People • Science • Regulation

PDA Letter

Volume L • Issue 6 www.pda.org/pdaletter June 2014

Drug Manufacturers Face More "How to Do" CMC/GMP Requirements in Europe 28

Register before June 30 for Largest Registration Savings!

The Parenteral Drug Association presents the...

2014 PDA/FDA Joint Regulatory Conference

Connecting Regulatory, Quality, Science & Compliance: Assuring Customer-Focused Outcomes throughout the Product Lifecycle

September 8-10, 2014

RENAISSANCE WASHINGTON HOTEL | WASHINGTON, DC

TOP REASONS WASHINGTON, DC WILL BE THE PLACE TO BE FROM SEPTEMBER 8-12:

1. From September 8-10, the conference will address **relevant topics, regulatory trends and information** with sessions devoted to **Compliance Updates** and **Center Initiatives**.

You'll hear from experts like:

- **Ilisa Bernstein,** Deputy Director, Office of Compliance, CDER, *FDA*
- **Bernadette Dunham,** Director, CVM, *FDA*
- **Martine Hartogensis,** Branch Chief, International Compliance, CVM, *FDA*
- **Mary Malarkey,** Director, Office of Compliance, CBER, *FDA*
- **Steven Silverman,** Director, Office of Compliance, CDRH, *FDA*
- **Doug Stearn,** Deputy Director, Policy & Analysis, ORA, *FDA*
- **Janet Woodcock,** MD, Director, CDER, *FDA*

2. The ***2014 PDA Drug Shortage Workshop,*** held on September 10-11, will focus on the technological improvements that can have a positive impact on preventing drug shortages, and discuss economic and regulatory barriers to implementation as well as potential incentives or regulatory changes that could improve the business case for quality improvements.

3. **PDA's Training and Research Institute will be hosting six training courses** on September 11-12 to complement what you learned at the conference on subjects such as:

- *GMPs for Manufacturers of Sterile and/or Biotechnology Products*
- *Role of the Quality Professional in the 21st Century*
- *Application of a Quality Systems Approach to Pharmaceutical CGMPS*
- *Preparing for Regulatory Inspections for the FDA and EMA*
- *Quality by Design for Biologics: A Practical Approach* – New Course
- *Managing the QC and R+D Laboratory in a GMP Compliant Manner* – New Course

Visit **www.pda.org/pdafda2014** to register for more information.

EXHIBITION: SEPTEMBER 8-10 | POST CONFERENCE WORKSHOP: SEPTEMBER 10-11 | COURSES: SEPTEMBER 11-12

UPCOMING LABORATORY AND CLASSROOM TRAINING FOR PHARMACEUTICAL AND BIOPHARMACEUTICAL PROFESSIONALS

AUGUST 2014

Fundamentals of Aseptic Processing

August 4-8 | Bethesda, Maryland
www.pda.org/APFundamentals

PDA has developed this new 5-day training course intended to provide individuals with an understanding of the fundamental principles governing aseptic processing.

Validation of Dry Heat Processes Used for Depyrogenation and Sterilization

August 12-14 | Bethesda, Maryland
www.pda.org/dryheat

This hands-on course focuses on the microbiology and engineering qualification of dry heat depyrogenation processes.

An Introduction to Visual Inspection

August 27-28 | Bethesda, Maryland
www.pda.org/visual

This course covers the fundamentals of visual inspection and their application to injectable products. The skills developed through this course may be applied to both manual and automated machine inspection.

2014 Aseptic Processing Training Program

August 18-22 and September 22-26 | Bethesda, Maryland
www.pda.org/2014aseptic

With almost 50 hours of hands-on laboratory training and group project work, in addition to extensive coverage of topics during the lecture sessions, this is the most complete aseptic processing training program offered.

SEPTEMBER 2014

2014 PDA Joint Regulatory Conference Course Series

September 11-12 | Washington, DC
www.pda.org/pdacourses2014

Immediately following the *2014 PDA/FDA Joint Regulatory Conference*, the PDA Training and Research Institute will host six courses to complement what you learned at the conference.

- GMPs for Manufacturers of Sterile and/or Biotechnology Products (September 11)
- Role of the Quality Professional in the 21st Century (September 11-12)
- Application of a Quality Systems Approach to Pharmaceutical CGMPS (September 11-12)
- Preparing for Regulatory Inspections for the FDA and EMA (September 11-12)
- Quality by Design for Biologics: A Practical Approach – *New Course* (September 12)
- Managing the QC and R+D Laboratory in a GMP Compliant Manner – *New Course* (September 12)

Fundamentals of an Environmental Monitoring Program

September 16-17 | Bethesda, Maryland
www.pda.org/EMFundamentals

The course will discuss, in detail, controlled environmental test methods, with a focus on microbiological control.

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

Laboratory Courses

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

PDA Letter

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Cover

Cover Art Illustrated by Katja Yount

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Contents

Features

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.

James E. Akers, PhD, Akers Kennedy & Associates

Gordon Personeus Award

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

Carol M. Lampe

Frederick J. Carleton Award

Presented as a tribute to past President **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.

John G. Shabushnig, PhD, Insight Pharma Consulting

Packaging Science Award

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

Edward Smith, PhD, Packaging Science Resources

Distinguished Service Award

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

David J. Cummings, U.S. FDA

Laurie Norwood, U.S. FDA

Erik van Asselt, PhD, Merck

Brigitte Reutter-Härle, Vetter

Nicholas R. DeBello, DeBello & Associates

Michael VanDerWerf, OrganoGenesis

Martin VanTrieste Pharmaceutical Science Award

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

Irving J. Pflug, PhD

PDA Europe Service Appreciation Award

This award is presented annually for special acts or contributions that have contributed to the success and strength of PDA Europe.

Harald Stahl, PhD, GEA Pharma Systems

Service Appreciation Award

The Service Appreciation Award is presented annually for special acts or contributions that have contributed to the success of PDA.

Maik W. Jornitz, G-Con Manuf

Arthur Vellutato, Jr., Veltek

Barbara Jentges, PhD, PhACT GmbH

Brenda Uratani, PhD, U.S. FDA

Don E. Elinski, RPh, Lachman Consultant Services

Greg Jordan, Box Hill Institute

Harold S. Baseman, ValSource

Janeen A. Skutnik-Wilkinson, NSF

Jeanne Moldenhauer, Excellent Pharma Consulting

Karen S. Ginsbury, PCI

Lothar Hartmann, PhD

Rina Yamin, Rina Yamin Pharmaceutical Consulting

Robert Sitrin, PhD, SitrinSolutions

Russell E. Madsen, The Williamsburg Group

Sabine Scheitlin

Saeed Tafreshi

Steven Mendivil, Amgen

Susan Schniepp, Allergy Laboratories

James P. Agalloco Award

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

Joseph J. Lasich

Rainer Newman

Brent Watkins, Veltek

Michael S. Korczynski Award

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

Tor G. Gråberg, Medical Products Agency Sweden

Yukio Hiyama, PhD, National Institute of Health Sciences, Japan

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.

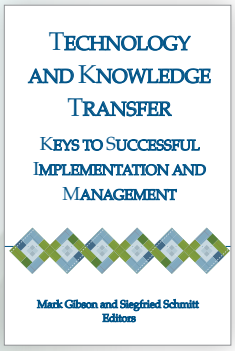
Bob Collier, PDA

Nadine Gold, PDA

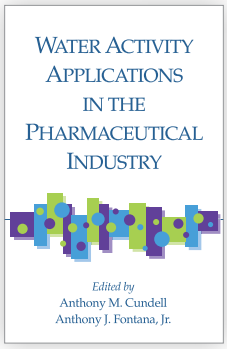
PDA's 2014 Summer Sale

June 15 – August 31

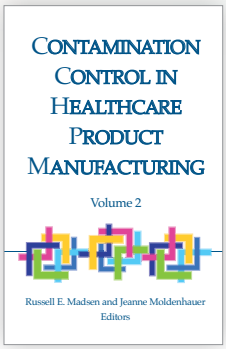
Save the green for the golf course when you take advantage of our hot deals! We will be offering deals on over 80 products.



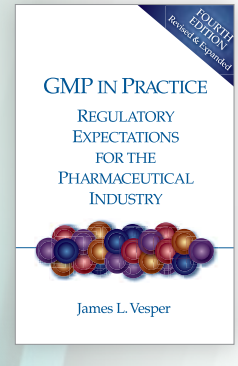
Technology and Knowledge Transfer: Keys to Successful Implementation and Management
Edited by Mark Gibson and Siegfried Schmitt
Item No. 17318



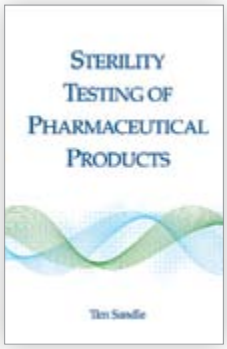
Water Activity Applications in the Pharmaceutical Industry
Edited by Anthony Cundell and Anthony Fontana
Item No. 17249



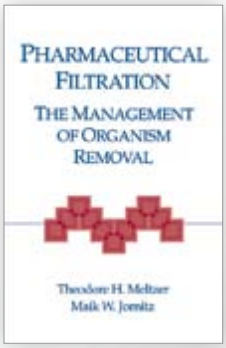
Contamination Control in Healthcare Product Manufacturing, Volume 2
Edited by Jeanne Moldenhauer and Russell Madsen
Item No. 17317



GMP In Practice: Regulatory Expectations for the Pharmaceutical Industry, Fourth Edition, Revised & Expanded
By James Vesper
Item No. 17269



Sterility Testing of Pharmaceutical Products
By Tim Sandle
Item No. 17315



Pharmaceutical Filtration: The Management of Organism Removal
By Theodore Meltzer and Maik Jornitz
Item No. 17235

Visit www.pda.org/bookstore for more information

Booklets for sale

Validation of Microbial Identification Systems
By Jeanne Moldenhauer
Item No. 17225

Environmental Impact on Media Fills
By John Lindsay
Item No. 17271

Training and Learning Critical Contributors to Quality
By James Vesper
Item No. 17259

Microbiological Validation Master Plan
By Trevor Deeks
Item No. 17230

Packaging Considerations for Steam Sterilization
By Edward Smith
Item No. 17274

Validation Procedures for the Bacterial Endotoxins Test
By James Cooper & Cheryl Moses
Item No. 17226

PDA Volunteer Spotlight

Emma Ramnarine

- Senior Director, Head, Global Biologics QC
- *Genentech/Roche*
- Member Since | **2001**
- Current City | **Fremont, California**
- Originally From | **Indore, India**

New, different, challenging, fast-paced, is what drives me

Emma has always admired Mother Teresa for her selflessness

You were selected to serve on PDA's Regulatory Affairs and Quality Advisory Board (RAQAB) after two years of membership. This followed 13 years as a PDA member and three years as an active volunteer. How have you been so successful?

I started volunteering with PDA as the Paradigm Change in Manufacturing Operations (PCMO[SM]) Task Force leader for the Technical Report No. 54 series on Quality Risk Management (QRM) for Pharmaceutical and Biotechnology Manufacturing Operations. This was invaluable for me, not only as an opportunity to learn and lead the development of the report and the associated training course with a diverse group of industry and regulatory colleagues, but it also enabled me to get more integrated into the PDA network, and from there into the RAQAB. PDA is a volunteer driven organization—you get out of it what you choose to put in.

How has preparing TR-54 contributed to your career?

Until a year and a half ago, I was Head of Global Quality Risk Management at Genentech/Roche. So when three years ago, PDA approached me asking if I would be interested in leading the PCMO[SM] Task Force on QRM for TR-54, , I said "why not?" I felt it afforded an excellent learning, benchmarking and knowledge sharing opportunity among different companies with varying levels of QRM experience and expertise.

Where do you see yourself in five years?

I see myself continuing to do what I love—staying on the leading edge of science, technology and systems thinking.

What piece of advice has been most helpful throughout your career?

One of the best pieces of advice one of my mentors gave me very early on was to make every day at work count as an opportunity to learn, grow and contribute, and to build lasting professional relationships based on respect and trust. Treat people and every interaction with care and make sure it brings value to all involved, because you never know which conversation can open doors to more learning, better opportunities and the next step in your career.

Volunteer Opportunities at PDA

Leadership

- PDA Executive Officers
- Director
- Scientific Advisory Board
- Biotechnology Advisory Board
- Regulatory Affairs and Quality Advisory Board
- PDA Committee Chair/Co-Chair
- Task Force Co-Chair

- Author/Contributor to the *PDA Letter*
- Author/Contributor to the *PDA Journal*
- Poster Presenter
- Attend Chapter Committee/Planning Meetings
- Technical Report Peer Reviewer

- Speaker
- Chapter Leader
- Task Force Member
- TRI Instructor
- Interest Group Leader

PDA Committees:

- Program Planning Committee
- Membership Committee
- PDA Letter Committee
- Education Committee
- Audit Committee

- PDA Membership
- Attend Global PDA Meetings
- Attend Chapter Events
- Survey Reviewer
- Interest Group Member
- Attend TRI Courses

Getting Involved

1,000 Over 1,000 volunteers worldwide actively carry out PDA's Mission

volunteer@pda.org

chapter update

Chapter Learns About PDA Quality Metrics Activities

Jeff Hargroves, ProPharma Group

The Missouri Valley Chapter held its Spring Meeting at the Airport Hilton in Kansas City, Mo., on April 21. Three great speakers addressed approximately 70 attendees.

Warren Lopicka gave information on the organization of the local FDA office region and Agency initiatives in the region.

Denyse Baker then gave an enlightening presentation on PDA's Regulatory Affairs and Quality Advisory Board (RAQAB). We learned where RAQAB fits into the overall PDA structure, how it interacts with external agencies such as the FDA, EMA, ICH and others, and Baker reviewed the specific process recently used to provide comments to the FDA regarding their quality metrics initiative.

Susan Schniepp then presented a detailed update on the background behind the quality metrics initiatives, the importance of these tools, areas of risk when trying to use quality metrics across a wide population of products/sites, and engaged the crowd with several real-life examples about how to implement quality metrics in a meaningful way.

The presentation concluded with a look at PDA's future quality metrics activities. These include collecting feedback from members on specific definitions, updating PDA's Points to Consider document, conducting a survey and holding a follow-up conference to the *2013 PDA Pharmaceutical Quality Metrics Conference.*

We look forward to our next meeting in the fall in St. Louis, Mo.!

[Editor's Note: Updates on PDA's quality metrics activities will be forthcoming in subsequent issues of the *PDA Letter*. For an overview of PDA's Points to Consider document and the *2013 PDA Pharmaceutical Quality Metrics Conference,* see the cover story of the February 2014 issue.**]**

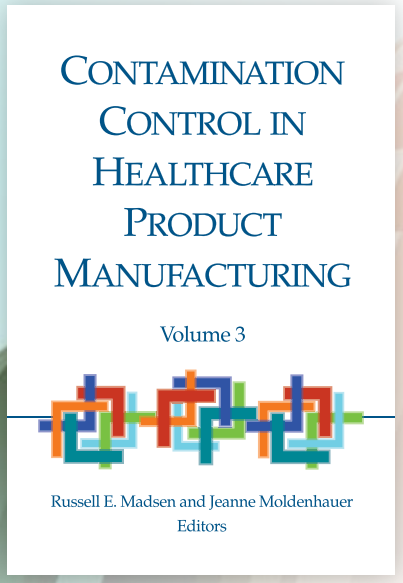
PDA Who's Who

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

Susan Schniepp, VP, Quality and Regulatory Affairs, Allergy Laboratories

Warren Lopicka, Supervisor, Consumer Safety Officer, U.S. FDA, Kansas City District Office

New Release at the PDA Bookstore



Contamination Control in Healthcare Product Manufacturing, Volume 3

Edited by Russell E. Madsen and Jeanne Moldenhauer

Volume 3 discusses extensive subjects related to water considerations and also includes invaluable advice regarding:

Item No. 17321

- Design and Sanitization of Water Systems to Prevent Contamination
- Real Time Microbial Analyzer for Water
- Use Of Ozonated Water as an Aid to Contamination and Biofilm Control
- Testing and Verification of Ventilation Systems for Biosafety Level 3 (Bsl-3) and Animal Biosafety Level 3 (Absl-3) Facilities
- Microbiology Laboratory Spearheading Microbial Contamination Control
- Understanding, Preventing, and Remediating Mold in Cleanrooms
- Contamination Control Considerations for Microaerophillics in Controlled Aseptic Manufacturing Areas
- The Problem of Burkholderia Cepacia
- Cleaning Validation: Process Life Cycle Approach
- Risk Management of Microbial Contamination Control in Aseptic Processing and Interventions Risk Assessment Model (Irem): The Use of Critical Thinking to Make Informed Decisions
- Understanding Cleanroom Classifications
- Disinfection Qualification Testing Consideration for Aseptic and Cleanroom Manufacturing Environments

All chapters are written by subject matter experts, each of them bringing their extensive knowledge and experience to all personnel involved in aseptic contamination control.

Own the entire collection today! When you purchase Item no. 17322, you'll own Volume 1, 2 and 3.

The first volume of Contamination Control series contains chapters that are predominantly centered on microbial issues. Volume 2 addresses some microbial issues, but also focuses on other types of contamination.

go.pda.org/CCHPM3

In Memory of Masamichi Sudo – President of Daikyo Seiko Ltd.

Patty Kiang, PhD, Kiang Consultant Services

When I received an email from **Kunihiro Noto** (Vice President, Sales and Marketing, Daikyo Seiko Ltd.) that informed me that **Masamichi Sudo,** President of Daikyo Seiko, had passed away, I was shocked and very saddened by this news.

I had the good fortune to see him one month ago in Sano, Japan when I accompanied my client to perform an audit at Daikyo. He was 89 years old and still remembered me and was very friendly and kind to me. His mind was still very sharp. He was telling me about his new development project and was very happy to receive recognition from around the globe. His lifelong goal was always in developing the highest quality and cleanest pharmaceutical primary containers and packaging systems.

Sudo was a dedicated person; he lost four fingers from rubber manufacturing when he founded Daikyo in 1954. I'd known him since 1978, when I visited Daikyo in Tokyo for the first time. He was a hands-on person, very much involved with new technology and new product development. At that time, Daikyo's rubber formulation was not as clean as today. Sudo developed the unique washing process after the manufacture of rubber stoppers. The washing process is very effective; alkaline autoclaving virtually eliminates microorganisms and WFI final washing removed visible particles. This process can also extract low molecular weight substances, processing aids and some reaction products from the molded rubber stoppers to make the stoppers clean and compatible with drug products. Over the past three decades, he led Daikyo to be the highest quality pharmaceutical container closure manufacturer in the world. Many state-of-the-art, clean rubber formulations have been developed with no postwashing process required. Flurotec laminated stoppers, CZ plastic containers and prefillable syringes with 100% automated vision systems have also been developed. Some of the products are viewed as the gold standard in the industry. He had the vision and perseverance to develop new container closure systems for the pharmaceutical industry. The pharmaceutical industry is very conservative and slow in accepting changes.

Daikyo is willing to spend the long development time and effort, waiting for pharmaceutical clients' long compatibility, stability and regulatory approval time. Sudo was not just focused on short term profitability, he was also passionate in developing the best and cleanest parenteral packaging systems for the world. I had the privilege to work on the CZ product development with Daikyo when I was working at West Company. Every time I needed some instrument or funding, he was always very responsive and very supportive, and I really enjoyed the collaboration with Daikyo.

Daikyo has achieved the goal of being the leader in the pharmaceutical container closure industry; all Daikyo competitors are trying to come up with similar products such as the coated stoppers and high quality plastic containers.

Sudo was passionate with his work and interested in new technologies, every time I visited Daikyo, there were always some new products, new technologies or new expansion. "Continuous improvement" is the normal practice at Daikyo. Always a great leader, he led by example to establish this culture for Daikyo.

Daikyo under his leadership was very active with the PDA and other industrial or social activities; He was very kind and generous to its employees and colleagues, the love and respect from Daikyo workers toward him was always present.

It is very sad to lose Mr. Sudo, a great leader for the pharmaceutical primary packaging industry, his vision and perseverance to lead successful new products and Daikyo's top quality standards cannot be easily replaced. The pharmaceutical industry is in debt to him for improving the quality of parenteral drugs, especially by lowering extractables and leachables and reducing particulates issues. He will be greatly missed by the pharmaceutical industry.

It was my great honor to consider Masamichi Sudo my friend and I would like to give my respect and condolences to his family and members of the Daikyo family.

[Editor's Note: Masamichi Sudo served on the board of the PDA Japan Chapter from 1994–1996. In addition, his father served on the board of the Japan Chapter when it was started.**]**

スドウ・マサミチ氏を追悼して ～株式会社大協精工取締役社長

キアン コンサルタント サービス、パティ・キアン博士

ノト・クニヒロ氏（株式会社大協精工営業部長）からEメールで、大協精工代表であるスドウ・マサミチ氏が亡くなられたと知らされたとき、その知らせは私にとって大変ショックで悲しいものでした。

幸いにも、ひと月前に大協にて会計監査を行うため日本へクライアントと出向いた際に、佐野で彼にお会いする機会がありました。スドウ氏は当時89歳で私のことをまだ覚えておられ、私に対しとても友好的で親切でした。思考はまだ非常にさえておられました。新規開発プロジェクトの話をされ、国際的な評価を受けることにとても喜んでいました。彼がいつも掲げていた生涯目標は最高品質と、最も清潔な薬剤一次容器・包装システムの開発でした。

スドウ氏はひたむきな方で、1954年に大協を設立された時にゴム製造で指を4本失くされました。彼と出会ったのは1978年で、私が初めて東京の大協へ訪れた時でした。とてもまっすぐなスドウ氏は新しい技術や製品開発に大変深く関わっておられました。当時、大協のゴム形成は現在のものほど清潔ではありませんでした。スドウ氏はゴム製ストッパーの製造後、独自の洗浄プロセスを開拓されました。その洗浄プロセスは非常に効果的で、アルカリ性高圧蒸気殺菌法によって微生物は事実上除去され、WFI最終洗浄では目に見える粒子が取り除かれました。また、このプロセスでは低分子量物質の摘出が可能で、エイズや他の反応生成物を成形ゴム製ストッパーで処理し、ストッパーを清潔にして薬剤に適合させます。過去30年以上を経て、スドウ氏は大協を世界で最も高品質な薬剤容器蓋を製造する会社へと導きました。最先端の無菌ゴム形成の多くが後洗浄過程なしで開発されています。同様に、Flurotecラミネートストッパー、CZプラスチック容器、そして100%自動視覚システムを備えた事前充填可能なシリンジも開発されました。業界において代表的な存在として見なされている製品もいくつかあります。スドウ氏は薬剤産業のために新しい容器蓋システムを開発するビジョンと粘り強さをお持ちでした。薬剤界は変化を受け入れることに対して大変保守的なのです。

大協は開発に長い時間と多大な努力を費やすことを厭わず、薬剤関連のクライアントとの適合、信頼、規制認可にかかる時間など、長くとも待つ姿勢を持っています。スドウ氏が重きを置いていたのは短い期間での利益性だけではなく、世界に向けての最高質で最も清潔な非経口包装システムの開発に情熱を注いでおられました。私は、名誉なことに、ウェストカンパニーで働いていた当時大協と共にCZ製品開発に取り組みました。スドウ氏は私が機器や資金が必要な時はいつも即座に対応してくださり、支援してくださいました。大協との協働は本当に楽しいものでした。

大協は薬剤容器蓋産業界においてリーダーになるという目標を達成しました。すべての競合者たちは、コーティングストッパーや高品質プラスチック容器など、類似品を開発する努力をしています。現在のCOP、COCプラスチック容器または事前充填可能なシリンジはCZ製品のジェネリック版です。しかし、CZは競合品よりもいまだより優れた材料特性を誇っています。

スドウ氏はご自身のお仕事に対し情熱的で新しいテクノロジーに興味を持っておられ、私が大協を訪れる度にそこには常に新製品や新技術、あるいは新規展開がありました。大協において「持続的発展」が通常の慣行なのです。偉大なリーダーであるスドウ氏は、この文化を大協に確立するべく模範を示して指導されました。

彼のリーダーシップの下で大協は、PDA（非経口製剤研究協会）やその他産業活動、社会活動に積極的に関与しました。スドウ氏は従業員や同僚に対し非常に親切で寛大であり、大協の社員らは彼に対し常に愛と尊敬の念を抱いていました。

薬剤一次包装産業の偉大なリーダーであるスドウ氏を失ったことは大変悲しいことであり、上出来な新製品につながる彼のビジョンと粘り強さ、そして大協の最高品質の標準は、簡単に置き換えられるものではありません。薬剤業界は非経口薬剤の品質改善、特に抽出物および侵出物の減少ならびに微粒子の問題を減らすことにおいて彼に恩義があります。彼は薬剤界にとても惜しまれることでしょう。

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『編集者注：スドウ・マサミチ氏は1994年～1996年の間PDA日本支部の理事を務める。加えて、日本支部が設立された当時はスドウ氏の父が理事を務めた。』

+ 2014 PDA Annual Meeting

Plenary Sessions

Opening Remarks

PDA Chair Hal Basman, Valsource, opens the meeting

Opening Remarks

PDA President Richard Johnson dicusses PDA's 2013 highlights

P1: Global Patient Access and Global Strategies to Medicines

(l-r) Mark McClellan, MD, PhD, Brookings Institution; Ursula Busse, PhD, Novartis; Rahul Singhvi, Takeda Vaccines

P2: Science and Innovation

(l-r) Michael VanDerWerf, OrganoGenesis; David Shanahan, Gradalis; Wilfried Dalemans, PhD, TiGenix

Closing Plenary: Emerging Technologies and Markets

(l-r) Jose Goin, PhD, Genentech; J. Christopher Love, PhD, MIT; Martin VanTrieste, Amgen

D: Advances in Analytical Testing for Large Molecules

(l-r) Pin Yee Wong, Genentech; Steven Cockrill, Amgen, Jose Goin, PhD, Genentech

A: Biosimilars

(l-r) Morten Munk, CMC Biologics; Lisa Skeens, PhD, Hospira; Jean-Marie Geoffroy, PhD, Hospira

E: Facilities

(l-r) Maik Jornitz, G-Con; Robert Dream, HDR; George Wiker, US Life Sciences

B: Globalized Supply Chain

(l-r) Ken Drost, Amgen; Melissa Banning, Amgen; Warren Horton, DSM

C: Inspection Trends

(l-r) Edwin Rivera-Martinez, Sanofi; Douglas Campbell, InterPro QRA; Karen Takahashi, CDER, U.S. FDA; Katherine Eban, *Fortune* magazine

F: Quality Systems

(l-r) Bryan Liptzin, Amgen; Susan Schniepp, Allergy Laboratories; David Cummings, CDER, U.S. FDA; Kate Gillespie, Johnson & Johnson

+ 2014 PDA Annual Meeting

Tuesday Breakout Sessions

L: Process Analytics Technology (PAT)

(l-r) Christopher Watts, PhD, VolPal; Morten Munk, CMC Biologics; Ali Afnan, PhD, Step Change Pharma

K: Process and Product Quality – Control and Detection of Particulates

(l-r) John Shabushnig, PhD, Insight Pharma Consulting; Julianne Wolfe, RJ Lee Group; Jeffrey Hartman, Merck

G: Protection Strategies for Biologics

(l-r) Igor Gorsky, ConcordiaValsource; Michele Creech, Grifols; Hank Rahe, Containment Technologies Group

I: Process Validation/Lifecycle Approach and FDA Guidance

(l-r) Karthik Iyer, PhD, CDER, U.S. FDA; Alex Viehmann, CDER, U.S. FDA; Jason Orloff, PharmStat; Hal Baseman, ValSource

J: Balancing Quality and Productivity in Biopharmaceutical Drug Substance Manufacturing Processes

(l-r) Michael DeFelippis, PhD, Eli Lilly; Annemarie Möritz, PhD, Novartis; Tongtong Wang, PhD, Eli Lilly

H: Sterile Processing

(l-r) Miguel Nogueras, Abbott; Carol Lampe, Consultant; Byron Lambert, Abbott

Wednesday Breakout Sessions

M: Combination Products

(l-r) Roger Asselta, Genesis Packaging Technologies; Andrea Straka, West; Lee Leichter, P/L Biomedical; Miguel Nogueras, Abbott

O: Parametric Release

(l-r) Robert Tomaselli, RPT Medical Products Consulting; Michael Sadowski, Baxter; Jeffrey Weber, Pfizer

N: Technology Transfer

(l-r) Christopher Watts, PhD, VolPal; Willow DiLuzio, PhD, Takeda; Jean-Marie Geoffroy, PhD, Hospira

Annual Walk/Run

Damian Waters (right), husband of Australia Chapter President Kim Waters (left), won first place in the run portion of the Walk/Run

Board member Jette Christensen won first place for the walk portion

Participants in the 8th Annual Walk/Run, with PDA's contribution, raised $3,000 for The Arc of San Antonio

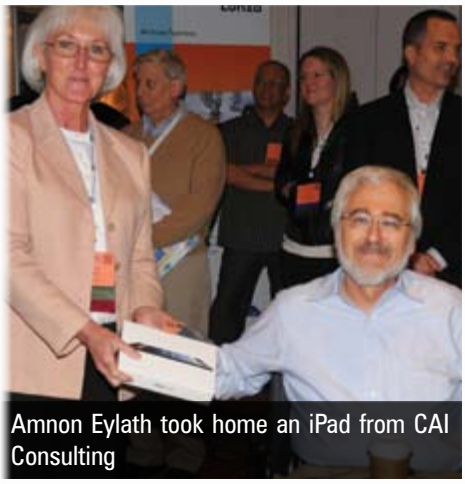
+ 2014 PDA Annual Meeting

Drawing Winners


Alpaslan Yaman, PhD, won a Kindle Fire from Cytovance


Rocco Duran wins a bottle of rum from Coldstream


Mike Avram received an opportunity to attend a free course from PDA TRI


Amnon Eylath took home an iPad from CAI Consulting


PDA presented Wendy Severs with a gift card


Jill Armstrong recieves an iPad curtousy of Lonza


PDA Europe presented Michele Creech with a Buddy Bear statue


Midi Labs presented Mico Holguin with a $200 American Express Gift Card


Debra Cortner won an iPad from Associates of Cape Cod

Gala

snapshot

TR-56 Update Reflects Annex 2 Revision

Jahanvi (Janie) Miller, PDA

As new technologies are presented and new concepts are used to manufacture drugs, it's imperative that our technical report teams keep our literature and resources updated with these changes. In January 2013, the European Commission issued the revised draft of Annex 2, *Manufacture of Biological Active Substances and Medicinal Products for Human Use*. The authors of *Technical Report No. 56 (2012): Application of Phase-Appropriate Quality Systems and CGMP to the Development of Therapeutic Protein Drug Substance* felt this revision should be incorporated into the technical report and requested PDA initiate the revision process. The team will be revising TR-56 in 2014 and hopes that this revision effort will help support the biopharmaceutical industry in maintaining best manufacturing processes.

Taking a step back, development of TR-56 began in April 2012 when PDA provided comments on the European Commission's concept paper, the *Delegated Act on the Principles and Guidelines of Good Manufacturing Practice for Active Substances in Medicinal Products for Human Use* **(Editor's Note:** These comments can be viewed at tinyurl.com/kvrtlyy**)**, which proposed extending medicinal product GMPs to drug substances. In turn, some of these recommendations were taken into consideration in the creation of TR-56.

We are excited by this opportunity to update TR-56, making it a "living document," if you will, reflecting changes in the global regulatory environment. Members will be notified when the revised version is available.

Journal *Preview*

May–June Issue Offers Two Virus-Centered Meeting Reports

This issue includes two meeting reports from two different conferences exploring virus safety concerns. **Hannelore Willkommen,** et al. offer overviews of both the *2013 PDA Virus & TSE Safety Forum* and the workshop on virus removal by filtration; the latter was held in conjunction with the *2011 PDA Virus & TSE Safety Forum.*

Editorial

Anurag S. Rathore, "The Scare of Adventitious Agents in Therapeutic Products"

Conference Report

Hannelore Willkommen, et al., "Meeting Report: 2013 PDA Virus & TSE Safety Forum"

Review

Sâmia Rocha de Oliveria Melo, et al., "Advice on Degradation Products in Pharmaceuticals: A Toxicological Evaluation"

Technology/Application

A. Hamid Mollah, et al., "A Practical Discussion of Risk Management for Manufacturing of Pharmaceutical Products"

Martha Folmsbee, et al., "The Development of a Microbial Challenge Test with *Acholeplasma laidlawii* To Rate Mycoplasma-Retentive Filters by Filter Manufacturers"

Research

Dennis Jenke, et al., "The Use of TOC Reconciliation as a Means of Establishing the Degree to Which Chromatographic Screening of Plastic Material Extracts for Organic Extractables Is Complete"

Hannelore Willkommen, et al., "Meeting Report—Workshop on Spike Characterizations and Virus Removal by Filtration: Trends and New Developments"

Suzan Mohammed Ragheb, Luis Jimenez, "Polymerase Chain Reaction/Rapid Methods Are Gaining a Foothold in Developing Countries"

Eva Gefroh, et al., "Use of MMV as a Single Worst-Case Model Virus in Viral Filter Validation Studies"

Tech *Trend*

Alt Method Vendors Should Provide Documentation Supporting Implementation and Validation Efforts

Mary Beth Anheuser, bioMeriéux

Acceptance of alternative microbiological methods for use in pharmaceutical and biotechnology laboratories is gaining momentum due to regulatory support conveyed through the U.S. FDA's PAT initiative, 21 CFR 610.9, the FDA's draft guidance *Validation of Growth-Based Rapid Microbiological Methods for Sterility Testing of Cellular and Gene Therapy Products* and Ph. Eur. Informational Chapter 5.1.6. Alternative Methods for Control of Microbiological Quality.

Laboratories implementing alternatives to the traditional culture methods are required to demonstrate the suitability of the new method through a comparison study. USP General Information Chapter <1223>, Ph. Eur. Informational Chapter 5.1.6, and *PDA Technical Report No. 33 (Revised 2013) Evaluation, Validation and Implementation of Alternative and Rapid Microbiological Methods,* define performance attributes that should be established during validation and subsequently used to determine equivalency with an existing method. For qualitative methods, these attributes include ruggedness, robustness, detection limit (LOD) and specificity.

Continued at top of page 22

Report From 2014 PDA ANNUAL MEETING

Task Force *Corner*

Responding to Bioburden/Biofilm Contamination

Rebecca Stauffer, PDA

During a breakfast roundtable session at the *2014 PDA Annual Meeting,* Bioburden and Biofilm Management Technical Report Team member **Kalavati Suvarna,** PhD, U.S. FDA, emphasized the technical report's role in identifying the causes of bioburden/biofilm contamination and how to control for it in pharmaceutical systems.

"It affects multiple industries," she said of bioburden. "In terms of public health impact…it impacts drug efficacy and drug safety."

For this reason, Suvarna stressed that "prevention is key," adding, "The technical report basically provides you some practical guidance on this issue. It also includes some case studies."

These case studies were taken from contamination events that have occurred over the past five years and also offer a useful take home message. These case studies encompass both upstream and downstream processes as well as pharmaceutical water systems and the role of equipment. The first case study examines the role of the mammalian cell culture process and the second looks at bulk drug product hold. The third case study explores equipment cleaning and storage.

Continued at bottom of page 22

PDA Journal *Award*

2013 Best Paper

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

For 2013, PDA recognizes the following recipients for their article, "Identification and Root Cause Analysis of Cell Culture Media Precipitates in the Viral Deactivation Treatment with High-Temperature/Short-Time Method," which was published in January/February 2013:

Xiaolin Cao, PhD

Gregory S. Stimpfl, P.E.

Zai-Qing Wen, PhD

Gregory T. Frank, PhD

Glenn Hunter

Xiaolin Cao, PhD (left), accepts the Frederick D. Simon award from PDA Journal Editor-in-Chief **Govind Rao**

Special *Recognition*

PDA Honors LAL Test Codiscoverer

At the *2014 PDA Annual Meeting* awards dinner, PDA bestowed special recognition to **Jack Levin,** MD, in honor of the 50th anniversary of his pioneering discovery of the Limulus Amebocyte Lysate (LAL) reagent, which revolutionized tests for bacterial endotoxin. In addition to this trailblazing work, Levin has contributed extensively to research on the physiological effects of endotoxin and chronic diseases associated with Gram-negative bacteria.

PDA President **Richard Johnson** (left) presents **Jack Levin** with a plaque honoring his achievements

Tech Trend continued from page 21

The onus is on the alternative method supplier to support proof of concept (POC) or feasibility activities and to provide documentation that supports implementation and validation efforts. Documentation can include guidance on IQ, OQ, and PQ activities, a bibliography of supplier and user study data demonstrating the performance of the method, and a Drug Master File (DMF).

The guidance documents suggest that attributes such as ruggedness and robustness are best determined by the supplier. In addition, during initial discussions, potential users require information on specificity and LOD. Vendors are challenged to provide generic, scientifically, and statistically relevant data to assess the method for use with the diverse products tested by biopharma companies.

[Author's Note: The author bases this article on bioMeriéux's BacT/ALERT® 3D systems (BTA). Documentation for the systems has been developed and is available to users to support the implementation and validation efforts.**]**

About the Author

Mary Beth Anheuser has worked in the field of microbiology for over 25 years. Her experience includes pharmaceutical, food and clinical microbiology. For the past seven years, she has focused on sterility test applications for testing biopharma products on the BTA systems.

Task Force Corner continued from page 21

Remediation strategies from these case studies include analyzing microbes and cleaning effectiveness, looking into the factors promoting the formation of biofilms and redesigning processes and equipment in response to contamination.

In addition, the technical report will include literature on new technologies, such as novel steam vapor systems and early detection systems.

Suvarna said she hopes that the data pulled from these case studies can prove useful to both industry and regulatory.

"I think that as a whole, we should try and double up best practices and find ways to integrate all of this information through periodic review," she said.

The technical report is expected to be available sometime in June. It can be purchased from the bookstore at www.pda.org/bookstore. PDA members will be able to download the report for free.

About the Expert

Kalavati Suvarna, PhD, is a Consumer Safety Officer in FDA/CDER's Office of Compliance, Office of Manufacturing and Product Quality, Biotech Manufacturing Assessment Branch.

Combination Products Offer Challenges, Opportunities for Industry

Lee Leichter, P/L Biomedical

The number and types of drug delivery combination products under development are growing rapidly, fueled by the increasing trend towards self-administration and the shifting of healthcare treatment from the clinic to the home environment.

Integration of the medical device quality system requirements for drug delivery combination products has been a challenge since the publication of the U.S. FDA's draft guidance in 2004. The draft rule on GMPs for combination products (21 CFR Part 4a) reinforced FDA's position on what would be required, but it was not clear on what products would be affected and enforcement of the rule. With the publication of the final rule in 2013, which became effective July 22, 2013, some of FDA's positions were stated and/or reinforced.

Some key issues that were clarified in the final Rule:

- The Rule did not create any new GMP requirements, only provided a method of implementing a streamlined system for compliance.
- All manufacturers have already been responsible for compliance with the CGMP requirements that apply to each constituent part of their combination products.
- FDA intends to apply a risk-based approach to facility inspection and, consistent with ensuring protection of the public health and in light of the specific circumstances, to offer manufacturers a reasonable opportunity to correct deficiencies before taking further compliance or enforcement actions.
- Prefilled syringes are combination products; however, distinctions between devices and containers/closures will be addressed in further detail in later guidance.
- A kit that includes two or more types of medical products is a combination product and thus subject to this rule.

The *2014 PDA Drug Delivery Combination Products Workshop,* Oct. 8, will offer real-life experiences from companies who have addressed these challenges, both postmarket and during development and approval. To learn more, visit www.pda.org/drugdelivery2014.

2014 PDA UPCOMING EVENTS

JUNE EVENTS

2
Manufacturing and Testing Challenges of ATMPs
Madrid, Spain
https://europe.pda.org/WSATMPs2014

2-6 and 23-27
2014 Aseptic Processing Training Program – Session 3
Bethesda, Maryland
www.pda.org/2014aseptic3

3-4
Advanced Therapy Medicinal Products
Madrid, Spain
https://europe.pda.org/ATMP2014

3-5
2014 PDA/FDA Pharmaceutical Supply Chain Conference
Washington, DC
www.pda.org/supplychain2014

4
PDA Capital Area Chapter Event – FDA Expectations: Multi-product Facility Considerations for Biological Products
Gaithersburg, MD
www.pda.org.capchevent

5
PDA Ireland Chapter Meeting on Visual Inspection
Dublin, Ireland
https://europe.pda.org/IRVisInsp2014

5-6
2014 PDA Pharmaceutical Supply Chain Course Series
Washington, DC
www.pda.org/supplychaincourses2014

9-11
2014 PDA/FDA Virus & TSE Safety Conference
Bethesda, Maryland
www.pda.org/virus2014

12-13
2014 PDA Virus & TSE Safety Course Series
Bethesda, Maryland
www.pda.org/viruscourses2014

17-18
2014 PDA Aseptic Processing-Sterilization Conference
Chicago, Illinois
www.pda.org/aseptic2014

19-20
2014 PDA Aseptic Processing-Sterilization Course Series
Chicago, Illinois
www.pda.org/sterilizationcourses2014

24-25
Parenteral Manufacturing
Istanbul, Turkey
https://europe.pda.org/ParMan2014

26
GMP and Quality Systems for Parenterals
Istanbul, Turkey
https://europe.pda.org/GMP&Quality2014

26
Cleaning & Disinfection
Istanbul, Turkey
https://europe.pda.org/TCCleaning2014

26
Fill & Finish Operations for Parenterals
Istanbul, Turkey
https://europe.pda.org/fill&finish2014

26
Technology Transfer – PDA Technical Report 30
Istanbul, Turkey
https://europe.pda.org/TechTransfer2014

26-27
Environmental Control
Istanbul, Turkey
https://europe.pda.org/EnvironControl2014

www.pda.org

For an updated PDA calendar of events please visit
www.pda.org/calendar

Save these dates!

JULY EVENTS

14-18
2014 DoE Week for Process Design and Process Optimization
Bethesda, Maryland
www.pda.org/DoEweek2014

29-31
Validation of Moist Heat Sterilization Processes
Bethesda, Maryland
www.pda.org/moistheat

AUGUST EVENTS

4-8
Fundamentals of Aseptic Processing – Session 2
Bethesda, Maryland
www.pda.org/apfundamentals2

12-14
Validation of Dry Heat Processes Used for Depryogenation and Sterilization
Bethesda, Maryland
www.pda.org/DryHeat

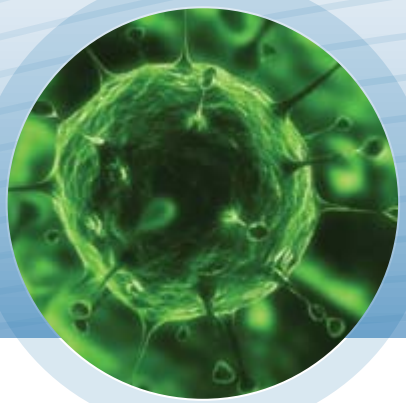
18-22 and
September 22-26
2014 Aseptic Processing Training Program – Session 4
Bethesda, Maryland
www.pda.org/2014aseptic4

27-28
An Introduction to Visual Inspection – Session 2
Bethesda, Maryland
www.pda.org/visual2

PDA Conference Recordings – Interactive Online Learning

Recordings from PDA's 2013 events are now available for purchase.

For more information on all PDA conference recordings, please visit **www.pda.org/onlinelearning**



Pharma Prepares for Smartphones—But Are We Ready?

Brigitte Reutter-Haerle, Vetter Pharma

Smartphones and their related applications—commonly known as "apps"—have taken over many of the tasks in our daily lives that once required a variety of tools and a great deal of effort. Monitoring of the news and weather, designing ideal gym workouts, finding the best restaurants and routes to destinations, and not to mention, instantaneous communication with friends and colleagues, are now easily achieved with the help of a smartphone app. Can it be possible that there is also a role for the smartphone in the world of device technology, particularly prefilled syringes and injection devices?

Recently, pharmaceutical companies, always quick to adopt differentiation opportunities for their products, have begun marketing products that include electronic functions and apps that access social media and offer direct user feedback from patients. In some cases, this information can actually affect a drug device's development. Smartphone technology has even reached a new level of sophistication that has enabled the integration of various reusable or disposable drug delivery devices.

Improved connectivity standards, simplified data exchange, and the automatic start of customized applications with smartphones have offered our industry options in the management of patient data and education that not very long ago were cumbersome and, sometimes, inaccurate. With this new technology, almost anything is now possible from a technical perspective including electronic product information in different languages, application videos, online recall and product expiration warnings, and reminder and dose-tracking apps, to name a few the industry is working on. And best of all, each of these apps can be readily available on your smartphone.

> Immediately following the *2014 PDA Universe of Prefilled Syringes and Injection Devices,* the PDA Training and Research Institute will host four courses. To learn more, visit www.pda.org/pfscourses2014.

But is the industry ready to adopt the technology and changes afforded by the smartphone? And what are the regulatory hurdles that we will encounter when dealing with medical applications? Certainly, regulatory agencies such as the U.S. FDA are sharply focused on the use of mobile medical apps. Issues such as data privacy and lifecycle management must be addressed, not to mention the complexity caused by a rapidly changing market with thousands of different smartphone devices using different operating systems.

Don't just listen in. Be a part of the conversation and stay abreast of this trend by planning on attending a session devoted to the topic at the *2014 PDA Universe of Prefilled Syringes and Injection Devices* conference in Huntington, Calif., Oct. 6–10. Not only will you hear more on what is happening in this exciting area, but you will also be introduced to a variety of different classes of medical devices, and receive guidance on handling the organizational structure when dealing with mobile medical apps and medical devices. Learn more at www.pda.org/prefilled2014.

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Drug Manufacturers Face More "How to Do" CMC/GMP Requirements in Europe

Ursula Busse, PhD, Novartis and Stephan Rönninger, PhD, Amgen

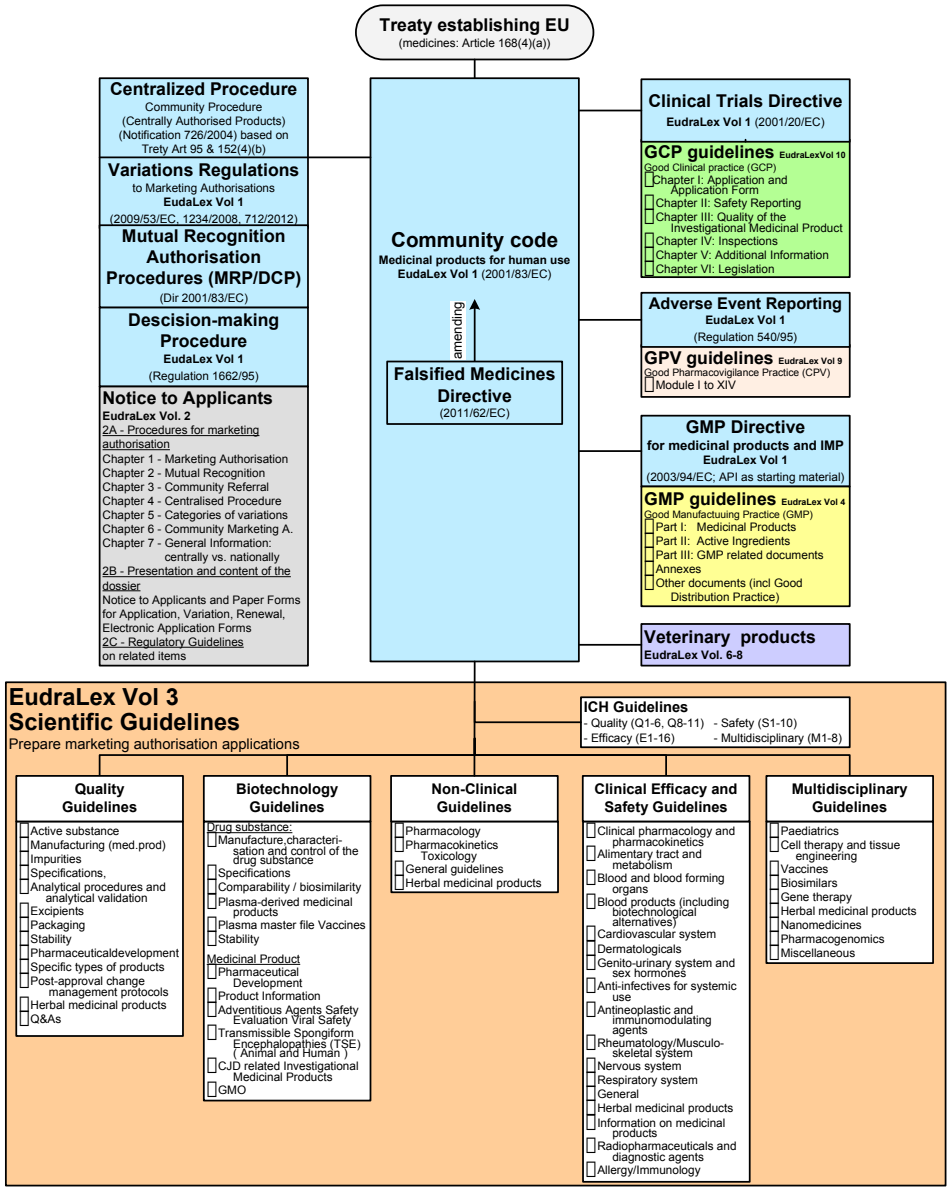
Pharmaceutical manufacturers increasingly are facing more detailed "how to do" requirements focusing on a widening scope of activities (e.g., distribution) in Europe as the European Union continues to upgrade CMC and GMP requirements.

There are three major drivers for regulatory change in the European Union in recent years:

- The new ICH quality paradigm on "*a harmonised pharmaceutical quality system applicable across the lifecycle of the product emphasizing an integrated approach to quality risk management and science*" (ICH Brussels, 2003) and the respective guidelines on ICH Q8, Q9, Q10, and Q11.
- The revised Clinical Trials Directive (CTD)
- Regulations such as the Falsified Medicines Directive (FMD, 2011/62/EC), amending the Community Code (2001/83/EC) **[Editor's Note:** See "Unprecedented EU Rule Changes Shake Industry," page 34 of this issue for more on this Directive and the Clinical Trials Directive. Plus, **Figure 1** outlines how this and other guidelines fit into the legislative framework.**]**

With more "how to do" (prescriptive) regulation, industry is now expected to apply updated guidance not just to newly licensed products, but also to legacy products and processes following a transitional

Figure 1 EU Legislation and Guidelines for Pharmaceuticals



period of a few years. The focus on supply chain oversight for all activities is raising the bar as well as costs in Europe

CMC Updates (Scientific Guidelines)

The CMC Guidances are intended to help in preparing the marketing authorization. Following the revision of several of these guidelines, applicants now have the opportunity to file either according to the "traditional approach" or the "enhanced approach" to development. The enhanced approach is characterized by implementing Quality by Design (QbD) and/or Process Analytical Technology (PAT). This is intended to provide industry more flexibility and allow for quicker implementation of innovative, science- and risk-based approaches to development, manufacturing and release.

The CMC dossier should be clear and support the overall development story. Applicants are required to completely describe the manufacturing process, including identification of critical manufacturing steps and references to non-critical aspects. The applicant should demonstrate full understanding of the process, the lifecycle approach and continual improvement. The dossier should be simple and understandable, and use ICH terminology for increased clarity.

The Quality Working Party at EMA will focus this year on updating filing related procedures to include the ICH Q8–Q11 principles, such as guidelines on the manufacture of the finished dosage form, the chemistry of active substances, genotoxic impurities (see ICH M7), quality risk management for the assessment of applications, stability testing for applications for variations to a marketing authorization and metal impurities (ICH Q3D).

Article at a Glance

- "Traditional" vs. "enhanced" approach to development
- EU GMPs aligned with PIC/S GMPs
- New pharmacovigilance guidelines streamline roles between EMA and member states

Most of the recent and future changes have similar drivers

EU GMP updates

Over the last two years, more than 50% (18/35) of the guidelines in the EU GMPs (*EudraLex Vol 4*) have either been updated or are under revision. It is important to highlight that the PIC/S GMPs will also be updated accordingly to ensure similarity to the EU GMPs, with the exception of Annex 16 on qualified persons and GDP regulations as these are not overseen by health authorities in some member inspectorates.

In **Part I of the EU GMPs** for Medicinal Products, Chapter 1, "Pharmaceutical Quality System" has changed to align with ICH Q10 and to implement quality risk management (QRM) principles. The guidance is clear that the product quality system (PQS) is regarded as a framework to manage all GMP topics, such as appropriately qualified and trained personnel, adequate premises and space, suitable equipment and services, correct materials, containers and labels management, approved procedures and instructions, suitable storage and transport and quality control. Chapter 2, "Personnel" now includes training requirements for senior management.

Revisions to Chapter 3, "Premises and Equipment" as well as Chapter 5, "Production" are about to be issued, potentially addressing appropriate risk reduction measures (e.g., single-use or dedicated facilities) for the issue of cross-contamination. The discussions between agencies and industry with regard to taking safety aspects into account are ongoing. Other prominent changes include traceability of supply chain and testing of starting materials.

Chapter 6, "Quality Control," contains a new section on technical transfer of testing methods and handling out-of-specification results. Chapter 7, "Outsourced Activities," was also updated to include a focus on assessments of suppliers and contractors prior to outsourcing an operation. Emphasis is placed on defining the responsibilities and the communication processes among the parties. Monitoring and review of the performance of suppliers is expected as well as oversight of incoming ingredients and materials.

The requirements for complaints and product recalls outlined in Chapter 8 have been updated with the expectation to implement risk management principles and workflows.

While ICH Q7 is the basis for **Part II of the EU GMPs** (GMP of APIs), Chapter 2.2 was recently added to include two principles from ICH Q9 on risk management. At this time, there is an ICH Implementation Working Group developing a Q7 Q&A document. The key message is that the ICH Q7 document is intended to be read in its entirety regardless of the nature of the manufacturing activities being conducted, in order to fully understand the links between certain sections and successfully implement appropriate GMPs at all stages of the API supply chain, including distribution.

In **Part III, "GMP related documents,"** several guidance documents have been added such as Pharmaceutical Quality Systems (ICH Q10) and Quality Risk Management (ICH Q9) to underline the importance of harmonization within the ICH parties of the United States, European Union, Japan and beyond.

For harmonization purposes the "MRA batch certificate" has been updated to present specifications in a format acceptable to both EU and Mutual Recognition Agreement countries. The template for the Site Master File (SMF), originally developed by PIC/S, is widely used for explaining details of a site and is now included in the EU GMPs. The template for "written confirmation" for active substances exported to the European Union now follows the requirements of the Falsified Medicines Directive (FMD).

The **Annex** section contains several specific guidances. Unfortunately, the recent updates have added more administrative burden and, in our opinion, unproductive activities. Most of the new elements in these guidances provide a different interpretation than the guidance given in the other parts of the EU GMPs. Recent updates focused on GMPs for biologics (Annex 2), and require the zone classifications at the final stage of API manufacturing to be equivalent to the first step in the finished dosage form manufacturing. For air quality and facility design, this might be the case; in many companies, however, not with regard to the intensive testing during operation.

Annex 15, "Qualification and Validation," was open for commenting until May 31. It discusses Stage 3 of the lifecycle, which is called "Ongoing Process Verification," instead of "Continued Process Verification"—the term used in the U.S. guideline. The draft allows implementation of both the traditional and the enhanced development approaches.

The draft guideline on batch certification and release procedures (Annex 16) implements the additional clarification of the 2009 Qualified Persons (QPs) discretion paper from EMA and widens the scope to include QP oversight of the supply chain. This expands the areas of involvement for QPs which, previously, was not part of their education and experience.

One positive change allowed by the revised Annex 16 is the reliance on the quality system and related activities of a company. On the other hand, the draft requires that the sampling for import testing must be done in the European Union, which will have a major delay on the availability of the drugs due to additional time needed after shipment.

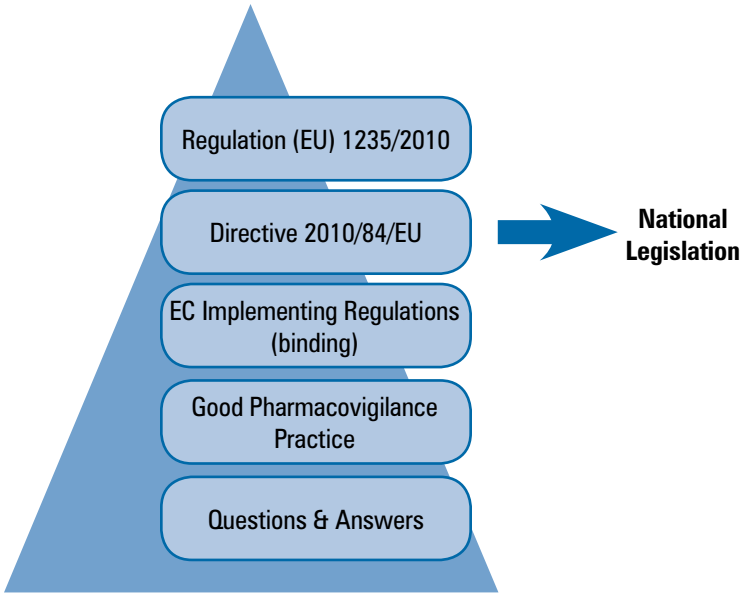
The revision of Annex 17 on parametric release now allows for the implementation of real-time release testing, if applied. This provides more flexibility to companies even if an established product is manufactured and a variation is filed.

The section **Other documents related to GMP** updates the GDP requirement. Major changes focus on supply chain and cold chain oversight as well as transport validation. The extensive content of the *Compilation of Community Procedures on Inspections and Exchange of Information* document was updated with new EU formats and procedures, including a series of guidances for regulators. These documents describe the regulators' procedures and provide relevant templates (e.g., inspection reports) seldom considered in the past.

Recent Changes in Pharmacovigilance Legislation

Adopted by the European parliament and the European Council in December 2010, the new pharmacovigilance legislation came into effect across the European Union in July 2012 as a result of changes set out in Regulation (EU) No1235/2010 and Directive 2010/84/EU. The legislation is reinforced by the legally binding Commission Implementing Regulation No 520/2012, published in June 2012 which provides details on the operational aspects for the new legislation and a series of modules on Good Pharmacovigilance Practice. Most of the legislation had to be implemented within 18 months of becoming law or by July 2012 (**Figure 2**).

Figure 2 Pharmacovigilance Legislation in the European Union



The new pharmacovigilance legislation represents the biggest change to the legal framework for human medicines in the European Union since 1995. The change was prompted by the need to strengthen the European safety monitoring system, establish a clear legal framework for postauthorization monitoring, and to reduce the number of potentially fatal adverse drug reactions.

In 2011, the legislation was tightened even further after the scandal involving Servier's diabetes drug Mediator (benfluorex), suspected to have caused more than 500 deaths in France. Amendments were published in October 2012 in Regulation (EU) No 1027/2012, applicable as of June 2013 and Directive 2012/26/EU, which applies as of October 2013. The amendments aim to further strengthen the protection of patient health by allowing prompt and appropriate regulatory action.

The new legislation streamlines respective roles and responsibilities between EU Member States and the EMA. It strengthens transparency rules related to pharmacovigilance data and establishes clear standards (Good Pharmacovigilance Practices, or GVP) for the conduct of pharmacovigilance by both industry and regulators. GVP guidelines have been released by EMA and replace the EC's pharmacovigilance guidance for human medicinal products (*EudraLex Volume 9A*).

The new pharmacovigilance legislation has significant implications for applicants and holders of EU marketing authorizations. Some examples are given below.

Safety Monitoring

Periodic Safety Update Reports (PSURs) have a single assessment for the same active substance or a combination of active substances. Routine PSUR reporting is no longer necessary for products with low risk or for established products unless concerns arise. PSURs are sent directly to EMA in standardized electronic format. Format and content are based on the Periodic Benefit Risk-Evaluation Report (PBRER) described in the ICH E2C (R2) from 2012. ➤

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There is a strengthened legal basis for requesting Post-Authorisation Safety and Efficacy Studies (PASSs/PAESs) from the pharmaceutical industry. EMA's Pharmacovigilance Risk Assessment Committee (PRAC), formed in 2012, is responsible for assessing the protocols of imposed PASSs and for evaluating their results. Risk management systems are required for all newly authorised medicines. Companies must submit a risk management plan to the Agency at the time of application for a marketing authorization. Risk management plans are continually modified and updated throughout the lifetime of the medicine as new information becomes available.

Safety Referrals

All pharmacovigilance referrals are discussed by the PRAC and the Committee for Medicinal Products for Human Use (CHMP) or the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh). Opinions are adopted as a result.

Adverse Event Reporting

Following a successful audit, marketing authorization holders submit adverse event reports only via EudraVigilance, a centralized Web-based information system designed to manage information on safety reports. Previously, reports were sent via the individual national competent authority.

Inspections and Pharmacovigilance Systems

The new legislation requires the introduction of a Pharmacovigilance System Summary in the marketing authorization and removes the requirement for new applications to contain a Detailed Description of the Pharmacovigilance System (DDPS). Marketing authorization holders are required to maintain a pharmacovigilance system master file (PSMF) permanently available for submission or inspection by the national competent authority. The file has to include all significant internal audit findings which can only be removed once corrected.

Products Under Additional Monitoring

Under the new pharmacovigilance provisions, some medicinal products for human use are subject to additional monitoring due to their specific safety profile. Those products have to bear a black inverted triangle on the package and package leaflet. With this measure, the EC aims to improve the safety of medicines and also to highlight to patients the importance of reporting suspected side effects to the medicines they are taking.

In early 2014, a three-year EU initiative, Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE), was launched to support implementation of the new legislation. SCOPE will help member states to harmonize pharmacovigilance activities, while ensuring that member states implement best practices and maintain the highest possible standards, measured against agreed benchmarks. The U.S. FDA and EMA have also initiated a new "cluster" on pharmacovigilance topics. Clusters are regular collaborative meetings between the EMA and regulators outside of the European Union, which focus on specific topic areas that have been identified as requiring an intensified exchange of information and collaboration. This cluster will provide a forum for a more systematic and focused exchange of information on the safety of medicines.

Final thoughts

The European Union's legislative framework for pharmaceuticals is undergoing major changes. Most of the recent and future changes have similar drivers: an expansion of the European Union to 28 member states—all with different national legislation—and the necessity for EU-wide harmonization; rapid progress in innovation which is giving rise to new technologies and novel therapies that need to be covered by additional regulations; and finally, globalization and the need to align with regulations outside of the European Union. Revised regulations focus on risk-based approaches and introduce a number of new requirements meant to support product quality and protect patient safety.

Acknowledgement

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Unprecedented EU Rule Changes Shake Industry

Peter Gough, NSF International

The rate of ongoing changes to European pharmaceutical legislation and guidance are at an unprecedented level. Many are likely to have a profound impact on the industry over the next five years and some will require significant investment.

Clinical Trials Regulation Proposal

On April 2, the text of a new Clinical Trials (CT) Directive, which will repeal the 2001 Directive, was approved by the European Parliament. The regulation is expected to be published in the *Official Journal of the European Union* shortly. The fact that the new legislation will take the legal form of a regulation will ensure that the rules for conducting clinical trials are identical throughout the European Union. This is vital in ensuring that Member States adhere to identical rules in authorizing and supervising the conduct of a clinical trial.

The European Parliament rewrote the CT Directive because the 2001 version failed to ensure harmonization among Member States (MS). An enormous bureaucracy associated with running clinical trials developed in order to manage specific MS requirements, resulting in a significant decline in the number of clinical trials conducted in the European Union.

A key change has to do with the selection of a MS to lead the assessment of the CT authorization submission. Sponsors can suggest the "reporting" MS to lead the assessment from among the MS in which the trials are to take place. If the concerned states do not agree on which nation should lead, the sponsor's selection is chosen.

The revised CT Directive creates:

- A "low intervention" clinical trials category
- An EU e-portal for CT authorization (CTA) submission
- Maximum allowed timeframes for assessment process steps

In addition, the Directive harmonizes the content of the CTA dossier, ensuring all MS have the same information available. This is intended to simplify the application process.

Falsified Medicines Directive (FMD) Implementation

In February 2014, it was reported that the European Commission had completed its impact assessment regarding the safety features required by the Falsified Medicines Directive and was proceeding to draft a delegated regulation to propose that:

1. The composition, format and carrier of the unique identifier will be fully harmonized across the European Union. The unique identifier will be placed in a 2-D barcode and contain the manufacturer code, a serialization number, a national reimbursement number (if present), the batch number and the expiration date.
2. Medicine authenticity will be guaranteed by an end-to-end verification system supplemented by risk-based verifications from wholesale distributors. Medicines will be systematically verified before being dispensed to patients. Medicines at higher risk of falsification (returns or medicines not being distributed directly by manufacturers) will be additionally checked at the wholesaler level.
3. The repository containing the unique identifiers will be set up and managed by stakeholders (i.e., in the European Stakeholder Model). National competent authorities will be able to access and supervise the database.

It is likely that the provisions of the delegated regulation would not have to be implemented before 2018 by the time it winds its way through the process.

Of course, the European Union is not alone in implementing serialization and tracking of medicinal products. When taken together with the requirements of other markets, the implementation of this aspect of the FMD is going to require significant investment from the industry over the coming years.

Revised Process Validation Guidance

On Feb. 27, the EMA published the final version of the revision of the Committee for Medicinal Products for Human Use (CHMP) *Guideline on Process Validation for Finished Products* that replaces the existing CHMP guidance on this topic. The revised version becomes effective Aug. 27.

Unlike the 2011 U.S. FDA guidance on process validation, the EU guidance states that it does *not* introduce new requirements for medicinal products already authorized and on the market *nor is it* applicable to APIs.

The final CHMP guidance states that the product lifecycle consists of three stages and that this guidance covers Stage 2 **(Table 1).**

The scope of this draft revision covers both human and veterinary products, including biological products (on a case-by-case basis in view of their complex nature and inherent variability).

The guidance allows different approaches to process validation: the traditional approach, a "continuous process verification" approach, and a "hybrid approach" that combines the two.

The number of batches required for process validation has been a subject of much debate since the FDA finalized its guidance in January 2011. The revised CHMP guidance states:

> *The number of batches should be based on the variability of the process, the complexity of the process/product, process knowledge gained during development, supportive data at commercial scale during technology transfer and the overall*

Table 1 Three stages and the applicable guidance

Lifecycle Stage	Applicable EU Guidance
1 – Product development	ICH Q8R2
2 – Process validation	This new CHMP guidance
3 – Ongoing process verification	EU GMP Annex 15

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experience of the manufacturer. Data on a minimum of 3 production scale batches should be submitted unless otherwise justified. Data on 1 or 2 production scale batches may suffice where these are supported by pilot scale batches and a justification...

So, the EMA appears to still be wedded to the traditional approach and the magic three batches, which is disappointing. The 2011 FDA guidance on process validation moved the whole concept of process validation away from being a one-time event, conducted around the time of submission of the regulatory dossier to obtain a marketing authorization, to a lifecycle process

The new approach given in section 5.2 of the guidance is called "continuous process verification" and is essentially one part that has become more generally known as the QbD approach, following the implementation of ICH Q8.

Section 5.3 is titled "Hybrid approach" and allows for the use of the traditional approach for some steps in a manufacturing process and the continuous process verification approach in others. Section 5.4 gives requirements for design space verification.

EU GMP Annex 15: Validation

A draft of a revised Annex 15 was published for comment on Feb. 6. Comments were due May 31.

The section on process validation makes reference to the CHMP's *Note for Guidance on Process Validation* and uses the same terminology as the aforementioned *Guideline on Process Validation for Finished Products* to describe traditional and continuous verification approaches to product development.

Draft Annex 15 requires that "the basis by which process parameters and quality attributes were identified as being critical or noncritical should be clearly documented…" The validation protocol must define the "critical process parameters, critical quality attributes and the associated acceptance criteria which should be based on development data or documented process knowledge."

Products that have been developed by a QbD approach can follow a continuous process verification approach as an alternative to traditional process validation. A hybrid approach using the traditional approach and continuous process verification for different production steps can also be used.

The section "Qualification stages of equipment, facilities and utilities" addresses user requirements specification (URS), which was a glaring omission in the 2001 version. The URS is an essential starting point because, as the new draft states, "The URS should be a point of reference throughout the validation life cycle." This section also has new requirements for factory acceptance testing/site acceptance testing.

There is a section that is analogous to Stage 3 of the 2011 FDA guidance on process validation, but the FDA description of continued process verification for this stage is replaced by '"ongoing process verification" in the draft Annex 15. Presumably, this change of terminology is to avoid confusion with the continuous process verification approach. This section states that "statistical tools should be used, where appropriate, to support any conclusions with regard to the variability and capability of a given process and ensure a state of control."

The revised section on cleaning validation requires that "limits for the carryover of product residues should be based on a toxicological evaluation to determine the product specific permitted daily exposure (PDE) value." This aligns with the draft changes to EU GMP Chapters 3 and 5 and the draft CHMP *Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities* that was published in January 2013.

Other changes to the cleaning validation section include the need to assess the influence of the storage time before cleaning and the time between cleaning and use, which should be taken into account when defining hold times (dirty and clean) for the cleaning validation. The maximum length of a campaign (in both time and number of batches) should be the basis for cleaning validation exercises.

EU GMP Chapter 6–Quality Control

The final version of a revised Chapter 6 was published in late March 2014 and becomes effective Oct. 1, 2014.

The final version is almost identical to the draft revision that was published on January 17, 2013. This revision adds more emphasis on the need to investigate out-of-specification and out-of-trend results, including adequate procedures for OOS/OOT results.

Other revisions involve test method validation and technical transfer. In particular, the chapter now calls for validation of test methods that were not originally validated by the laboratory using them. It also states that reference standards must be certified, qualified and verified as suitable for the intended use.

There are new requirements relating to the use of secondary reference standards, the preparation and verification of culture media, and the control of animals used in testing.

Conclusion

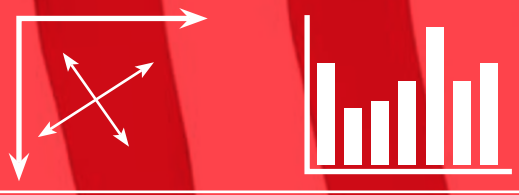
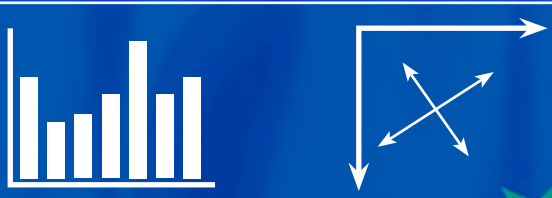
The rate of change is probably higher than it has ever been. If pharmaceutical companies are to keep up and remain in compliance, it is essential that they keep abreast of the numerous changes and make the necessary investments in people, capabilities and facilities that these changes will require.

About the Author

A chemist with a master's degree in analytical chemistry, **Peter Gough** has over 35 years' experience of pharmaceutical manufacture, control and quality management. He has broad experience, particularly with quality control laboratories and the manufacture of solid dosage forms and active pharmaceutical ingredients.

U.S. vs EU PROCESS VAL GUIDANCES

= indicates where the two guidelines are exact
≠ indicates where the two guidelines suggest differences
≈ indicates where the two guidelines share similarities

2011 U.S. FDA Guidance		2014 EMA CHMP & Annex 15 guidelines
DEFINITION: "The collection and evaluation of data, from the process design stage through commercial production, which establishes scientific evidence that a process is capable of consistently delivering quality products."	≈	**DEFINITION:** "The documented evidence that the process, operated within established parameters, can perform effectively and reproducibly to produce a medicinal product meeting its predetermined specifications and quality attributes." (ICH Q7)
Process Performance Qualification (PPQ) introduced with concurrent release as a goal	≈	Performance Qualification recognized for Stage 3
Nonstandardized drugs defined as orphan drugs, radiopharmaceuticals, etc.	≠	Nonstandardized drugs defined as biologicals, biopharmaceuticals, special dosage forms, etc.
Emphasizes importance of statistics throughout lifecycle 	≈	 Statistics only emphasized as an option in an ideal situation
Clearly endorses continuous process verification for Stage 3	≈	Calls ongoing process verification "an alternative approach" for Stage 3
Purports to align with ICH Q8/11, Q9 and Q10	=	Purports to align with ICH Q8/11, Q9 and Q10

Special thanks to **Stephan Rönninger,** PhD, Amgen, for his assistance with this infographic.

GDP and GSP Regulatory Changes: Impact on your Logistics

Peter Norton, DeltaTrak, and Ding Enfeng, Shijiazhuang Lonzeal

In September 2013, the EU Good Distribution Practices (GDP) guideline for medicinal products became effective. Also in 2013, the Chinese FDA (CFDA) implemented their new Good Supply Practice (GSP) guidelines with the expectation that all Chinese drug distribution companies should be able to pass GSP certification after June 30, 2016.

Both of these new regulations are very similar in content and contain recommendations related to total supply chain risk aversion planning for all products covered under these guidelines. They also include specific supply chain management recommendations for cold chain and ambient products, with added directives and control initiatives aimed at preventing falsified medicinal products from entering the supply chain at any point.

The focus of both these regulation is on ensuring a secure supply chain with an aim to maintaining the quality, safety and efficacy of products from "source to patient."

Similarities in Supply Chain Guidelines

Quality Management System (QMS): Both require a fully documented QMS with a documented risk mitigation plan, appropriate and focused Standard Operating Procedures (SOPs) and Work Instructions (WIs) with a program for self-audits.

Personnel, hiring and training: Both require that all personnel hired have the background, qualifications and experience to perform the tasks they are hired for. Additionally, there should be ongoing training, and the European Union requires identifying a "responsible person" who manages compliance.

Documentation: Both require that all processes and procedures are documented, change control processes are in place and all documents are signed off to the appropriate level of authority—in the European Union, this includes the "responsible person."

Risk management: Both require drug distribution companies establish risk management plans and related SOPs.

Facilities: Both require conditions be maintained and monitored to ensure that products are stored and kept in conditions recommended by the manufacturers to maintain peak efficacy and quality. This includes cold chain, other controlled products, and products in quarantine. Both also define facility security and outline methods for preventing animals and bugs from entering the facility.

Transportation: Both require that medicinal products transported outside the controlled facility match the same environmental controls defined for their storage and these conditions are maintained until delivery to the patient.

Operations: Both include strict rules on where to obtain products, including approved packaging. Products can only be purchased via authorized distribution channels.

Complaints, returns, and suspected falsified medicinal products: Both require that all such products must be recorded and handled carefully according to written procedures, with records available for the appropriate authorities. All supply chain partners should have a consistent approach to controlling the entry of falsified medicines into the supply chain.

Outsourced activities: These should be correctly defined and controlled with a written contract outlining each party's duties. The services provider should have their own quality system in compliance with regulations subject to audit.

Sales and purchase records: Both require that accurate records are maintained for all sales and purchase transactions which match quantity, type of products (lot and serial number) and have the appropriate signatures from responsible parties.

Computerized systems and electronic data management: Both require drug distribution companies to implement strict management procedures for computerized data systems, in order to ensure data integrity and product quality.

Differences in Local and Global Impact

In regards to the local impact, the EU regulation clearly states that this will apply to any "actors" involved in distribution, wholesaling, and brokering of drugs—right back to the manufacturer, if they perform direct distribution of their own products.

Wholesale distribution activities are defined as including all activities relating to: procuring, holding, supplying or exporting (global impact) medicinal products. Therefore, the primary focus is on finished goods and patient protection.

It should be noted, however, that this regulation only applies to medicinal products, not APIs.

There are existing regulations within the European Union related to APIs requiring that these must have a certificate of authenticity and quality provided with them when shipped from countries other than Australia, Japan, Switzerland and the United States.

The new Chinese FDA regulation goes a lot further toward preventing falsified medicines from entering the supply chain by total verification of suppliers, review of vendor licenses, and documentation controls on what is ordered compared to what is delivered; in essence, a basic level of a "drug pedigree."

To this end, audits and compliance will be highly regulated under Article 79 of the Chinese Drug Administration Law that allows for heavy fines and potential loss of operating licenses for manufacturers, distributors, or wholesalers that do not comply.

Domestic API manufacturers within China do not need a GSP certificate to support API distribution. Foreign API importers will need a GSP certificate to support distribution. ➤

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Additionally, the Chinese GSP regulation has five annexes to address specific topics, two of which relate solely to temperature and humidity environmental monitoring for drug storage and shipment, including cold chain, or frozen drug storage, and transportation management.

Harmonization and Global Impact

Even though a life sciences company may be based in one region of the world, it is highly likely that they will ship products to different global locations. Therefore, with the new regulations being similar in content and structure, the approaches that global manufacturers, shippers and distributors implement for ensuring global compliance should be harmonized.

Within the European Union, there are 18 member countries that have accepted the new GDP regulations but may have slight variations on how they interpret compliance.

Raw materials and goods coming into the region from ICH countries, like Australia, the United States, Japan, etc., are exempt by the level of their own accepted standards and controls. But other regions exporting APIs and raw materials to the European Union will need a certificate of quality and authenticity, preferably from a regulatory authority.

Note: CFDA also requires that all API and finished drug importers should obtain an import license and submit the imported products for testing to be conducted at the Beijing, Shanghai or Guangzhou drug control institutes.

No matter what changes may be pending, or recently introduced, there are certain and basic key activities to ensuring compliance with all forms of global compliance. These are:

- Keeping up to date on new regulations
- Education and self-audits
- Maintaining a fully documented QMS—including a fully documented risk mitigation plan
- Appropriate staff training

These activities are recommended, at a minimum, for any medicinal product producer, warehouse operator, wholesaler or distributor that manages cold chain products.

About the Authors

Peter Norton is currently employed as the Business Development Director for DeltaTrak. He has had previous global program and project management responsibilities gained from advising clients on more efficient approaches to monitoring/managing cold chain logistics.

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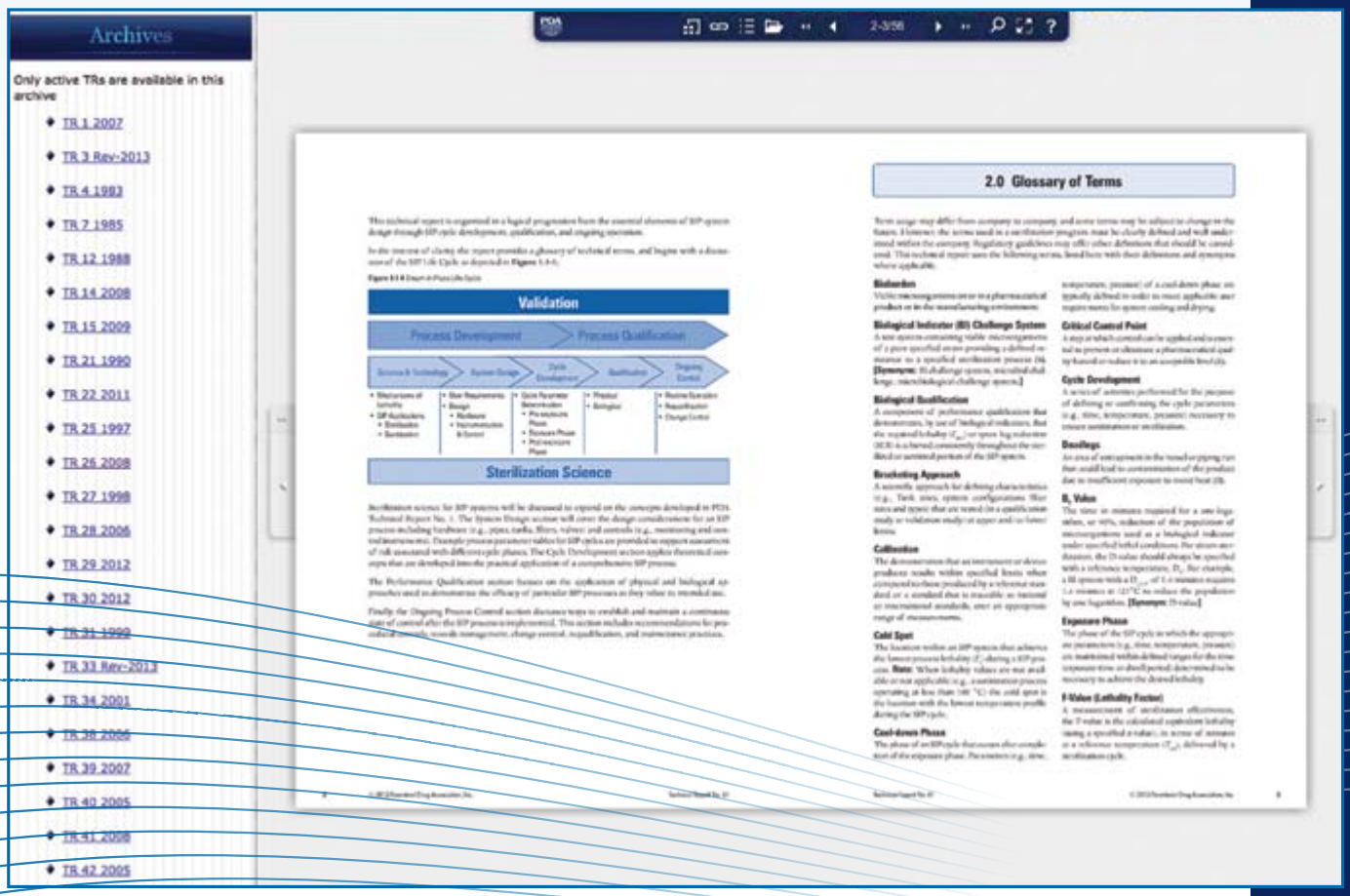

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Today's Challenges for QA Personnel

Robert Kieffer, PhD, RGK Consulting

Perhaps it's a cliché to say that it is a rapidly changing world, but in the world of pharmaceutical quality assurance, it is rapidly changing, or at least in my opinion, the role of QA should be changing.

It is well known that quality practices in pharma have lagged behind best practices in other industries. ICH Q10 Pharmaceutical Quality System, along with ICH Q8 Pharmaceutical Development, ICH Q9 Quality Risk Management, ICH Q11 Development and Manufacture of Drug Substances, and the U.S. FDA's 2011 process validation guidance, have revolutionized our thinking about quality, or better said, brought our thinking about quality up to date.

What are some of the challenges today for QA?

- Quality is the responsibility of all employees. The pharmaceutical quality system is the responsibility of senior management. How does QA fit in this scenario?
- Moving from Quality by Inspection (the concept of quality in the mid-'50s) to Quality by Design
- Moving from policing quality to promoting quality
- Moving from a reactive mode to a proactive one and the shift to prevention in our CAPAs
- Thinking of quality as not just compliance with regulations and passing an inspection, but as adding value to the patient (cost, service, and product safety and efficacy) and to the company
- Reducing the Cost of Quality; especially the costs of failure and appraisal.

In my opinion, this requires a change in mindset for QA personnel and the acquisition of new skills. The transition to the new world of quality needs to start with changes in the quality department.

One of the new desirable skills is the design of better processes. QA has little responsibility for the design of the production process, but does have control of the design of many supporting processes, such as documentation, change control, investigation of failures, auditing, etc. Furthermore, QA can influence the design of processes such as training, supply chain/materials management and validation. Many failures or deviations are assigned to human error, but in reality the cause is a poorly designed process. Processes must be designed to be simple and fail-safe. It should be difficult for an operator to make an error. Process design or process reengineering is usually a team activity. QA needs to possess an effective methodology for process design and have the capability to facilitate teams.

Another aspect of process thinking for QA is process assessments. Processes are audited not departments. It is a process that delivers the desired output; all important processes are cross-functional. Frequently, the weak links in the process are the communication steps between departments. The process assessment consists of

several factors: (1) Is the process well designed to prevent errors and achieve its desired output efficiently and effectively? (2) Is there a designated process owner who has the responsibility to manage, monitor and improve the process? (3) Has the process been implemented and all users understand it? (4) Is the process integrated with other processes so that they form one system? (5) What are the results? Each process should possess a set of metrics ***(1).***

Since senior management is responsible for the Pharmaceutical Quality System (PQS), what can QA do to help senior management? First, the PQS consists of processes—the production process, the supplier process, supporting processes and management processes; so, one thing that can help is the QA expertise in designing good processes as mentioned above. Furthermore, since QA has the expertise on best quality practices they can assist management in the development of the quality policy and the quality manual.

An important activity for management is the periodic review of the PQS, hopefully, monthly. QA is an ideal candidate to be secretary of this meeting and set the agenda along with the plant manager and the team leader, as well as provide a summary of the data/metrics on the PQS. The collection of data on the performance of the PQS and the analysis—root cause and risk analysis—of this data is a very important activity which QA can facilitate ***(2).***

Finally, QA must have credibility. It must show a high level of competence in the areas described above. It must demonstrate the power and capability to make tough decisions. Furthermore, it must be seen as understanding the business dynamics and the problems of production and other departments; as contributing to improving processes; as serving as a trusted member of the team; as having exceptional expertise in the areas of quality, etc. QA needs to be seen as a department that can help and even train senior management.

[Author's Note: An article on this topic will be published by the author in the July/August 2014 *PDA Journal of Pharmaceutical Science and Technology*.**]**

Robert Kieffer will be teaching a course on the role of the quality professional following the *2014 PDA/FDA Joint Regulatory Conference.* Go to www.pda.org/pdacourses2014 to learn more.

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Jette Christensen, Novo Nordisk A/S

PDA Members Support Numerous Science Activities

"Science" is one of the three pillars in our strategic plan, but obviously it interacts with the other two: People and Regulation. PDA is a global organization and currently we have 24 chapters throughout the world where science-based activities are executed. We have interest groups in both the United States and Europe that also are involved in science activities.

PDA's vision is "to be the foremost global provider of science, technology and regulatory information and education for the pharmaceutical and biopharmaceutical industry" and PDA's mission is "to develop scientifically sound, practical information and resources to advance science and regulation for the pharmaceutical and biopharmaceutical industry through the expertise of our global membership."

As you can see, science is a key part of our foundation.

My personal experience with science activities in PDA has been very positive. Being active, I meet a lot of very knowledgeable colleagues from whom I have learned a lot. My involvement also allows me to possibly influence the content of a conference or technical report as well as the general scientific development within PDA.

Of science-based deliveries, technical reports are one of my favorites. Recent improvements to benefit the members include substantial modifications in the workflow, meaning that the time to prepare a technical report has been brought down from several years to 18 months. This has led to a record number of ten technical reports published in 2013—and expectations for 2014 are that we will maintain the same high level.

Science is a central part of PDA's vision and mission. And when it comes to living out the vision and mission we are doing it, first and foremost, because the dedicated members and the competent staff of PDA are bringing forward these activities.

Your Local PDA Connection

Are you curious about the issues unique to your region?

Another layer of PDA leadership resides at the grassroots level in the Chapter organizations. Regional PDA Chapters provide local services to the membership, including translations of PDA publications, networking social events, student scholarship and annual regulatory and technical conferences. Each Chapter is managed by volunteer leaders.

Learn more about your local Chapter at www.pda.org/Chapters

Sophomore Trip to Annual Meeting Bears More Fruit

A big component of being one of the editors for the *PDA Letter* involves attending PDA meetings. In April, I attended my second *PDA Annual Meeting*, and this time around was a totally different experience. As a neophyte in 2013, I was still too new to PDA and didn't know what to expect at the large event. This year, I enjoyed every aspect of the meeting—the informative talks, poster presentations, vendor exhibits, networking opportunities and even some of the sights in San Antonio, Texas. You may have even seen me attempting to dance at the Monday night gala!

But what I enjoy most about the Annual Meeting, in particular, is having an opportunity to speak with and learn from PDA members around the world. This year, I talked to members hailing from Germany, Belgium, Switzerland, Italy, Canada, Taiwan, Israel, Japan...just to name a few of the locations. I also, along with *PDA Letter* Editor **Walter Morris,** had the opportunity to grab some beers with plenary speaker **Wilfried Dalemans,** who clarified some points he made in his talk. This relaxing discussion helped me prepare last issue's cover story. It's amazing to see that while we may be in different places scattered across the globe, we all face the same challenges of striving to meet quality goals in a shifting regulatory environment.

In keeping with our goal of providing more globally focused content, this issue looks at recent changes in the European regulatory space. **Ursula Busse** and **Stephan Rönninger** look at CMC and GMP updates, in addition to pharmacovigilance changes, in our cover story, while **Peter Gough** examines the Clinical Trials Directive, the Falsified Medicines Directive, process validation requirements and updated quality control guidance (see page 34).

For the issue's Infographic, we worked closely with Stephan Rönninger to compare the EU and U.S. process validation regulations—an update to the Infographic in the April 2013 *PDA Letter* based on new information and updated guidance.

In our Regulation section, **Peter Norton** and **Ding Enfeng** compare the similarities between EU and Chinese supply chain regulations.

Staff at PDA were saddened to learn of the recent passing of Daikyo Seiko President **Masamichi Sudo.** Member **Patty Kiang** was gracious enough to submit an obituary for him, which we translated into Japanese for the benefit of readers located in Sudo's home country of Japan (p. 13).

Speaking of the Annual Meeting, check out the PDA Photostream for pictures from the conference, exhibits and networking events. We hope that you'll consider joining us next March for the *2015 PDA Annual Meeting* in Las Vegas!

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

The *PDA Letter* podcast is available at www.pda.org/pdaletter.

PDA Letter

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