People • Science • Regulation

PDA Letter

Volume LI • Issue 5 www.pda.org/pdaletter May 2015

Key Considerations for Successful Technology Transfers 28

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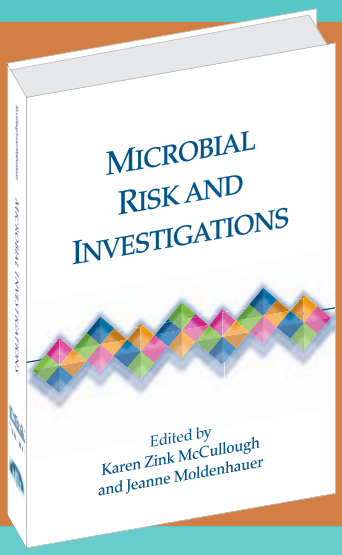
PDA Bookstore New Release

PDA Parenteral Drug Association



Microbial Risk and Investigations

EDITED BY: KAREN ZINK MCCULLOUGH AND JEANNE MOLDENHAUER

PDA MEMBER PRICE: $260
ITEM NO. 17328

go.pda.org/MRIG

The Barr Decision (Barr, 1993) forever changed how pharmaceutical companies look at data that is out-of-specification (OOS). Following issue of this legal decision, many companies and regulators worked to determine how this decision affects microbiological test results.

Microbial Risk and Investigations, written by authors with years of industry experience and edited by industry experts Jeanne Moldenhauer and Karen Zink McCullogh, provides a wealth of information on microbial investigations and dealing with aberrant data. Many of the chapters include case studies that can provide guidance for common situations that may occur at your facility.

Some of the many topics covered include:

- Types of Investigations
- The Microbiologist's Tool Box
- Quality Metrics
- Contamination Risk Evaluation
- Sterility Testing
- Objectionable Organisms
- Particulates
- Rapid Microbiology Methods

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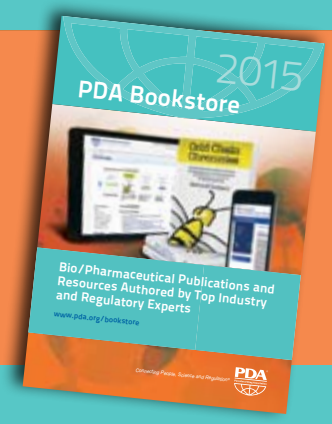

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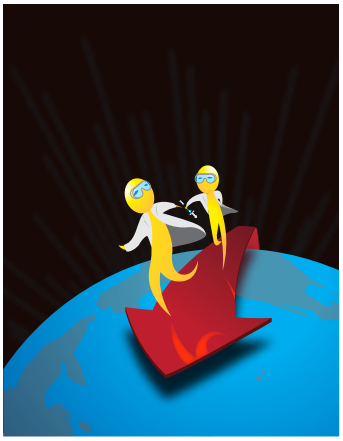
PDA Letter

Volume LI • Issue 5 www.pda.org/pdaletter

Cover



Cover Art Illustrated by Katja Yount

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Voices of PDA

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PDA's Mission

To develop scientifically sound, practical technical information and resources to advance science and regulation for the pharmaceutical and biopharmaceutical industry through the expertise of our global membership

PDA's Vision

To be the foremost global provider of science, technology, and regulatory information and education for the pharmaceutical and biopharmaceutical community

PDA® Parenteral Drug Association

Connecting People, Science and Regulation®

The Parenteral Drug Association presents...

PDA 10th Annual Global Conference on Pharmaceutical Microbiology

Inspiring innovation and exploring current trends and challenges to product quality and infection control in the global market

October 19-21, 2015 | Bethesda, MD

Bethesda North Marriott Hotel and Conference Center

Exhibition: October 19-20 | Courses: October 22-23

2015 Theme: Promoting Excellence: Past Lessons, Present Solutions and Future Visions

Register by August 10, 2015 and save up to $400!

PDA's 10th Annual Global Conference on Pharmaceutical Microbiology will address pressing challenges to product quality and infection control in today's global market. Hear from regulatory and industry experts from around the world as they highlight the hottest topics, case studies and current trends in pharmaceutical microbiology.

Keynote addresses will focus on The Future of Science and The Science behind Ebola. Concurrent tracks will explore the latest in new technology and contamination control. Additional sessions will take an in-depth look at current hot topics, including

- Urban Myths
- USP Updates
- Regulatory Updates – What's Going On within FDA and PIC/S?
- Ask the Regulators Panel Discussion
- And Much More!

Learn more and register at pda.org/microbiology2015

Following the conference, attend *PDA's 10th Annual Global Conference on Pharmaceutical Microbiology Course Series*. Over two days (October 22-23), PDA Education will host three courses on topics of the utmost importance to pharmaceutical microbiology:

- *Investigating Microbial Data Deviations* (October 22)
- *Evaluation, Validation and Implementation of Alternative and Rapid Microbiological Testing Methods* (October 22-23)
- *Regulatory Aspects of Microbiology in a Non-Sterile Environment* (October 23)

Learn more and register at pda.org/microcourses

PDA Honors Contributors at Annual Meeting Banquet

Each year, PDA recognizes members whose contributions have helped the Association fulfill its mission. Honored members are recognized at the PDA Awards Dinner, held during the Annual Meeting. PDA congratulates each winner and thanks them for their service to the Association.

Honorary Membership

This is PDA's most prestigious award, conferring lifetime membership benefits to the recipient. The award is usually given in recognition of very long service of a significant nature to PDA.

John Shabushnig, PhD, Insight Pharma Consulting

Gordon Personeus Award

Presented in memory of the late **Gordon Personeus,** past PDA President and long-time volunteer, this award is intended to honor a PDA member, other than a member of the PDA Board of Directors, for long-term acts or contributions that are of noteworthy or special importance to PDA.

Hannelore Willkommen, PhD, RBS Consulting

David Matsuhiro, Cleanroom Compliance

Frederick J. Carleton Award

Presented as a tribute to lifetime contributor, past President, past Executive Director and Honorary Member **Frederick J. Carleton,** this award is designated for a past or present member of the PDA Board of Directors whose services on the Board are determined by his/her peers as worthy of such recognition.

Susan Schniepp, Regulatory Compliance Associates

Steven Mendivil, Amgen

Packaging Science Award

This award is given in recognition of extraordinary contributions to PDA and the packaging science.

Nicholas DeBello, DeBello & Associates

Distinguished Service Award

This award is given in recognition of special acts, contributions or services that have contributed to the success and strength of PDA.

Osama (Sam) Elrashidy

Michael DeFelippis, PhD, Eli Lilly

Anthony Cundell, PhD, Microbiological Consulting

Robert Repetto, Pfizer

Steffen Gross, Paul-Ehrlich-Institut

Martin VanTrieste Pharmaceutical Science Award

Established in honor of long-time contributor and Chair-Elect, **Martin VanTrieste** this award is given annually for outstanding contributions to the advancement of pharmaceutical science.

Maik Jornitz, G-Con Manufacturing

PDA Europe Service Appreciation Award

This award is presented annually for special acts, contributions or services that have contributed to the success and strength of PDA's European activities.

Derek Duncan, PhD, Lighthouse Instruments

Service Appreciation Award

The Service Appreciation Award is presented annually for special acts, contributions or services.

Kim Ngan Waters, GlaxoSmithKline Australia

Lara Soltis, Ansell Healthcare

Roland Bizanek, PhD, Compass Pharma Consulting

Melissa Seymour, Biogen Idec

Elaine Eborall, Genentech

John Finkbohner, PhD, AstraZeneca-MedImmune

Junko Sasaki, Sumitomo Dainippon Pharma Co

Christopher Smalley, PhD, Merck

James P. Agalloco Award

The James P. Agalloco Award is presented annually to the PDA faculty member who exemplifies outstanding performance in education.

John Geigert, PhD, BioPharmaceutical Quality Solutions

Piet Christiaens, PhD, Toxikon Europe

Michael S. Korczynski Award

An award established in recognition of contributions made toward the development of PDA's international activities.

Junko Sasaki, Sumitomo Dainippon Pharma Co

Karen Ginsbury, PCI Consulting

Frederick D. Simon Award

The Frederick D. Simon Award is presented annually for the best paper published in the *PDA Journal of Pharmaceutical Science and Technology.*

Yuh-Fun Maa, Wendy Shieu, Sarah Torhan, Edwin Chan, Aaron Hubbard, Benson Gikanga, and **Oliver Stauch,** for the March/April 2014 paper, "Filling of High-Concentration Monoclonal Antibody Formulations into Pre-Filled Syringes: Filling Parameter Investigation and Optimization"

Distinguished Editor/Author

This award recognizes the author or editor selected by PDA members for their contribution to PDA's technical books.

Kevin O'Donnell for his book *Cold Chain Chronicles*

President's Award

This award recognizes a PDA staff member, other than senior staff, whose exemplary performance has contributed to PDA's success during the previous year.

Melissa Pazornik and **Sylvia Becker**

PDA Volunteer Spotlight

Mirko Gabriele

- Technology Transfer Manager
- *Patheon*
- Member Since | **2011**
- Current City | **Latina, Italy**
- Originally From | **Isola del Liri, Italy**

There is a continuous osmosis of knowledge

What was the most rewarding aspect of your work on the Technology Transfer Technical Report Team?

Having the chance to work with experts from all over the world with different backgrounds and views on technology transfer.

How did you start volunteering for PDA?

I joined the interest group working on technology transfer. I was in contact with one of the members of the interest group. After hearing about the group's activities, I was so impressed that the next day I asked to join the team.

What is something you learned/gained from PDA that you couldn't have gotten anywhere else?

The possibility to fruitfully exchange experiences, ideas and thoughts down to the nitty-gritty of pharma topics.

What is the most challenging part of your job?

The most challenging, but also the most interesting, part is understanding the real drivers of a project. Sometimes they are hidden, sometimes they are more clear, and sometimes they are not and you have to figure them out.

What challenges do you foresee for your segment of pharma? And how can they be overcome?

Pharma processes and chemistry are becoming more and more complex. There is more potential for risks and mistakes. Regulators want to prevent bad outcomes for patients, therefore we need to highlight risks, properly evaluate those involved and put in place mitigation plans.

What is an issue or trend in your industry you think more people should be talking about?

Quality By Design and Risk Management

Tell us something surprising about you.

I like reading financial newspapers and fantasy books. You may think that's a bit strange as they are completely different topics; however, believe me, a financial newspaper is the best fantasy story you can read!

The Parenteral Drug Association presents...

2015 PDA Visual Inspection Forum

October 26-27, 2015 | Bethesda, MD

Bethesda North Marriott Hotel and Conference Center

Exhibition: October 26-27 | Courses: October 28-29

The leading meeting and exhibition dedicated to quality assurance of injectable products

Register before August 17, 2015 and save up to $400!

The *2015 Visual Inspection Forum* will provide presentations, case studies and discussions on new developments in the field of visual inspection, including a basic understanding of the sampling and inspection process, special aspects of biotech products, practical aspects of manual and automated methods and the regulatory and compendial requirements that govern them.

This program features two confirmed FDA speakers:

Stephen Langille, PhD, Branch Chief, Division of Microbiology Assessment, Branch 3, CDER, *FDA*

Ewa Marszal, Chemist, CBER, *FDA*

Other aspects of visual inspection to be covered include:

- New USP chapters <790> and <1790>
- Particle Control and Characterization
- Vaccines/Biologics Inspections
- Compendial Requirements, Current and Future Regulatory Requirements
- Selection and Qualification of Human Inspectors
- Challenging or Difficult to Inspect Products
- Packaging Materials/Container Closure Integrity/Leak Testing
- Case Studies on Validation for Visual Inspection Market
- And so much more!

Be sure to visit our exhibitors! See the latest in commercial inspection hardware and discuss production needs with key suppliers of inspection systems and services onsite during the exhibition days.

Do you wish to become an exhibitor at the *2015 Visual Inspection Forum*? Email **Dave Hall,** hall@pda.org, to learn more.

Immediately following the *2015 Visual Inspection Forum*, PDA Education will host the *An Introduction to Visual Inspection* (October 28-29) course. Learn the fundamentals of visual inspection and their application to injectable products. Through a combination of lecture, discussion and hands-on laboratory exercises, develop practical inspection skills that can be applied to both manual human and automated machine inspection.

Learn more, visit pda.org/visual2015

chapter update

Israel Chapter Explores New Regulations, Novel Therapies

Karen Ginsbury, PCI Consulting

The PDA Israel Chapter's 2014 *Annual Meeting* held last December proved to be chock-full of useful GMP and GDP information presented by industry experts and regulators.

Following a report from Chapter Treasurer **Karin Baer, Ofra Axelrod** delivered the first talk of the evening, offering an overview of recent activities from the Israeli Ministry of Health. The Ministry's improvement initiatives remain ongoing, particularly concerning its laboratory. EDQM provided certification for the laboratory, which was inspected by, and received accreditation from, the prestigious Official Medicines Control Laboratories network within Europe for ISO 17025 certification. This year, the laboratory will start a formal postmarketing surveillance program, testing samples and supporting the Ministry as it focuses on counterfeit products.

Additionally, the GMP inspectorate will also be focusing on inspections for Phase 3 manufacturers and importers of clinical trial materials. Israel is one of the most advanced countries in this respect, having passed legislation requiring a quality agreement between the sponsor or distributor/importer and the clinical site. The GMP inspectorate participates in EMA's Inspectors Working Group and follows up on implementation of EU legislation as well as performing inspections on behalf of PIC/S outside Israel. API legislation has also been passed and Israel is currently under evaluation to enter the white list of countries allowed to export APIs to Europe without a statement of compliance.

PDA Israel Chapter Executive Committee: Shlomo Sackstein, BioPharmax; Raphy Bar, BC Consulting; Karin Baer, Teva Pharmaceuticals; Einat Frydman, BTG, Ferring; Karen Ginsbury, PCI Pharma; Rachel Karpel, Karpel Consulting; Mark Kessler, Kessler Consulting; Moti Izhar, Ludan

The Ministry of Health also now participates in the WHO prequalification program and additionally collaborates with the U.S. FDA regularly. The ministry also works closely with Swissmedic as well. ➤

Next, Chapter President **Rachel Karpel** spoke on Israeli regulations in greater detail, taking participants on a lightning tour of regulatory changes outlined in 50 regulatory documents issued in 2014. API manufacturers must now allow for GMP inspections of their facilities and GDPs must include starting materials, not just actives. Pharmacovigilance is now a prerequisite for registration and a Qualified Person must be identified as part of this greater emphasis on pharmacovigilance. And there will be greater control of medicines imported under the compassionate usage clause.

Also, proposed GDP requirements would mirror the European approach to GDP.

The third lecture of the evening moved away from GMP and regulation, instead focusing on novel therapies. **Hermona Soreq** spoke in a unique and humorous manner about the challenge and promise of microRNAs as biomarkers, injecting some fascinating and encouraging scientific content to the evening.

The evening was closed out with two further lectures: **Shuli Bach** brought participants up-to-date on quality metrics and **Karen Ginsbury** provided some global regulatory updates based on her participation in PDA's Regulatory Affairs and Quality Advisory Board.

The Chapter sends a huge thanks to all the speakers and to Rachel Karpel for moderating and organizing the evening.

Ofra Axelrod from the Israeli Ministry of Health discussed ongoing initiatives within the Ministry

Who's Who

Ofra Axelrod, Director, The Institute for Standardization and Control of Pharmaceuticals, Israeli Ministry Of Health

Shuli Bach, Teva Pharmaceuticals

Karin Baer, Director of Quality Assurance, Omrix biopharmaceuticals Ltd

Karen Ginsbury, President, PCI Consulting

Rachel Karpel, Senior Associate, PCI Consulting

Hermona Soreq, Professor, Department of Biological Chemistry, Hebrew University

PDA Recognizes PCMO® Leaders for Achievements

Stephan Rönninger, PhD, Amgen, Veronique Davoust, PhD, Pfizer, Glenn Wright, Eli Lilly, and Jahanvi (Janie) Miller, PDA

PDA's Paradigm Change in Manufacturing Operations (PCMO®) program has led the way in moving pharmaceutical manufacturing into a new model of robust business and production processes, better quality, and state-of-the-art technologies by focusing on implementation of the lifecycle approach, quality systems, process management, and Quality Risk Management. Initiated by **Lothar Hartmann** in 2009, the PCMO® Steering Committee leadership—**Stephan Rönninger** (chair), **Veronique Davoust** (co-chair), and **Glenn Wright** (co-chair)—has maintained a large portfolio of best practice documents and guided the initiative's seven years of success.

PCMO® was a first of its kind program for PDA, as it focused the work of several existing Task Forces and created additional Task Forces to fulfill its mission.

Overall, 18 Task Forces operated under the PCMO® imprimatur, which under the leadership of the PCMO® Steering Committee and with contribution from PDA staff liaison **Jahanvi (Janie) Miller,** delivered 11 PDA technical reports with accompanying PDA Education courses, four *PDA Journal of Pharmaceutical Science and Technology* articles, two PDA conferences, and one PDA webinar. All of these projects significantly benefitted the PDA membership.

This year at the *2015 PDA Annual Meeting* in Las Vegas, PDA recognized the PCMO® Steering Committee leaders and the task force leaders, who served as the key factors to these accomplishments. During this recognition, PDA also announced the closeout of PCMO® as the Association will begin a revised focus on manufacturing through PDA's new Manufacturing Science Program (MSP℠).

Members of the PCMO® Steering Committee pose for a group photo March 16 at the *2015 PDA Annual Meeting*

Who's Who

Veronique Davoust, PhD, Manager, Global Quality Strategy, Pfizer

Lothar Hartmann, PhD, Head, Quality, Crucell Switzerland AG

Jahanvi (Janie) Miller, Senior Project Manager, PDA

Stephan Rönninger, PhD, Head, External Affairs Europe, International Quality, Amgen

Glenn Wright, Senior Director, Project Management, Eli Lilly

New Advisory Board Drives Strategic Plan for PDA Education

Brent Watkins, Veltek Associates

The new PDA Education Advisory Board (EAB) met at the *2015 PDA Annual Meeting* in Las Vegas. Formed in late 2014, EAB will support PDA's education courses by advising on strategic plans, initiatives and the best direction for positioning PDA Education programs.

Led by **Edward Trappler,** a longtime PDA volunteer and a 30-year industry veteran, **Brent Watkins** and **Bob Dana**, the EAB will strive to strengthen PDA's position as a leader in education and training for the pharmaceutical and biotech industry. Other members include: **John Shabushnig, John Brecker, Jim Vesper, David Matsuhiro, Michael Sadowski, Hal Baseman, Lisette Gilchrest, John Finkbohner** (RAQAB liaison), **Marsha Hardiman** (SAB liaison), and **John Geigert** (BioAB liaison). PDA representation also includes **Georg Roessling**.

EAB will develop a strategic plan for PDA Education that provides guidance to the PDA Board of Directors. Since the PDA brand is very strong in the industry, EAB believes the goal should be to build on this solid foundation. PDA Education currently offers:

- PDA's Training and Research Institute (TRI) located at PDA's global headquarters in Bethesda, Md. TRI currently offers more than 30 laboratory- and lecture-based courses each year at the facility, serving thousands of students over the last 18 years. TRI is the only standalone facility of its kind in the industry.
- Lecture education courses that accompany PDA's signature conferences.
- In-house training for a variety of subjects that can be customized to individual organizations.

The strength of PDA Education lies with the industry experts who help develop course material and instruct the classroom/laboratory sessions. PDA has recently developed an Instructor Handbook for both veteran and new instructors to provide a framework that helps to ensure consistent, high-quality instruction. PDA has developed a formal process of vetting instructors and course materials to provide the best product for students. Instructor reimbursement has also been standardized (usually in the form of an honorarium).

PDA Education also understands that PDA's library of technical reports supports an excellent source of relevant course material. Technical Reports will continue to be a focus of course development; the timely development of course material after a technical report is released or updated provides a valuable resource to the industry. When possible, technical report team members will be involved in course development.

The EAB also understands that PDA Education does not operate in a vacuum, and that there are other organizations and individuals who offer similar products. EAB will frequently benchmark these competitive offerings in order to improve our own.

EAB proposes offering online material including videos, whether free or at cost, as an added value to our industry.

PDA Education recently began offering students electronic versions of course material. Online and printable distribution of course material is still heavily controlled, but this allows more flexible access to course material. Overall, the response has been positive. In 2015, many students used their laptops or tablets to follow along with their instructors, as opposed to cumbersome course binders.

2015 will be an exciting year for EAB as it works to fulfill its mission:

> *"The Educational Advisory Board will provide guidance and support to the PDA in advancing effective and valuable educational programs for the benefit of our membership and the industry."*

PDA Who's Who

Edward Trappler, President, Lyophilization Technology

Brent Watkins, Southeastern Technical Manager, Veltek Associates

Bob Dana, Sr. VP, Education, PDA

John Shabushnig, PhD, Independent Consultant, Insight Pharma

John Brecker, Consultant, JB Consulting Micro

Jim Vesper, PhD, President, LearningPlus

David Matsuhiro, President, Cleanroom Compliance

Michael Sadowski, Director, Medical Products Sterility Assurance, Baxter Healthcare

Hal Baseman, COO, ValSource

Lisette Gilchrest

John Finkbohner, PhD, Senior Regional Policy Director, MedImmune

Marsha Hardiman, Senior Consultant, ConcordiaValSource

John Geigert, PhD, President, BioPharmaceutical Quality Solutions

Georg Roessling, PhD, Sr. Vice President, PDA Europe

2015 PDA Annual Meeting

Plenary Sessions

Opening Remarks

(l-r) Richard Johnson, PDA; PDA Chair Hal Baseman, ValSource

Chad Juros of Azzur Group demonstrated magic tricks. As a child, his father encouraged him to learn magic tricks as a way to deal with leukemia.

Members of the audience got to participate in Juros' act as he told his moving story of surviving cancer as a child

P1: Changing Manufacturing – Fulfilling Future Treatment Options and Financial Necessities

(l-r): Glenn Wright, Eli Lilly, Adwait Bhagwat, PricewaterhouseCoopers; Chad Juros, Azzur Group; Jeff Boyd, Novartis

P2: The Importance of Science & Technology to Building a Quality Culture

(l-r) Jeff Levy, PhD, Eli Lilly; Fran Zipp, Lachman Consultants; Ira Mann, FPC of Atlanta

Plenary Sessions

P3: Flexible Manufacturing – Current Solutions and Future Visions
(l-r) Michael O'Brien, Pfizer; Maik Jornitz, G-Con; Duncan Low, PhD, Amgen

P4: Biosimilars on the Doorstep – Challenges and Opportunities
(l-r) Sumant Ramachandra, MD, PhD, Hospira; Ursula Busse, PhD, Novartis; Joerg Windisch, Sandoz

Breakout Sessions

B1: Threats to Global Supply Chain
(l-r) John Geigert, PhD, BioPharmaceutical Quality Solutions; Thomas Pizzuto, J&J; Michael Dalton, ELI Lilly; Robert West, U.S. FDA

C1: Advances in Manufacturing
(l-r) Robert Repetto, Pfizer; Morten Munk, NNE Pharmaplan; John Bonham-Carter, Repligen

C3: Virus Contamination
Min Zhang, Genentech

A2: Methods for Improving Manufacturing Performance
(l-r) William Miele, PhD, Pfizer; Martin VanTrieste, Amgen; Sarah Horton, Pfizer; Kerry Ingalls, Amgen

2015 PDA Annual Meeting

Breakout Sessions

A3: The Value of Knowledge Transfer and Process Validation

(l-r) Vijay Chiruvolu, PhD, Kite Pharma; Walter Manger, Merck; Senthil Ranganathan, PhD, CMC Biologics

B2: Drug Shortages

(l-r) Emma Ramnarine, Susan Schniepp, Regulatory Compliance Associates; John Finkbohner, PhD, AstraZeneca-MedImmune

B3: Biologic Combination Products

(l-r) Michael DeFelippis, PhD, Eli Lilly; Manfred Maeder, PhD, Novartis; John Towns, PhD, Eli Lilly

C2: Cell Therapies – New Processes/New Challenges

(l-r) Ali Siahpush, PhD, Pharmefex Consulting; Knut Niss, PhD, Novartis; Michael DeFelippis, PhD, Eli Lilly; Vijay Chiruvolu, PhD, Kite Pharma

Passport Drawing

PDA Education presented a $100 giftcard to Wendy Shieu of Genentech

Mahesh Mohnani of AstraZeneca won a bottle of wine from Aptar

Kiyoshi Temmaru of Takeda got to take home a Windows Trio tablet from AWS Bio-Pharma

Janmeet Anant, PhD, from EMD Millipore won a bottle of bourbon whiskey from Coldstream Laboratories

Edwin Rivera-Martinez received a Samsung tablet from BioVigilant

An iFit from Lonza was presented to Mike Avram of Bayer

James Stumpff of PAREXEL got an iPad mini from CAI

+ 2015 PDA Annual Meeting

Annual Walk/Run

Participants in the 9th annual walk/run braved the desert heat to raise over $3,000 for the Cure 4 the Kids Foundation

Exhibit Hall/
Networking

snapshot

TR-65 Offers Best Practices for Tech Transfer Planning

Jahanvi (Janie) Miller, PDA

The transfer of knowledge, processes and best practices is critical in improving efficiency, effectiveness and quality. PDA recognized the need for a guide outlining the importance of including these aspects in a well-designed technology transfer project (TTP) plan, leading to publication of the 2014 *PDA Technical Report No. 65: Technology Transfer.*

Within this technical report, the technology being transferred is related directly and indirectly to a drug under development and related processes (manufacturing, analytical, packaging) during the lifecycle. Since all aspects of the development are considered, individuals working to develop a TTP must encompass a multidisciplinary background; these individuals also ensure the project is adequately supported through sufficient oversight. This technical report is one of the key elements in comprehensively establishing a program to ensure successful knowledge transfer.

Technology transfer refers to the conveyance of manufacturing processes, analytical methods, packaging components, etc., from an original site to a new one. This could be due to outsourcing or even migration to a new facility within the same company. The technical report offers best practices and case studies to ensure a successful technology transfer. In light of greater use of contract manufacturing organizations as well as the introduction of new forms of modular manufacturing, effective planning for technical transfer will be critical to the future of the industry.

This technical report was published under auspices of the Paradigm Change in Manufacturing Operations (PCMO®) initiative which has issued many technical reports relating to aspects of robust systems. PDA recently closed this initiative (see story on p. 12) to inaugurate the Manufacturing Science Program℠.

Members can read the technical report for free on PDA's online technical report portal. Technical Report No. 65 can also be purchased at the PDA Bookstore (www.pda.org/bookstore).

Journal *Preview*

May–June Issue Features Editorials from the BioPhorum Operations Group (BPOG)

This issue of the *PDA Journal of Pharmaceutical Science and Technology* includes an introduction and two editorials from the BioPhorum Operations Group (BPOG). Of these editorials, one provides an industry perspective on microbial monitoring for biologics and the other compares container closure integrity control with integrity testing.

Commentary

Jinshu Qiu, et. al., "Risk-based Strategy to Determine Testing Requirement for the Removal of Residual Process Reagents as Process-related Impurities in Bioprocesses"

Research

Marianne Lilletvedt Tovsen, et. al., "Physicochemical Stability of Emulsions and Admixtures for Parenteral Nutrition during Irradiation by Glass-Filtered Daylight at Standardized Conditions"

Scott F. Ross, et. al., "Microscopic Characterization of Brevundimonas diminuta in the Hydrated State"

Dennis Jenke, et. al., "A Means of Establishing and Justifying Binary Ethanol/Water Mixtures"

David Roesti, et. al., "Comparison of Different Calculation Approaches for Defining Microbiological Control Levels Based on Historical Data"

Héctor Santana, et. al., "Stability Studies of a Freeze-Dried Recombinant Human Epidermal Growth Factor Formulation for Wound Healing"

Yuh-Fun Maa, Wendy Shieu and Oliver B. Stauch, "Filling of High-Concentration Monoclonal Antibody Formulations into Pre-filled Syringes: Investigating Formulation-Nozzle Interactions To Minimize Nozzle Clogging"

Technology/Application

Flaviu Gruia, Arun Parupudi and Alla Polozova, "Practical Considerations for Detection and Characterization of Sub-Micron Particles in Protein Solutions by Nanoparticle Tracking Analysis"

Paul Genest, et. al., "Achieving a Successful Scale-Down Model and Optimized Economics through Parvovirus Filter Validation using Purified TrueSpikeTM Viruses"

BPOG Special Section Editorial

Darren Whitman, "Introduction to BioPhorum Operations Group (BPOG) Special Section Editorials"

David Bain, et. al., "Microbial Monitoring For Biological Drug Substance Manufacturing: An Industry Perspective"

Scott Ewan, et. al., "White Paper: Container Closure Integrity Control versus Intergrity Testing during Routine Manufacturing"

Automated Isolator with Robotic Arm Offers New Options

Rebecca Stauffer, PDA

It is no revelation to say that the age of robotics and automation is underway, as many assembly line industries have utilized production robots in one form or another for several decades. Yet pharma manufacturing remains heavily human. Robotic systems, however, can offer solutions to problems caused by the human element, such as the problem of microbial contamination in aseptic processes.

In a presentation at the Nov. 2014 PDA *Parenterals* conference in Munich, Germany, **Sergio Mauri,** Manager, Integrated Projects Business Unit, Fedegari Autoclavi, showcased his company's gloveless, fully sealed isolator that uses a robotic, GMP-compliant arm. This solution is currently in an advanced development phase and the company hopes to market it for small-scale manufacturing of personalized, cytotoxic materials used for clinical trials.

"If we are able to take personnel out from our process, then we will really reach the goal to have an advanced aseptic process," he said. "The isolator with the GMP robot can give a flexible and modular solution."

He added, "Our system is based on a batch system and it is completely sealed."

With no operator required, the isolator supports a completely automated fill/finish process. Without the need for gloves and the resulting glove ports and gauntlets, a greater level of sterility assurance is assured.

The equipment includes Wash in Place (WIP) capability to clean the contamination generated by the process. It also uses single-use material such as ready-to-use primary containers and closures, beta bags and disposal waste bags.

To ensure airtight construction, Fedegari's seven-axis robot arm—built by robotics manufacturer Kawasaki—is stainless steel and designed to be low particle shedding. It is also resistant to high pressures and temperature wash downs, fully compatible for decontamination using H_2O_2 vapors. The system can also support both positive and negative pressures. An electronic motor controls the strength of the arm's grip.

"This is really a breakthrough," emphasized Mauri.

External parts are decontaminated with steam sterilization. The tubs inside the isolator are decontaminated with H_2O_2 through a vaporizer that controls a dosing pump and heater for compressed air by means of saturated steam within the material transfer autoclave before entering the isolator.

Human Element Still a Factor

Fedegari, according to Mauri, is currently wrapping up development of the isolator. One company has already signed on to purchase the isolator and Mauri expects others to look into the system.

He stressed that "nothing is advanced with human intervention," and the company seeks to remove the human element from the aseptic environment except for loading and unloading the isolator.

Yet other industries have seen issues—and even crises—arise from becoming fully reliant on automation. In fact, overreliance on automated systems has been cited as a major factor in the 2009 crash of an Air France flight ***(1).*** In a separate interview with the *PDA Letter*, Mauri acknowledged this could be a potential risk. He said he would encourage a customer to use the Quality by Design approach to build a risk assessment regarding an operator's ability to correctly respond to the equipment.

"It's part of training, part of making all the safety requirements in devices in order to avoid problems due to a lack of control by the operator," he said.

While the isolator system is currently configured just for small-scale production, Mauri does see the potential for use in larger-scale manufacturing, particularly if manufacturers move to using smaller, parallel systems.

"We have to take an example from semiconductor manufacturing where they have a huge manufacturing output by adding in parallel, smaller clusters. So, even if one of these clusters is running out of operation there are another 50 working giving out all the outputs. While in pharmaceutical manufacturing, with big-scale manufacturing we have a line, and if the line is jammed and it stops for two or three hours, you are losing the production of two or three hours," he explained. "We have to learn from other businesses how to manage the efficiency of the pharmaceutical industry."

Reference

1. Langewiesche, W. October 2014. The Human Factor. *Vanity Fair*. www.vanityfair.com/news/business/2014/10/air-france-flight-447-crash

About the Expert

Sergio Mauri is a chemical engineer involved in contamination control technologies of viable and nonviable particles in cleanrooms and clean air devices since the early '80s. At present, he is in charge of the Integrated Projects Business Unit at Fedegari Group.

Regulators, USP Looking Increasingly at Visual Inspection

John Shabushnig, PhD, Insight Pharma Consulting, and Markus Lankers, PhD, rap.ID GmbH

For injectable products, visual inspection continues to be an important element of the manufacturing process and quality assurance. Product inspection provides necessary information for lot release, and, coupled with defect identification, contributes to a strategy of continuous process improvement. Not only that but in the past five years, regulatory citations in this area have risen; there were 55 recalls in the United States in 2014 due to foreign particles, making it the leading reason for recalls last year.

In addition to interest from the U.S. FDA, the United States Pharmacopeia (USP) has recently published several new or revised chapters that impact visual inspection and particles in injectable products. USP <790> Visible Particulates in Injections and USP <1790> Visual Inspection of Injections are especially relevant to this field. Protein aggregation in biopharmaceutical products, with its many facets, has also contributed to increased interest in particulate matter control, even if these inherent particles are product-related and not the result of a lack of manufacturing process control.

Since 2000, PDA has organized the Visual Inspection Forum to discuss new technical and regulatory developments in this field. This annual meeting alternates between the United States and Europe; this year's meeting will be held in October in Bethesda, Md. The meeting will provide a forum to present and discuss new developments in the field of visual inspection, including a basic understanding of the sampling and inspection process, special aspects of biotech products, practical aspects of manual and automated methods and the regulatory and compendial requirements that govern them. Special attention will be given to validation case studies for visual inspection market.

This is an excellent opportunity to learn more about visual inspection and to discuss inspection challenges with the experts. As in past years, the meeting will feature an exhibition where attendees can see the latest in commercial inspection hardware and discuss production needs with key suppliers of inspection systems and services. For more information about the meeting, visit www.pda.org/visual2015. Information about the PDA Education course following the event can be found at www.pda.org/visualcourse.

Examining the Current State of Monoclonals

Martijn van der Plas, Dutch Medicines Evaluation Board, and Michael DeFelippis, Eli Lilly

Three decades after the licensure of the first monoclonal antibody, interest remains strong in this product class. The top three blockbuster pharmaceuticals of 2013 were monoclonal antibodies. An estimated 300 compounds are currently in various stages of clinical development for treatment of cancers, inflammatory and autoimmune diseases and other disorders. The intense focus on monoclonal antibodies has, in turn, driven significant developments in the CMC aspects associated with commercial production. Scientific advances in molecular biology have enabled production of fully human monoclonal antibodies. The antibody structure also now serves as a framework to create related molecular entities, such as fragments, Fc-fusions, bispecifics and antibody drug conjugates. Improvements in expression systems and cell culture have boosted titers, and efficiency gains have been realized in manufacturing by adopting platform processes for upstream and downstream operations. Many manufacturers of monoclonal antibody products were early adopters of QbD-enabled control strategies.

Manufacturers of therapeutic monoclonal antibodies continue to invest in process development to accommodate a broader range of product types. Economic factors are strongly fueling efforts to further increase cell culture productivity, optimize operational efficiency and reduce overall manufacturing expenses to reliably produce larger quantities of high quality products at lower cost. Process development clearly remains an area of focus for manufacturers. For this reason, the planning committee of PDA's *8th Workshop on Monoclonal Antibodies* has selected this topic as the theme of this year's workshop. The objective of the workshop is to examine current methods for process development of monoclonal antibodies and explore technologies that will influence new CMC approaches.

The workshop program will consist of sessions covering both upstream and downstream process development, control strategy design, antibody related products and technology innovations. An entire session will be devoted to regulatory considerations with presentations by regulators involved in dossier review and inspection.

For more information, please visit https://europe.pda.org/monoclonals2015.

2015 PDA Upcoming Events

SAVE THE DATE for PDA's 2015 Events

MAY EVENTS

18-19
2015 PDA Pharmaceutical Packaging Conference
Baltimore, MD
pda.org/packaging2015

18-22
2015 Aseptic Processing Training Program – Session 3, Week 1
(Week 2: June 15–19)
Bethesda, MD
pda.org/2015aseptic3

19
PDA Metro Chapter Day Symposium
Somerset, NJ
pda.org/metrochaptersymposium

20-21
2015 PDA Drug Delivery Combination Products Workshop
Baltimore, MD
pda.org/drugdelivery2015

20-21
2015 PDA Pharmaceutical Packaging Course Series
Baltimore, MD
pda.org/packagingcourses

21
PDA Puerto Rico Chapter Spring Educational Event
Guayama, PR
pda.org/prchapterevent

22
Technical Development of Prefilled Syringes, Autoinjectors and Injection Pens
Baltimore, MD
pda.org/techdevelop

JUNE EVENTS

1-3
Management of Aseptic Processing
Bethesda, MD
pda.org/apmanagement

2-3
Advanced Therapy Medicinal Products
Amsterdam, The Netherlands
europe.pda.org/ATMPs2015

4
Process Simulation Testing for Aseptically Filled Products
Bethesda, MD
pda.org/simulation

9-10
2015 PDA Aseptic Processing – Sterilization Conference
San Diego, CA
pda.org/aseptic2015

9-10
GSA Schedule Contract GS-02F-113BA
Fundamentals of Cleaning and Disinfectant Programs for Aseptic Manufacturing Facilities
Bethesda, MD
pda.org/cleaning

9-11
2015 Virus & TSE Safety Forum
Lisboa, Portugal
europe.pda.org/Virus2015

For an updated PDA calendar of events, please visit:

pda.org/calendar

11-12
2015 PDA Aseptic Processing – Sterilization Course Series
San Diego, CA
pda.org/sterilizationcourses

23-24
Quality & Regulations
Brussel, Belgium
europe.pda.org/QuaReg2015

23-24
2015 PDA Single Use Systems Workshop
Bethesda, MD
pda.org/sus2015

25-26
2015 PDA Single Use Systems Workshop Course Series
Bethesda, MD
pda.org/SUSCourseSeries

25-26
Risk-based Prevention of Drug Shortages
Brussels, Belgium
europe.pda.org/DrugShortage2015

JULY

7
Application of Phase-Appropriate GMP to the Development of Protein Bulk Drug Substances
Bethesda, MD
pda.org/bulkdrug

8
A Former Investigator's Perspective on Conducting Effective Deviation Investigations, Root Cause Investigations, Corrective and Preventive Action (CAPA)
Bethesda, MD
pda.org/capa

21-23
Moist Heat Sterilization Week
Bethesda, MD
pda.org/moistheat

27-29
Risk-based Qualification of Sterile Drug Product Manufacturing Systems
Bethesda, MD
pda.org/risk

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Photo Source: Aseptic Vial Filling at Albany Molecular Research Inc.

Ebola Crisis Offers Lessons Learned for Industry, Regulators

Edward Balkovic, PhD, Genzyme

Throughout 2014, the world watched in anticipation as global healthcare workers sought to contain an outbreak of the Ebola virus throughout parts of West Africa. As of today, tens of thousands have died throughout the region, and even Western nations have not been spared, facing limited outbreaks in both the United States and Europe.

The industry responded to this crisis promptly, along with relevant regulatory authorities. GlaxoSmithKline, Johnson & Johnson, and Novavax are just some of the companies in the early phases of testing potential vaccines and treatments. The U.S. FDA, the National Institutes of Health, CDC, WHO, and other agencies are also working with industry to ensure efficient development of effective treatments for this gruesome disease.

Development of an Ebola vaccine and other treatments is a superb example of "true science," featuring regulatory collaboration to harmonize and accelerate production of a beneficial medicinal product. Manufacturers and regulators can use this sobering situation as an example of how to effectively seek solutions to the challenges of everyday production, particularly in the area of pharmaceutical microbiology.

Learn more about how the search for an Ebola vaccine is shaping new pathways for regulatory development at this year's *10TH Annual Global Conference on Pharmaceutical Microbiology* in Bethesda, Md. with a keynote speech from **Luciana Borio,** MD, Assistant Commissioner, Counterterrorism Policy and Acting Deputy Chief Scientist, Office of Counterterrorism and Emerging Threats, Office of Compliance, FDA on the first day. Borio will discuss the science behind the recent Ebola virus epidemic in West Africa and the global regulatory efforts to fight it.

The second day will begin with a presentation looking at untapped ecosystems for the discovery of microbes with different metabolite/antimicrobial profiles from **Alan Dobson,** PhD, Director, Environmental Research Institute and Professor, Microbiology, University College Cork, National University of Ireland. Other concurrent sessions will provide the latest information on contamination control, rapid micro methods, risk assessment case studies, biofilms, endotoxin detection, bioburden testing, global harmonization, and other innovative technologies.

For more information, visit www.pda.org/microbiology2015. To learn about PDA Education courses following the conference, visit www.pda.org/microcourses.

Tackling Sterility Concerns of Compounding

Austin Caudle, NSF Health Sciences

Prior to 2012, most Americans had never heard of compounding pharmacies, however, in the wake of the New England Compounding Center (NECC) tragedy, this changed overnight. Following this event, calls for greater control over compounding pharmacies spurred legislative activity in the U.S. Congress. State boards of pharmacy and the U.S. FDA increased regulatory scrutiny of these operations, resulting in closures of additional compounding pharmacies in multiple states. In addition, PDA has also been involved with compounding pharmacy regulation, notably with its review of the FDA draft guidance, *Current Good Manufacturing Practice – Interim Guidance for Human Drug Compounding Outsourcing Facilities under Section 503B of the FD&C Act.*

Historically, the role of compounding pharmacies has been to make drugs prescribed by doctors for specific patients with needs that cannot be met by commercially available drugs. But in the last several years, compounding pharmacies have stepped up their production in an effort to ease drug shortages and are now being utilized on a larger scale as drug manufacturing problems result in shortages of critical drugs. Given the sterility concerns at some compounding pharmacies, increased attention has been given to sterile manufacturing as it places extreme emphasis on equipment, personnel, quality systems, procedures and practices to obtain the largest sterility assurance possible, meaning compliance with USP <797> Pharmaceutical Compounding Sterile Preparations.

This year's *PDA Aseptic Processing – Sterilization Conference* will again look at recent updates and insight on compounding regulations. Given the high risk to patients and increased awareness by the public this topic continues to be an important part of the this conference. This time, two of the leading experts in the field, **Rich Kruzynski** President, PharMedium Services, and **Ken Latta,** President, Health System Consulting Group and Gates Healthcare, will delve further into this important topic.

For more information about this conference, please visit www.pda.org/aseptic2015. For information about PDA Education courses following the conference, go to www.pda.org/sterilizationcourses.

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Key Considerations for Successful Technology Transfers

Jose Caraballo, Bayer HealthCare

The pharmaceutical industry

is constantly engaged in transferring processes between organizations or locations; these transfers are critical to get product to market. The number of transfers is expected to increase as countries act on the need to manufacture drug products locally ***(1).*** This activity is part of the normal lifecycle of a drug product, and it can range from very successful transfers to problematic ones, based on a myriad of factors. Among them are process and product robustness, the readiness of organizations to engage in transfer activities, availability of experts, and the timely execution of all the work needed to complete a transfer.

The ICH Q10 ***(2)*** guidance states that a transfer of technology is an integral part of its product lifecycle model and identifies it as an activity that must be executed under GMP given its relevance to commercial manufacturing and impact on product quality. This emphasis is justified due to the complexities surrounding transfers of technology.

Article at a Glance

- Technology transfer refers to the process of moving knowledge between organizations
- Cultural boundaries can present challenges
- Analytical methods must be accounted for early on in the process

Overall, technology transfer can be characterized as a phase in the pharmaceutical product lifecycle and requires considerations for specific areas to focus on when planning and executing transfers of technology between organizations.

Technology Transfer in a Nutshell

There are many definitions that describe the technology transfer process for pharmaceuticals. Approaching this process as only transferring information (documents, lists of process parameters, etc.), however, is not a technology transfer. Per ICH Q10 ***(2),*** the objective of technology transfer is:

> *"…to transfer product and process knowledge between development and manufacturing, and within or between manufacturing sites to achieve product realisation. This knowledge forms the basis for the manufacturing process, control strategy, process validation approach and ongoing continual improvement."*

In summary, the goal is to transfer knowledge between organizations which will serve as the basis for a sustainable and controlled manufacturing of pharmaceutical products.

The process of transferring knowledge has recently received attention through the issuance of guidance documents that describe the expectations, approaches, and steps for executing transfers ***(2-5).*** These documents offer valuable guidance on how to plan, manage and execute a transfer for a pharmaceutical product.

A typical approach for a technology transfer can be summarized as follows:

Pretransfer – The organizations involved confirm that the process or product is well characterized, ready to be transferred, and a decision is made to initiate transfer activities. A transfer team is created, consisting of members from the sending organization (Sending Unit) and the receiving organization (Receiving Unit). The organizations involved then initiate information sharing between the Sending and Receiving Units. Project management tools are launched to support the transfer activities.

Knowledge Transfer Package — Information regarding materials, methods and procedures, process parameters, equipment requirements, training materials, systems, etc. is collected and prepared to support the knowledge transfer process.

Technology Transfer Planning — Risk assessments are conducted to analyze and manage the potential impact of limited information or differences between manufacturing sites (e.g., equipment, process, facility fit, systems, etc.). A transfer plan is created to identify key milestones and provide guidance regarding transfer scope, resource requirements, timelines and level of effort.

Transfer Execution and Verification — The transfer plan is executed. Process verification activities (e.g., small and full-scale verification runs, process qualification and conformance runs, etc.) are conducted to demonstrate successful information and process transfer. Data is collected to close transfer activities and to support technical reports, regulatory submissions and approvals.

Posttransfer Verification — Lessons learned are shared within the organizations. Continued process verification is implemented to demonstrate ongoing process control.

In many ways, each transfer is unique and requires integrated organizational structures, engaged team members, careful planning, effective communication and skillful execution to ensure the desired results.

Considerations for Tech Transfer Success

Some transfers are complex to execute due to unexpected constraints or challenges. The following areas are usually sources of issues if they are not anticipated and added to the overall transfer plan.

Changes to how a process is controlled should be assessed for impact to process performance and product quality

Organizational barriers, geography and culture: Transferring knowledge across cultural boundaries to other countries can be a challenging exercise if not planned carefully. To start, countries may have different safety and engineering standards that create the need for design changes and other adaptations as part of the transfer of processes and technical systems. These adaptations must be assessed for risks and documented as part of the transfer process for future reference.

The Receiving and Sending Units will most likely have different organizational structures. Finding the right role and function to engage in transfer activities will be critical to ensure knowledge is transferred to the right person. The Receiving Unit must have the human capital and infrastructure to receive the knowledge and technology. For example, in some projects, organizations use contractors to conduct the transfer of technology. This approach could weaken the completion of a robust knowledge transfer if these contracted personnel leave the Receiving Unit at the end of the project. Securing the transferred knowledge in the Receiving Unit should be one objective of the overall transfer plan.

Language and cultural behaviors will also play a significant role as transfer teams share design documents, qualification protocols, and reports or engage in active communication via online meetings or e-mails. Defining the documentation structure and language before initiating any transfer of information will save countless hours during execution and documentation closure.

The role of electronic systems: Electronic systems are pervasive in today's pharmaceutical industry. In addition

to distributed control systems, process control modules, data acquisition systems and manufacturing execution systems, there is an abundance of critical data elsewhere that may be relevant for a successful technology transfer. For example, electronic systems supporting supplier quality management, inventory systems, and material release processes most certainly contain important data and methods to be documented and transferred to the Receiving Unit. This transfer will need special consideration given that there are hardware and software elements that need to be defined and managed.

Of special importance to some biotech products is the process control software managing how process parameters are executed and controlled. Changes to how a process is controlled should be assessed for impact to process performance and product quality.

Scale-up, adaptations and small-scale verifications: In many cases, processes are scaled up or scaled down between transfers. Early in the planning stage, a detailed assessment of scale differences must be completed to evaluate these as part of the transfer. Ideally, process and equipment changes are avoided to increase the likelihood of a successful transfer. This, however, is usually not possible. Process adaptations are almost always needed; for example, to accommodate for different lengths of transfer lines (hold times) and different equipment features (control systems, gaskets, alarms, etc.).

Valid small-scale process verification models can be extremely useful for verifying some process aspects early, before initiating large-scale process verification or engineering runs. For complex processes, full scale verification should be completed prior to initiating process qualification or conformance runs. This will provide an opportunity to evaluate the effectiveness of the process transferred at a full scale.

Analytical methods: Analytical methods are needed early in technology transfer processes. Raw materials need to be purchased, tested and released to support process verification runs and process qualifications. There may be a need to conduct special technical studies to obtain data related to process adaptations. These studies will require analytical testing capabilities. Different quality control labs may need additional time to run side-by-side comparisons to detect and then correct lab-to-lab biases.

For example, a laboratory bias was detected during a method transfer for a biologics drug substance. Data from the Sending Unit laboratory was trended against data from the Receiving Unit laboratory, and a significant difference was observed between results for some methods. The investigation concluded that the handling of samples and sampling preparations between laboratory scientists was not equivalent. Additional side-by-side testing and training was conducted with technicians from both sites to define further requirements and share techniques for proper execution. This extra effort eliminated the biases between the labs in time to support the rest of the technology transfer efforts.

Change management: The adoption of a system that effectively tracks, evaluates and manages changes between the Sending Unit and the Receiving Unit will support future investigations as part of process of technology transfer execution and closure. The structured documentation of changes (planned or not) will help scientists and engineers interpret discrepancies between expected and actual values. A formal system is recommended to track these changes during the transfer process.

Conclusion

Technology transfer is a mature process in the pharmaceutical industry; however, it still provides many challenges for transfer teams. Each organization should adopt a policy or procedure to manage transfers of technology in a structured and consistent way. Some areas of the transfer process merit additional focus to ensure timely and successful transfers. Key recommendations include:

- Acknowledging cultural and geographical challenges
- Having a full understanding of all relevant data in electronic systems
- Verifying process transfer effectiveness via small-scale models and engineering runs
- Ensuring analytical testing capabilities early in the transfer process
- Tracking all changes to support investigations and future process optimizations

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3. ISPE. *ISPE Good Practice Guide: Technology Transfer.* 2nd Ed. Tampa: ISPE, 2014.
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About the Author

Jose Caraballo is Director of Global Quality, Biotech Product Supply at Bayer HealthCare, where he is responsible for providing strategic planning and support for new and existing operations for biotech products. He serves as a quality assurance expert on strategic project teams related to the expansion of biotech manufacturing capabilities.

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Portable Pods Part of New Strategy for Pfizer

Rebecca Stauffer, PDA

On March 17, the PDA Letter's ***Walter Morris*** *and* ***Rebecca Stauffer*** *interviewed* ***Michael O'Brien,*** *Vice President, Technology and Innovation, Worldwide R&D – PTx Pharmaceutical Sciences, Pfizer, following his presentation, "Portable, Continuous, Miniature, & Modular (PCM&M) Development and Manufacturing: The Foundation for a Transformational Development, Manufacturing & Distribution Model" at the* 2015 PDA Annual Meeting. *His talk provided an overview of Pfizer's new Portable, Continuous, Miniature, & Modular, or PCM&M, approach to manufacturing involving movable pods for manufacturing of oral solid dose products at the company's Groton, Conn. site. The April* PDA Letter *Podcast includes more from this interview.*

PDA Letter: Can you tell us more about what spurred the PCM&M program?

O'Brien: There were a combination of factors and events that actually led to the formal initiation of the program. Historically, I had even been involved in the development of some API continu¬ous processing technologies, so I had that general strong interest to begin with. Prior to my arrival at Pfizer, scientists from both Commercial and WRD Pharmaceutical Sciences had designed and fabricated a unique vertical powder mixing system that offered numerous advantages over twin screw technology which is the current industry standard. The vertical mixer was designed to operate in CSTR mode (continuously stirred tank reactor) which overcomes the conflict between high sheer rate and residence time that we see in the twin screw systems.

It was from that that starting point that one of our senior scientists decided that well; we can build a very interesting but simple CDC, or continuous direct compaction system, with feeders aligned over the mixer that drops powders directly onto a tablet press. This prototypical unit was built in their laboratory, duct tape and all. After seeing that unit operate, the vision was pretty clear that this type small system could actually be used in both a development and commercial settings since it could crank out a variable quantity of uncoated tablets with rapid start-up and shut down times. This would provide the ability to produce drug product on the basis of demand rather than forecast. Later I was introduced to G-CON, a manufacturer of autonomous, environmentally isolated cleanrooms or PODs and the PCM&M concept was born.

PDA Letter: There's lots of great technology out there. And the pharmaceutical industry is pretty notorious for not using practically any of it. What was your business case for this new model of manufacturing?

O'Brien: There were several business drivers. First and foremost, there has been a portfolio shift from high volume, blockbuster type products to one that is more dominated by lower volume drugs. In addition as our markets, that were traditionally European/U.S.-centric, have increasingly expanded to emerg¬ing markets around the globe, we are often required manufacture and distribute from inside individual countries and regions. And since we can't build plants in every country or region of the world, prefabricated, relatively low cost minifactories that could rapidly be deployed in grey space facilities seemed a very attractive concept. Finally, the industry's network of development and manufacturing facilities is distributed across the globe and utilizes equipment of every size, configuration and make.

Drug product production processes that initiate in development labs will later need to be run at multiple sites, and more importantly, in much different equipment trains. To make this work, sophisticated technical transfer paradigms have evolved that use a combination of science of scale tools, significant technical resources and an experimentation heavy model. Moving to the same equipment for development, clinical manufacturing and commercial manufacturing paradigm would simplify the process, lower costs and maximize robustness.

PDA Letter: So, is the next stage validation?

O'Brien: There'll be several stages that will ensue. First, assembly of the entire unit will occur, which is expected to take three to four days. Once this is completed and the various utility components are hooked up we will go through site acceptance testing or SAT. In essence, the engineers will be running nonactive powders through system at wide ranging parameters. Whatever it takes to actually go through a process that enables you to say 'okay, we can sign off on this' will be done. From that point, we would need to go through a validation and GMP readiness process while investigating a number of different potential, legacy and eventually NCE products on the PCMM system.

PDA Letter: Do you envision multiple products running through this system?

O'Brien: That's the goal. The objective at the outset was to design a multiproduct facility. Obviously, to have that you have to be able to rapidly changeover the line which we are still working through. You want to be able to change the whole system over in prob¬ably close to a day, or better yet a half day if possible.

PDA Letter: Do you plan to move these pods? ➤

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O'Brien: Initially, the prototype, that will be assembled in a Groton warehouse at an R&D site, would stay in place for quite some time. As we move forward we anticipate having PCM&M systems like this at our commercial sites and potentially at some of our regional sites. Whether the next unit is purchased and installed at another site or we move the Groton unit to the site has not been determined.

PDA Letter: This is not unlike what we've heard from other companies using these modular systems. And the goal is to use one location as sort of the innovator and then eventually spread the units across the enterprise.

O'Brien: That's right. And so, in some ways, I would comment that it's pretty amazing, the buy-up of the concept that we see from many parts of the Pfizer organization as well as other large and small Pharma companies, especially given that assembly has yet to occur.

PDA Letter: Why do you think there was a significant level of buy-in internally?

O'Brien: It's a combination of two or three factors…First we have confidence in the individual components of the PCM&M unit…..GEA's ConsiGma™ high-shear wet granulation technology and our vertical mixer have been previously tested in the field. The ConsiGma™ has been sold to a number of other pharma companies and we had previously built several CMTs, which is the terminology that we use for the vertical mixer, including a mixer that was operational at one of our commercial sites. Aside from the confidence factor, the technology has the promise to address a number of different issues, including high tech transfer costs, emerging market access, high inventory costs and most importantly better access of our medicines to the patients that need them. Then there was the matter of integrating the processing equipment into a POD. That was a tougher sell at the outset, but people warmed up to that as they better understood the consequential benefits.

PDA Letter: You stated that you accomplished this project by working 'step-in-step' with regulatory agencies. Can you tell us which ones you worked with?

O'Brien: We haven't necessarily worked in-step with them in an advisory capacity as we went through detailed design and fabrication of the equipment. What we have done, from the beginning, is try to articulate the concept to various regulatory agencies through presentations as association meetings and the like….most notably the [U.S.] FDA and EMA. Our own CMC regulatory organization has been involved since the beginning and has introduced PCM&M through a variety of channels and at mutually attended meeting venues. It is our intent to bring the FDA down to Groton for a workshop sometime after the unit is fully operational, perhaps in early to late June of this year.

PDA Letter: You mentioned that you eventually want to use this new system not just for the oral solid doses but also for fill-finish product. What are the technical challenges you foresee?

O'Brien: The concept itself—which is to utilize the same equipment for development *and* for clinical and commercial manufacturing, to minimize the costs and complexity of technical transfer, to be able to rapidly deploy what is in essence a factory module in less than a year etc.—these and other elements that I spoke of in today's presentation—you can apply those concepts to API, whether they be large molecule or small molecule and theoretically to any dosage form. You certainly can apply those concepts to sterile fill-finish for example. There's no reason in the world why we can't [take] a fill-finish operation and put it into a POD. You're going to have to weigh the pros and cons. you don't want to force fit a technology if it does not make good technical and business sense.

PDA Letter: What you're doing with the pods is almost identical, so is that a tech transfer benefit?

O'Brien: So, a company for example would have an oral solid dose unit in their R&D facility, and the reason they have that is because they can do the…post-Phase I development in that unit. And they can go through the Phase II a/b clinical batches and all of that. Then as you get to Phase III supplies and the actual commercial process, you could either transfer the process over to identical unit that's sitting in a commercial site already. So, it's just an apple-to-apple transfer, same exact equipment. In theory, if you wanted to, you could say 'we're going to bring a new unit into the R&D facility, and we're going to take this unit and ship it over to wherever it is we might want to manufacture.'

I think it'll work itself out differently in different situations and cases.

About the Expert

Michael O'Brien is the head of the PTx Pharmaceutical Sciences Technology & Innovation Group. His group oversees a range of functions, including informatics, technology strategy/technology development, and the leveraging of internal innovation and science to develop external networks focused on the delivery of horizon 2/3 technology advances.

Quality's Role as Financial Officer – Can you speak $, €, £, ¥, CHF?

Jennifer Magnani, Sanofi Pasteur, and Anders Vinther, PhD, Sanofi Pasteur

Why is it that Finance and Quality are seen as immiscible as oil and water? Rarely do you experience a financial discussion in a Quality meeting setting. Likewise, rarely do you see a cGMP compliance or quality discussion when the organization gets together to discuss budget. Having financial discussions with Quality professionals is generally linked to production volumes and the cost of the Quality organization as overhead. We all have the same goal of providing quality products to patients and wanting our companies to be successful, so why don't we change the focus of the dialogue to also include how Quality can deliver financial benefits? At present, the traditional stereotypes of Finance and Quality professionals prevents us from improving financial results for the company. It's now time to shift the dialog from a cost-based conversation to a value-based conversation. It's time for a change!

The Language of Finance

Have you ever heard a conversation similar to the following one between the Head of Quality and the CEO?

Barbara, Head of Quality: *"We are not compliant with 21 CFR 211.46 and need to put a couple of CAPAs in place to reduce our deviations in this area. I need to hire five more people in my area."*

Paul, CEO: *"I am sorry, Barbara, but you know we have a fixed budget, and you really just need to manage this issue within your budget".*

Now, imagine the conversation with Barbara speaking the language of Finance.

Barbara: *"We are losing 5% of our batches due to environmental monitoring excursions in our facilities, which are costing our company $28 million per year. Additionally, this is a compliance risk that we must address or run the risk of serious enforcement action. I think we should invest in hiring five more people, do a few design changes at a total cost of $3 million in CAPEX and an annual cost of $750,000. This would essentially eliminate the batch failures and the annual write-offs of $28 million."*

How do you think Paul, the CEO would reply? It's obvious, isn't it? So how do we move away from speaking different languages?

When we speak different languages there is a possibility of a message being misinterpreted, or as they say, "lost in translation," which could then lead to a failure or error.

Well, we believe it all starts with Quality learning to speak the "language of finance." But how do you do that?

Bringing Financial Visibility into Quality Operations

It sounds trivial but it all starts with understanding where the money goes, which can be thought of as a cost-of-quality model that provides the organization with the data needed to analyze the cost of "poor quality."

We suggest something as simple as the following four categories: preventive, appraisal, internal and external failure costs.

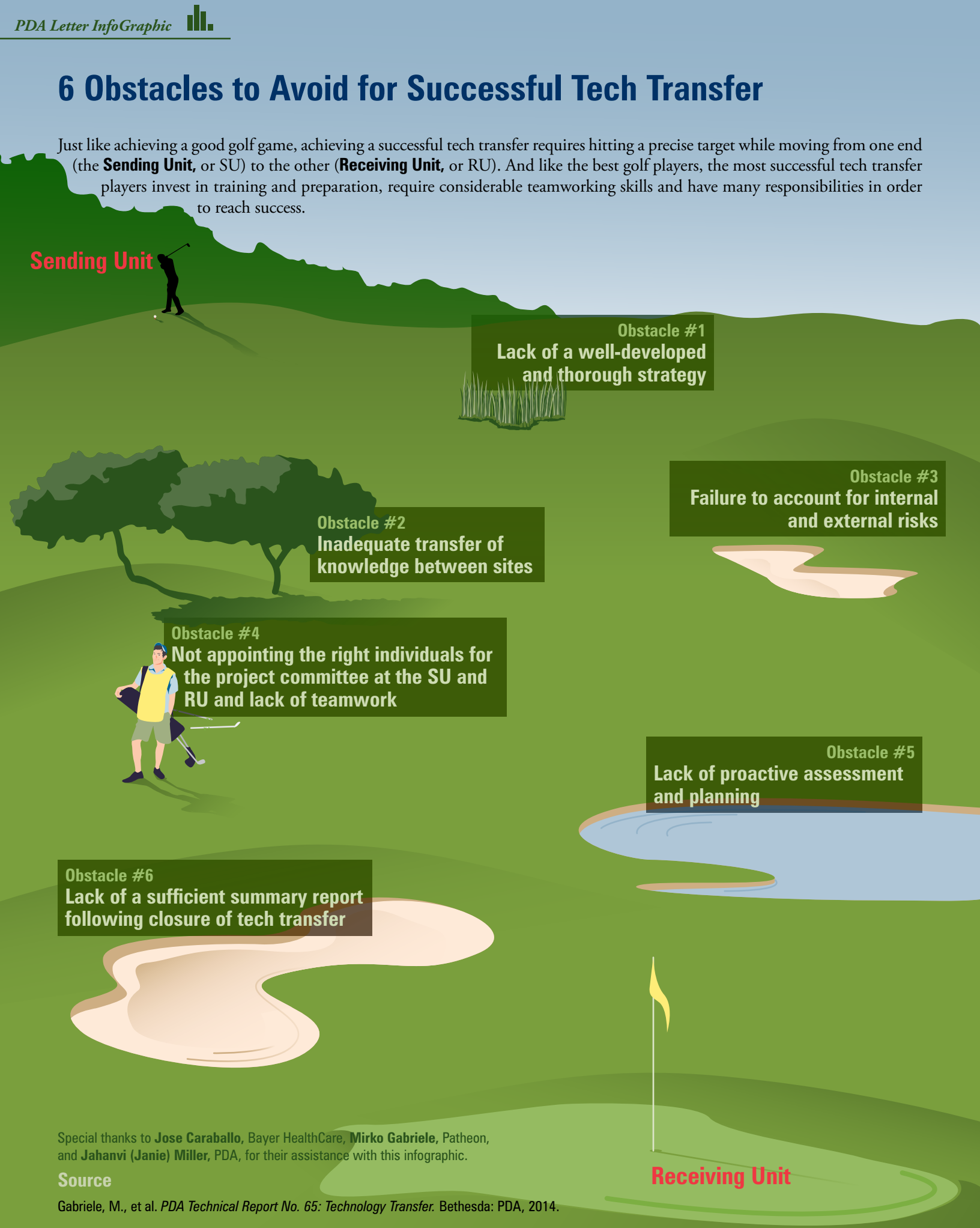
Don't spend a lot of time making it 100% accurate or comprehensive—it should be directional and an assessment of where to dig deeper. What expenses, costs and losses should be explored? It should help you identify the cost of quality activities like investigations, QC testing for batch release, validation, etc.

Armed with this data, you will be able to provide your organization a different perspective and prioritize quality, not only in terms of cGMP compliance gaps, but also in terms of financial opportunities. This is accomplished by educating the Quality organization and other relevant departments on these quality costs. Then, by incorporating this information into daily operational procedures, processes and documents, the organization

Continued on page 43

6 Obstacles to Avoid for Successful Tech Transfer

Just like achieving a good golf game, achieving a successful tech transfer requires hitting a precise target while moving from one end (the **Sending Unit,** or SU) to the other (**Receiving Unit,** or RU). And like the best golf players, the most successful tech transfer players invest in training and preparation, require considerable teamworking skills and have many responsibilities in order to reach success.



Special thanks to **Jose Caraballo,** Bayer HealthCare, **Mirko Gabriele,** Patheon, and **Jahanvi (Janie) Miller,** PDA, for their assistance with this infographic.

Source

Gabriele, M., et al. *PDA Technical Report No. 65: Technology Transfer.* Bethesda: PDA, 2014.

2015 Glass Quality, Visual Inspection and Foreign Material Identification Week

September 14-18, 2015 | Bethesda, MD
PDA Training and Research Institute

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Three courses are offered during the *2015 Glass Quality, Visual Inspection and Foreign Material Identification Week* to help you develop a comprehensive program designed to identify and classify nonconformities, visually inspect your final product and to analyze foreign material isolated during your inspections!

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Provides valuable knowledge related to the quality of glass containers, the development of standardized quality criteria and sampling plans for use in the quality decision-making process.

An Introduction to Visual Inspection (September 15-16) THIS COURSE FILLS UP FAST! SIGN UP NOW!
Covers the fundamentals of visual inspection and their application to injectable products. This course is a combination of lecture/discussion and hands-on laboratory exercises used to develop and practice practical inspection skills.

NEW COURSE **Foreign Particulate Examination, Isolation and Analysis** (September 17-18)
Demonstrates the advantages and disadvantages of polarized light microscopy, infrared spectroscopy and scanning electron microscopy for particulate analysis.

Discounts apply when registering for multiple courses!

To register and for more information, visit www.pda.org/glassqual

Denotes Laboratory Course

snapshot

RAQAB Represents the Globe at Annual Meeting

Denyse Baker, PDA

RAQAB members joined the early bird March 15 in Las Vegas with a 9 a.m. meeting the Sunday prior to the *2015 PDA Annual Meeting*. Members brought a breadth of knowledge with regional liaisons representing India, Russia, Japan, Europe, North America and Israel. The group also welcomed two new members: **David Perkins** and **Steven Lynn**.

Members of the RAQAB posed for a group photo in the Las Vegas sun.

PDA President **Richard Johnson** attended the meeting and led off with a discussion on improving PDA project prioritization and how the Advisory Boards can have more input into the strategic planning of the PDA Board of Directors.

Elizabeth Meyers presented an overview of new regulations in Russia intended to strengthen the local manufacturing base but which also create challenges for foreign manufacturers, including new requirements for GMP inspections and issuance of GMP certificates by Russian authorities. The requirements are set to take effect July 1, even though it remains unclear which body will be responsible for those inspections–RZN, MinProm-Torg or a third party.

RAQAB reemphasized its commitment to build stronger working relationships with WHO and is exploring how best to engage with the USP. PDA has sponsored several commenting teams on WHO draft guidances already in 2015 including Good Distribution Practices and Good Pharmacopeial Practices and is monitoring USP draft publications as well. Data integrity has become a hot topic and RAQAB is sponsoring several initiatives to provide more information to members and regulators about best practices.

In the meantime, RAQAB is always open to ideas and feedback. Contact **Denyse Baker** at baker@pda.org if you have a suggestion.

2015 Regulatory Affairs and Quality Advisory Board (RAQAB) Members

Susan Schniepp, Fellow, Regulatory Compliance Associates (chair)

Jeffrey Broadfoot, Senior Director, Quality Assurance, Emergent BioSolutions (vice-chair)

Ruhi Ahmed, PhD, Senior Director, Regulatory Affairs, Ultragenyx

Claudio Correa Cappai, Supply Chain Quality Manager, Roche

Robert Caunce, Quality Manager, Technology Transfer, Hospira

Veronique Davoust, Senior Manager, Global Quality Strategy, PhD, Pfizer

John Finkbohner, PhD, Senior Regional Policy Director, AstraZeneca-MedImmune

Mirko Gabriele, Technology Transfer Manager, Patheon

Karen Ginsbury, President and CEO, PCI Consulting

Jeffrey Hartman, Senior Consultant, ConcodiaValSource (Science Advisory Board liaison)

Hongyang Li, Vice President, Quality, Novartis

Steven Lynn, Global Head of Compliance and Auditing, Novartis

Edwin Rivera-Martinez, Vice President, U.S. Quality Liaison, Global Quality

Elizabeth Meyers, Senior Manager, QA, Amgen

Shin-ichiro Mohri, Director, Sakai Plant Kyowa Hakko Kirin

David Perkins, Director, Quality and Compliance, AbbVie

Emma Ramnarine, Senior Director, Head, Global Biologics QC, Genentech

Stephan Rönninger, PhD, Head, External Affairs Europe, International Quality, Amgen (BoD Liaison)

Junko Sasaki, Quality Principal, Investigational Drug Quality, Dainippon Sumitomo Pharma

Anil Sawant, PhD, Vice President, Enterprise Regulatory Compliance, Johnson & Johnson

Siegfried Schmitt, PhD, Principal Consultant, PAREXEL

Janeen Skutnik-Wilkinson, Staff Associate, Compliance and Standards, Biogen Idec

Jacqueline Veivia-Panter, Consultant (Interest Group Liaison)

Wendy Zwolenski Lambert, Global Validation Leader, Novartis (Biotechnology Advisory Board liaison)

Denyse Baker, Senior Advisor, Scientific and Regulatory Affairs, PDA

Rich Levy, PhD, Senior Vice President, Scientific and Regulatory Affairs, PDA

Georg Rössling, PhD, Sr. Vice President, PDA Europe

Morgan Holland, Coordinator, Scientific and Regulatory Affairs, PDA

FDA, Industry Entering Changing Times: Are You Prepared?

Steven Mendivil, Amgen, and Alicia Mozzachio, U.S. FDA

Change is in the regulatory air! The U.S. FDA's focus on pharmaceutical quality systems, risk management and Quality by Design has fundamentally changed the way quality is assessed today as compared to ten years ago.

The Agency began its official move to a more quality-focused and risk-based organization with the launch of the Office of Pharmaceutical Quality in January. Further restructuring at the Agency includes moving to commodity-based inspections. From now on, inspectors will be assigned to a product-sector, like pharma manufacturing, instead of generalizing over all FDA-regulated product types.

Change is also impacting other regulatory areas, including supply chain security, biosimilars, quality metrics, and GMPs for APIs (ICH Q7 Q&A) and more.

It is difficult staying abreast of all these changes, particularly, as industry faces its own changing paradigms. Personalized medicines, combination products, small-scale manufacturing, greater use of contract manufacturing organizations and new technologies s are driving changes in the regulatory compliance landscape.

The convergence of a changing industry along with the evolving regulatory framework makes knowing whether you are meeting the regulatory requirements much more difficult. So how can you help your company keep track of all these changes? And how can those in industry learn from regulators how to meet regulatory requirements?

Very simply. Join your colleagues at the *2015 PDA/FDA Joint Regulatory Conference* and take the unique opportunity to interact with FDA representatives and industry experts face-to-face to discover firsthand how to comply with regulatory global strategies and industry strategic initiatives from leaders and advocates who are shaping the global regulatory compliance landscape and take home best practices for compliance. Each year, FDA speakers provide updates on the current state of efforts impacting the development of global regulatory strategies, while industry professionals from some of today's leading pharmaceutical companies present case studies on how they employ global strategies in their daily processes.

To learn more and to register, visit www.pda.org/pdafda2015. For information about PDA Education courses following the conference, go to www.pda.org/2015-regulatory-course-series.

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Specific Example Needed for Advanced Therapies Guidance

For the comments grid, visit www.pda.org/regulatorycomments

February 23, 2015

Division of Docket Management (HFA-305)

Food and Drug Administration

5630 Fishers Lane, Room 1061

Rockville, MD 20852

Reference: Minimal Manipulation of Human Cells, Tissues, and Cellular and Tissue-Based Products; Draft Guidance for Industry and FDA Staff Docket No. FDA-2014-D-1696

Dear Sir/Madam,

The Parenteral Drug Association (PDA) commends FDA for addressing and characterizing the important concepts of minimal manipulation and related terms for HCT/P products. These concepts are difficult and undoubtedly will continue to be challenged as new, innovative tools are introduced to process cellular and tissue-based products. The format of questions followed by discussion in this guidance makes it easy to find information and follow the logic of the applicable regulation. Such guidances, with a very directed and limited scope, are a helpful means to communicate FDA's latest thinking in a timely and efficient manner.

To further clarify FDA intentions and enhance the value of this guidance, PDA recommends a more specific example be provided in section 7. It would be very useful to have at least one real-life example of minimal manipulation for readers to wrap their minds around to clarify the phrase "extraction or separation of cells from structural tissue in which the remaining structural tissue's relevant characteristics relating to reconstruction, repair, or replacement remain unchanged" (from the last paragraph of page 5 in the draft guidance). Examples, such as the one presented in Example 10-1 of a separation procedure that is more than minimal manipulation, clarify the meaning of the text. For instance, would extracting muscle tissue and removing surrounding adipose tissue be considered to satisfy the criteria for minimal manipulations being referred to in this section?

PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological, and device manufacturing and quality. Our comments were prepared by a committee of experts with experience in gene and cell based therapies including members representing our Board of Directors and our Biotechnology Advisory Board and our Regulatory and Quality Advisory Board.

If there are any questions, please do not hesitate to contact me.

Sincerely,
Richard Johnson
President, PDA
cc: Denyse Baker, PDA

PDA Commenting Task Force

Michael VanDerWerf, Organogenesis (Chair)

Karen Ginsbury, PCI Consulting

Karen Walker, Novartis

Allen Burgenson, Lonza

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

Former FDA Commissioner Now at Institute of Medicine

Former U.S. FDA Commissioner **Margaret Hamburg,** MD, is now Foreign Secretary for the Institute of Medicine, an arm of the National Academy of Sciences. She will advise the Institute on international health matters. Her term began April 6 and lasts until June 30, 2019.

OGD Director Stepping Down Temporarily

On March 30**, Kathleen Uhl,** MD, temporarily stepped down from her role as Director of the U.S. FDA's Office of Generic Drugs for an extended medical leave. In her absence, **John Peters,** MD, Acting Director, Office of Bioequivalence, will assume her responsibilities.

Bill Would Require Shorter Time for FDA to Review Products Approved in Europe

A bill was recently introduced in Congress that, if passed, would require the FDA to review drug products approved by EU authorities within 90 days. This bill, the Speeding Access to Already Approved Pharmaceuticals Act, seeks to address the lag between approval of a drug product in Europe and in the United States. Currently, the shortest time between approvals is six months.

USP Elemental Impurities Chapters to Align with ICH Q3D

USP announced that the chapters pertaining to elemental impurities, <232> Elemental Impurities—Limits and <2232> Elemental Contaminants in Dietary Supplements, will be applicable Jan. 1, 2018 in order to align <232> with implementation of ICH Q3D.

United States Seeks to Strengthen Device Postmarket Surveillance

The U.S. FDA released a report with the Brookings Institution in mid-Q1 outlining recommended steps to develop a National Medical Device Postmarket Surveillance System. This report offers a strategy for developing a nationwide system that harnesses data, analysis and stakeholder participation to optimize surveillance in an effort to achieve optimal patient care.

This report has its origins in CDRH's 2012 initiative to strengthen the U.S. surveillance system for devices. This initiative also includes efforts to implement unique device identifiers for devices. The report can be accessed here: tinyurl.com/llczeez.

Europe

EMA Management Board Elects New Vice Chair

The EMA's Management Board has elected **Christa Wirthumer-Hoche** as its Vice-Chair. She replaces **Walter Schwerdtfeger,** and is currently Head of the Austrian Medicines and Medical Devices Agency.

EMA GMP Guide Revisions Account for Cross-Contamination and Toxicological Assessments

Effective March 1, Chapters 3 and 5 of the EMA GMP Guide covering premises and equipment and production respectively have been updated to account for improvements to the guidance on cross-contamination and references to toxicological assessment. These chapters were updated as part of an effort to align with the EMA guideline *Setting Health Based Exposure limits for Use in Risk Identification in the Manufacture of Different Medicinal Products in Shared Facilities.*

European Commission Updates API GDP Guidelines

On March 21, the European Commission announced changes to its *Guidelines on GDP for APIs,* aimed at API importers and distributors. These changes include: requirements for API distributors to implement a quality system featuring a designated person with risk management responsibility at each point in the distribution chain, a traceable supply chain, suitable cold chain conditions, documented and investigated deviations to established procedures, effective CAPAs in place, one-year record retention policies and examinations of all API deliveries for damage.

The new guidelines become effective Sept. 21.

Excipient Guidelines to Become Stricter in 2016

The European Commission announced on March 21, an updated and more detailed version of its *Guidelines on Risk Assessment of Excipients*. Under these new guidelines, manufacturing authorization holders are required to implement risk assessments of their entire supply chains from raw material sources to packaging.

The steps taken for maintaining quality of an excipient must be extensively documented with a track-and-trace system fully in place. A quality control expert is now required to assess the excipients and release batches.

These guidelines become effective March 21, 2016.

Quality's Role as Financial Officer – Can you speak $, €, £, ¥, CHF?
continued from page 35

will have complete picture. This education should go down to the shop floor level so everyone thinks about quality differently.

If employees at all levels have a foundation of quality compliance and understand that delivering safe products is the top priority, the addition of being aware of financial impacts can be a great benefit to the company. Suggestions made by those involved can be the most effective way to make improvements.

Compare Costs of Failure to Quality to Drive Value

Another strategy for disseminating the financial impact of poor quality is to include the cost of failures into deviation and investigations reports, including the number of hours investigations took (in terms of $, €, etc.) and the value of any rejected material (recommend using the market value). Compare these costs to the cost it would have taken to avoid the deviation. You will automatically drive the conversation from cost to value.

We know the costs of failed batches, write-offs, scrap, recalls, etc., but rarely do we speak about it during quality reviews as a means to look for improvement opportunities. Those reviews simply catalogue the number of recalls, investigations, etc., and notes trends. While these reports also help you link the causes to the failure, they fail to provide the financial link.

When decisionmakers link the cause of the failure with associated financial losses, allocating money to fix the issue is easier to justify. This information also helps the company determine where the compliance improvement would have the biggest financial impact. A common fact about these types of costs is that they often are not included fully into the budget and therefore hit finances directly.

Conclusion

The cost to react by far exceeds the cost to avoid an issue. According to PDA's *Business Case for Pharmaceutical Quality* survey, more than 50% of respondents said that the cost of failure was at least five times higher than the cost of prevention, yet most companies choose to stay in the reactive mode. We need to make different choices here!

In the next issue, we will talk about teaching compliance in financial terms.

About the Authors

Jennifer Magnani is currently Head of Sanofi Pasteur Quality Academy and Leader of the PDA Quality System Interest Group.

Anders Vinther is Chief Quality Officer, Sanofi Pasteur. His experience includes QC, QA, executive and strategic management in a variety of cultures and a number of companies ranging from start-ups to large biologics companies.

Rebecca Devine, PhD, Regulatory Consultant

PDA Strives to Better Serve the Vaccine Industry

As a microbiologist and ex-regulator with many years of involvement in the regulatory, quality and compliance spaces as they relate to biological products including vaccines, the manufacture and regulation of vaccines is a topic of continued interest to me. I know there are many PDA members that also share this interest. Vaccine production provides numerous scientific topics in need of technical and regulatory guidance.

PDA is well suited to serve our members in this area, and the Board of Directors is committed to supporting activities for that purpose.

In 2010, PDA held its first U.S. conference solely focused on vaccines. This conference built upon PDA Europe's vaccine conferences. This was followed by a second U.S. conference in 2012. Building on these important offerings, PDA will continue to host these conferences periodically.

These conferences are designed to delve into the unique issues of the vaccine industry. This is an area not fully served by other organizations in the areas of manufacturing science and regulation. Vaccines have served the public well in diminishing the morbidity and mortality associated with infectious diseases. But new emerging diseases and the complexity of the vaccine approval process now present challenges for manufacturers and regulators. Focused vaccine conferences and topics will therefore continue to be a part of PDA conference and scientific agendas in the years to come in order to help facilitate vaccine development and approval.

This December, PDA will host a vaccines conference concurrently in both the United States and Europe. Here, speakers will interact with participants at both locations simultaneously through virtual communication. This is an exciting new approach intended to capitalize on our excellent speakers, and will allow attendees in both locations to hear important information intended to address global issues affecting the vaccine industry. It will also allow participants access to such speakers while attending in their home region. Such innovative ideas will allow PDA to support this sector of the pharmaceutical industry.

Other topics that impact the vaccine industry are also being addressed by PDA. These include new techniques for adventitious agent testing and viral contamination risk mitigation strategies. These are ever-evolving scientific areas. PDA generated technical guidance will continue to address emerging problems that affect the vaccine industry. Such topics will also be important for the biotechnology industry as a whole since they impact all products manufactured using cell culture.

Other initiatives such as the aging facilities initiative will also provide support to the vaccine industry. Many vaccine manufacturing facilities have been in use for decades; modernization is a topic that, when coupled with regulatory impact, provides unique challenges for vaccine manufacturers. Technical information and guidance that PDA is working on will contribute to solutions for updating aging and outdated processes, facilities and analytical methods. I am looking forward to the work products from these teams.

PDA will also continue to support the vaccine industry through the activities of the Biotechnology Advisory Board (BioAB) and the Vaccines Interest Group.

I look forward to seeing many of you in one or more of these upcoming vaccine events!

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We Want to Hear From You!

At its essence, technology transfer is simply the transmittal of knowledge between two organizations, be it from one facility to another within the same company, or from one company to another, such as a contract manufacturing organization. The sharing of knowledge is important in our industry, particularly as new production models are under development.

Knowledge sharing is also important for us, the editors of the *PDA Letter.* So we invite our readers to share their thoughts with us in our 2015 *PDA Letter* Readership Satisfaction Survey (www.surveymonkey.com/s/2015pdaletter). Tell us what you think of the Letter. How could it be better? What do you like about it? Are there any pertinent topics in your field that are not being covered? Don't hold back! Tell us! We want to know.

The *PDA Letter* is your membership benefit and touches upon most segments of our industry. We want to be sure that it captures the issues and interests of our audience.

Returning to the topic of technology transfer, this issue features some valuable content on this important area. *PDA Letter* Editorial Committee member **Jose Caraballo** wrote this issue's cover story, which offers a useful guide for those involved in, or considering, tech transfer. Our infographic also looks at obstacles, or "sandtraps," that could ensnare even a veteran of many tech transfers.

The editors also interviewed Pfizer's **Michael O'Brien** following his talk at the *2015 PDA Annual Meeting.* He discussed Pfizer's development of portable pods for modular manufacturing at the company's Groton, Conn. site. You can also hear excerpts from this interview in our April *PDA Letter* podcast.

And speaking of the Annual Meeting, check out the PDA Photostream to view some photos taken from this year's exciting conference and consider attending next year's Annual Meeting in San Antonio, Texas.

— **Rebecca Stauffer,** filling in for **Walter Morris** this issue.

PDA Letter

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Subscriptions are not available.

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pda.org/2015aseptic4

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Register now for the
2015 Aseptic Processing Training Program – Session 5
Week 1: October 5-9 | Week 2: November 2-6
pda.org/2015aseptic5

Validation of Dry Heat Processes Used for Depyrogenation and Sterilization
August 12-14 | Bethesda, MD
pda.org/depyro

GMP Week
August 17-19 | Bethesda, MD
pda.org/GMP

- GMPs for Manufacturers of Sterile and/or Biotechnology Products (August 17)
- Application of a Quality Systems Approach to Pharmaceutical CGMPs (August 18-19)

SEPTEMBER 2015

Fundamentals of an Environmental Monitoring Program
September 9-10 | Bethesda, MD
pda.org/enviro

Establishment of a Risk Based Environmental Monitoring (EM) Program
September 11 | Bethesda, MD
pda.org/EMP

2015 Glass Quality, Visual Inspection and Foreign Material Identification Week
September 14-18 | Bethesda, MD
pda.org/glassqual

- Identification and Classification of Nonconformities in Molded and Tubular Glass Containers for Pharmaceutical Manufacturing (September 14)
- An Introduction to Visual Inspection (September 15-16)
- Foreign Particulate Examination, Isolation and Analysis – New Course (September 17-18)

Utilization of Statistical Methods for Production Monitoring
September 22 | Bethesda, MD
pda.org/statistics

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