quality risk assessment have significant impact on strategies for process development, quality management and regulatory compliance in manufacturing of biopharmaceuticals. Our conference will provide an update on the most recent development of EU and U.S. regulations, especially on process validation with case studies from leading companies sharing their expert knowledge. In our question & answer sessions, we want to encourage you to share your experience and to come up with your comments on new technologies, guidelines and regulations.

Parenterals 2012 will serve as an op-

Continued at bottom of page 54

Just Added!
New half-day post conference workshop: Understanding the Requirements for Cleanrooms Workshop



The Parenteral Drug Association presents...

PDA's 7th Annual Global Conference on Pharmaceutical Microbiology

Everyday Microbiology – It's All About Control!

October 22-24, 2012

Bethesda North Marriott Hotel | Bethesda, Maryland

The PDA annual global conference on pharmaceutical microbiology is the only place where pharmaceutical and industrial microbiologists come together from all over the world to learn from each other and exchange valuable experience. Don't miss this excellent opportunity to meet and interact with fellow microbiologists, regulatory representatives, key product vendors and other global leaders in pharmaceutical microbiology.

In between the opening and closing sessions, the conference will offer great plenary sessions that include:

- Outbreaks Associated with Pharmaceutical Products: Steps for Prevention
- Biofilms and Tribute to Professor Bill Costerton, BSc, PhD
- Urban Myths in Aseptic Processing and Objectionable Organisms
- And many more

There will also be an opportunity to *Ask the Regulators: Expert Panel Discussion:* The panel will consist of representatives from the FDA with a broad range of expertise, including cGMP field inspections and the review of chemistry, manufacturing and controls information related to sterile drug products.

Hear directly from experts, such as:

- **Matthew J. Arduino,** Dr. PH, Lead Microbiologist, Chief Clinical and Environmental Microbiology Branch, *Centers for Disease Control and Prevention (CDC)*
- **John Metcalfe,** PhD, Senior Microbiology Reviewer, *CDER, FDA*
- **Philip Stewart,** PhD, Director, Center for Biofilm Engineering, *Montana State University*
- **Kalavati Suvarna,** PhD, Consumer Safety Officer/Microbiologist, *CDER, FDA*
- **Anders Vinther,** PhD, Vice President, Roche Quality Biologics Operating Unit (PTQB), *Genentech, Inc.*

Immediately following the conference PDA's Training and Research Institute (PDA TRI) will be hosting five stand-alone courses on-site on October 25-26.

Visit **www.pda.org/microbiology2012** for more information and to register

Exhibition: October 22-23 | Courses: October 25-26

Challenges, Opportunities for Providing Vaccines to the World

PDA/FDA Vaccines Conference • Bethesda • Dec. 3-4 • pda.org/vaccines

Co-chairs Norman Baylor, PhD, Biologics Consulting Group and Michael VanDerWerf, GlaxoSmithKline

After the success of the inaugural PDA/FDA Vaccines conference in 2010, we are inviting all to join us at our second Vaccines Conference in December of 2012. The conference will focus on both our responsibility to provide vaccines to the world and the regulatory and technical challenges to effectively produce and supply these needed medicines. The conference will include industry, regulatory and vaccine experts from non-governmental organizations, such as the World Health Organization, PATH and the National Vaccine Program Office, along with many FDA speakers. This important event will provide a great venue to both hear about and actively discuss the many important vaccine development, manufacturing and regulatory issues we face today.

While advances in science and technology are leading to research and development of a wide array of new vaccines and novel manufacturing approaches, technical, logistical and regulatory challenges continue to face the vaccine industry. This is especially true for vaccines needed in developing countries and other international markets. Come hear about novel industry approaches to supply vaccines along with international regulatory approaches to manufacturing and distribution issues, all discussed by industry and regulatory subject matter experts.

This two day event includes many information-packed sessions, vital for today's vaccine professional. Here are just some of the sessions that will be of high interest:

- Hear about global responsibilities and challenges by distinguished speakers from the World Health Organization and the National Vaccines Program Office
- Discuss global regulatory challenges for manufacturing in and for developing countries with Cathy Hoath form Merck, along with Akira Homma, PhD from Bio-Manguinhos/ Fiocruz (BRAZIL)
- Learn how to naivigate the multiple regulatory requirements and guidances for adventitious agent testing and cell substrate characterization with Arifa Khan, phd, from CBER, FDA and Laurent Mallet, PhD, of Sanofi Pasteur, Ltd.
- Discuss high-profile supply chain problems and proposed strategies to solve them with Martin Vantrieste, Senior Vice President of Quality, *Amgen, Inc.*
- Learn about the Challenges of Assuring Consistent Supply of High-Quality Excipients and controlling the end product supply chain with real world examples and case studies from recent industry experience .
- Explore emerging trends in vaccine manufacturing and developments and better understand FDA and industry perspectives regarding the development, quality and regulatory challenges associated with the use of non-traditional production methods.
- Understand issues around standardization and testing in a global environment as explained by FDA and industry speakers
- Review global regulatory challenges with Marion Gruber, PhD, Director, OVRR, CBER, *FDA* by understanding the regulatory environments around the globe including licensing requirements, immunizations schedules, lot release, and pharmacopeial specifications.

Please join us for these topics and more! This is a must-attend event for all involved in the manufacture and testing of vaccines for preventive and therapeutic purposes. Pharmaceutical and biopharmaceutical professionals with responsibilities in development, manufacturing, preclinical, quality assurance, quality control and regulatory affairs are encouraged to participate.

TRI will also hold two one-day courses on December 5 and 6.

Discuss Special Biotech Issues continued from page 52

portunity for international knowledge exchange and late stage technology and regulatory. Our speakers will provide an overview on aseptic processing techniques in barrier and isolator systems, media fill strategies and associated environmental monitoring programs. You will be able to meet and listen to regulators from U.S. and Europe, experts from pharmaceutical industry, medical device manufacturers, primary packaging material and technology / machinery industry. These sessions will cover the use of flexible manufacturing concepts including single-use materials for fill and finish and related problems with extractable studies, the impact of primary packaging components on quality, and practical developments on primary packaging containers and device selection. In addition to this, we will also discuss how superior electronic systems allow for improvement of process control, and we will also address current standards and the future of visual inspection of parenteral drug products.

We look forward to seeing you there!

WHO Trainer Highlights Global Training Landscape

Biennial Training Conference • Bethesda • Oct. 8-9 • pda.org/biennial2012

Tim Gillum, PhD, Baxter Healthcare

The *PDA Biennial Training Conference* is one of the top industry conferences addressing the evolving training landscape within regulated environments. You will have the opportunity to gain insight to processes and tools that provide you the opportunity to immediately enhance your respective training programs. Additionally, scheduled round table sessions and networking forums will afford each participant the opportunity to work through issues specific to your current situation.

Recognizing the realities of our changing industry, with common budgetary constraints and travel restrictions, this year's conference has packed as much as possible into two days. With this in mind, I ask that attendees come to the conference ready to participate from two lenses: The lens of training compliance and the lens of the business of training. Enhancing our training systems in these two areas will ensure safe and effective products for our patience and catalyze our efforts from training to learning.

Taking a systemic view to training is vital to our organizations as a result of generational changing of the guards, the evolution of technology at a more rapid rate than ever before and evolving global regulatory expectations. This conference provides two plenary sessions, 27 concurrent sessions presented by industry practitioners, and a series of round table discussions focusing on the entire training system. The conference will offer a session by **Richard Sands** addressing why supervisory training needs to be different and **Nadine Rozowsky,** Global Training System Manager at Baxter Healthcare, will present her experiences in leading the use of a single LMS for roughly 50,000 employees in over 100 countries.

The closing plenary session will be presented by Dr. Umit Kartoglu, MD. Dr. Kartoglu is responsible for training for the World Health Organization. His session will offer the attendees the opportunity to learn about the regulatory perspective on pharmaceutical training from the lens of the World Health Orga-

The closing plenary session will be presented by Dr. Umit Kartoglu, MD. Dr. Kartoglu is responsible for training for the World Health Organization

Continued at bottom of page 56

Pharma Micro Event Looks at Careers

Global Conference on Pharmaceutical Microbiology • Bethesda • Oct. 22-24 • pda.org/microbiology2012

Marla Stevens-Riley, U.S. FDA

How many pharmaceutical microbiologists does it take to change a microscope light bulb? None, because chemists were hired instead of microbiologists.

This is a bit provocative, but there is some truth in the details. Employment opportunities for all scientists have decreased over the past decade. Positions for pharmaceutical microbiologist are decreasing as pharmaceutical companies must make difficult financial decisions when determining the types of scientist to hire. In addition, as more of the "Baby-Boom" generation reach retirement age, there is a need to accelerate our development of future pharmaceutical microbiologists who are highly skilled and trained to maintain excellence in the field. Pharmaceutical microbiologists must continue to voice the importance of their role in ensuring the microbiological quality of pharmaceutical products. In the most extreme cases, without microbiological quality, the resulting product can lead to death.

How can these goals be achieved? By offering quality microbiology education and having pharmaceutical companies invest in the continued training of microbiologists. This year's P*DA Global Pharmaceutical Microbiology Conference* is offering a unique session called "Preparing the Quality Control Microbiology Workforce of the Future" to address some of these issues. Speakers in this session will discuss how academic training prepares (or not) students for microbiology in the pharmaceutical industry, what types of skill-sets are needed for the pharmaceutical microbiologist, and how industry provides on the job training for new QC microbiology employees.

Pharmaceutical microbiologists must continue to voice the importance of their role in ensuring the microbiological quality of pharmaceutical products

For a contrast to discussion of the newly hired microbiologists, mid-level managers in the microbiology lab will describe their successes in solving some of the unique day to day challenges in the "Future Leaders" session. Other unique interactive sessions available at this year's conference will be the "Do the Math" session that will allow attendees to follow along with session leaders performing mathematical calculations related to most probable number and endotoxin testing and the "Ask the Regulators Expert Panel Discussion" that will allow attendees to pose questions to a panel of representatives from the FDA about cGMP field inspections and the review of chemistry, manufacturing, and controls information related to sterile drug products.

In addition, there will be other plenary and concurrent sessions discussing the current microbiological research available on pyrogen/endotoxin testing, control of raw materials and bulk solutions, package integrity, microbial control of biopharmaceuticals, biofilms, rapid microbiological methods, urban myths of pharmaceutical microbiology, and regulatory updates related to the microbiology laboratory. For more informal microbiological discussions, attendees can view poster presentations and visit with vendors exhibiting the latest in pharmaceutical microbiology technologies.

WHO Trainer Highlights Global Training Landscape continued from page 55

nization Cold Chain on Wheels course is a recent example of his balanced understanding of the training expectations of the global regulatory community and applications of true adult learning. The Program Planning Committee is extremely excited to provide attendees the opportunity to gain greater insight to the global landscape of training.

Join us at this year's conference in Bethesda, Md. October 8-9 and learn from leading industry practitioners in the craft of compliance training, learning and workplace performance. This is a great opportunity to actively engage as a part of the global training community.

Immediately following the *conference,* PDA's Training and Research Institute will be hosting three courses from October 10-11.

To learn more about the conference, courses or to register, visit www.pda.org/biennial2012.

The 2012 Aseptic Processing Training Program is **SOLD OUT!** Visit **www.pda.org/aseptic** to sign up to receive an email notice when registration opens for the next session.

Parenteral Drug Association Training and Research Institute (PDA TRI)

Upcoming Laboratory and Classroom Training for Pharmaceutical and Biopharmaceutical Professionals

October 2012

Developing a Moist Heat Sterilization Program within FDA Requirements
October 2-4 | Bethesda, Maryland
www.pda.org/moistheat2012

Developing and Validating a Contamination Control, Cleaning and Disinfection Program for Controlled Environments
October 9-10 | Bethesda, Maryland
www.pda.org/contamination2012

2012 PDA Biennial Training Conference Course Series
October 10-11 | Hyatt Regency in Bethesda, Maryland
www.pda.org/biennialcourses2012

- Qualifying Your SMEs as Trainers | October 10
- Learning, Knowledge Management and Impact: Moving from Theory to Practice | October 10-11 – New Course
- FDA Inspection Readiness for a Training Systems Audit | October 10

The Universe of Pre-filled Syringes and Injection Devices Course Series
October 18-19 | Red Rock Resort and Spa in Las Vegas, Nevada
www.pda.org/prefilledcourses2012

- Combination Products: Principles, Regulations, Current Issues and Solutions | October 18
- Technical Development of Pre-filled Syringes, Autoinjectors and Injection Pens | October 18
- Syringes and Elastomers: Understanding the Effects on Quality and Demonstrating the Production Process, Influences and Needs | October 19

PDA's 7th Annual Global Conference on Pharmaceutical Microbiology Course Series
October 25-26 | Bethesda North Marriott Hotel in Bethesda, Maryland
www.pda.org/microcourses2012

- Alternative Methods for Mycoplasma Testing | October 25 – New Course
- Biofilms | October 25 – New Course
- Evaluation, Validation and Implementation of Alternative and Rapid Microbiological Testing Methods | October 25 – New Course
- Microbiological Issues in Non-Sterile Manufacturing | October 26
- Investigating Microbial Data Deviations | October 26 – New Course

Validation of Biotechnology-Related Cleaning Processes
October 30-November 1 | Bethesda, Maryland
www.pda.org/biotechnology2012

November 2012

Steam in Place
November 2 | Bethesda, Maryland
www.pda.org/steam2012

2012 PDA FDA Pharmaceutical Supply Chain Conference Course Series
November 12 | Bethesda, Maryland
www.pda.org/supplychaincourses2012

- Developing a Robust Supplier Management Process | November 12

DoE Basics for Validation by Design
November 13-14 | Bethesda, Maryland
www.pda.org/doe2012

Single-Use Systems for Manufacturing of Parenteral Products – New Course
November 14-15 | Bethesda, Maryland
www.pda.org/suscourse2012

Qualification of Pharmaceutical Systems – New Course
November 27-29 | Bethesda, Maryland
www.pda.org/pharmasystems2012

December 2012

Risk Management in Aseptic Processing
December 4-5 | Bethesda, Maryland
www.pda.org/riskmanagement

For more information on these and other upcoming PDA TRI courses please visit www.pda.org/course

Laboratory Courses

The PDA Training and Research Institute is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education.

Editor's Message

Job Aids Facilitate Publishing Process

As I set out to work on the September *PDA Letter* solo for the first time in six years (see **Emily Hough's** farewell message in the July/August issue), I was shocked at how much I had forgotten about all the steps involved with putting together the issue. This got me thinking about incoming writer/editor, **Rebecca Stauffer,** who starts in September, and all the things I will have to teach her about the job. While Rebecca is an experienced publishing pro, we have our own procedures and steps to follow here at PDA.

Thankfully, it did not take me long to reacquaint myself with all the editing tasks Emily had performed with increasingly little oversight during her five years on the Letter. Making the task less formidable was the various checklists we had developed to help her perform standard work that was routine—so routine, it was easy to forget to do some of the tasks prior to the existence of the checklist. This job aid really helped me, and it helped Emily improve the editorial quality of the *PDA Letter* over the last five years. After working through the issue and using the checklists, I am confident that Rebecca will have a smooth transition into our workflow for the October issue.

For this reason, I really enjoyed interviewing the four experts for the cover story, "Job Aids Slowly Evolve from Paper to Electronic, From Shop Floor to Office Suite Tools." It struck me how the experts reinforced the idea of linking job aids to procedures and version-controlling them. I'd go further to say that job aids, like checklists, are a work in progress. The first version might not capture all the relevant steps to a standard procedure. Indeed, it took several iterations to get the editing checklist right.

Editing an article is not a one-time, one-shot job. It takes several passes to edit an article properly. The first step is a read through. Next, we tackle language and syntax to ensure every sentence in the article makes sense and can be easily understood. After that, we look at standard style, grammar and punctuation. Finally, after it is formatted for the Letter, we look at the headlines, bylines and the overall layout. Well, after we struggled with some editing mishaps even after Emily started using an editing checklist, we sat down and examined them. We came to the conclusion that she needed multiple checklists—one for each read-through. We met several more times, and eventually we deployed four separate checklists for editorial, and the result was a marked improvement in our work—fewer typos, spelling, style and other types of mistakes in the Letter. The success was so good, I worked with the Letter's designer to develop a checklist she is to use when creating each issue.

One can be truly expert in their field, yet still forget to perform the most standard work functions on a routine basis. Job aids, whether checklists, flow charts, or pictures, are for everyone.

PDA Letter

The PDA Letter is published 10 times per year, exclusively for PDA members.

Subscriptions are not available.

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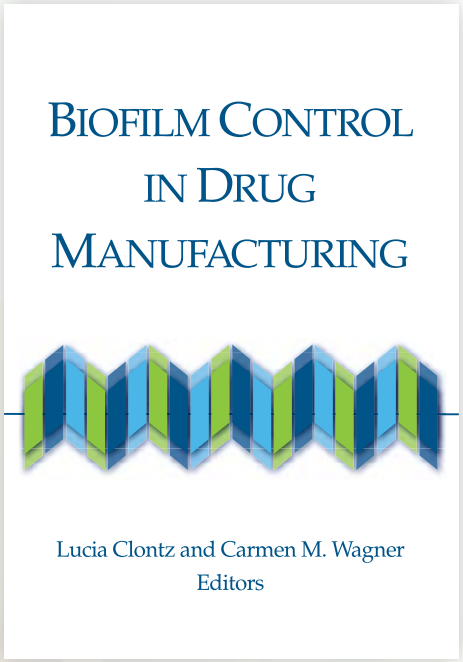
New Release at the PDA Bookstore



Biofilm Control in Drug Manufacturing

Edited by **Lucia Clontz and Carmen M. Wagner**

Pre-order your copy by **Sept. 30, 2012** and Save 20%

This book provides guidance in preventing and controlling biofilm contamination in pharmaceutical and biopharmaceutical processing. Twelve chapters contributed by global experts and useful appendices cover topics such as:

- The contamination control by design model
- The impact of biofilms on pharmaceutical manufacturing
- Establishing microbial contamination control
- Controlling biofilms in drug manufacturing equipment
- The link between process equipment colonization and drug safety
- Detection and prevention control of biofilms in pharmaceutical water
- Sanitization
- And much, much more

www.pda.org/bcdm

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By James L. Vesper
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Edited by Dr. Siegfried Schmitt
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