

PDA Letter

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October 2007




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Quality Systems



November 1-2, 2007 | Bethesda, Maryland
December 10-11, 2007 | Dublin, Ireland
April 21-22, 2008 | Beijing, China
April 24-25, 2008 | Shanghai, China

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QbD: Still in Design?

A Report from PDA's QbD Workshop

Bert Frohlich, Amgen

Organized by general themes, this report summarizes the presentations, discussions and experiences shared by participants at the May 21-22 Quality by Design for Biopharmaceuticals workshop in Bethesda, Md. The pharmaceutical and biopharmaceutical industries and two regulatory agencies were represented.

Although the quality by design (QbD) for biopharmaceuticals concept was introduced to the biopharmaceutical industry relatively recently, it was acknowledged by both the U.S. FDA and industry that QbD is not a new concept. To some degree, this rational design approach has been used previously by practitioners of process development. There was, however, fairly wide agreement that a need exists to establish a structured framework that stimulates innovation and continuous improvement for the design of products and manufacturing processes for biopharmaceuticals, as well as small-molecule drugs. It was stressed on multiple occasions that this quality initiative is not a revolution but simply an evolution in drug design and specification and of the relationship between industry and its governmental regulators.

The main objective of this initiative is to build quality into manufacturing processes and product release rather than testing it in. The ultimate goal, as envisioned by FDA, is the *desired state*, defined as follows: [Cherney]

Maximal efficient, agile, flexible pharmaceutical manufacturing sector that produces reliable high-quality products without extensive regulatory oversight.

This state would encourage:

[Cherney]

- *A regulatory process that is consistent, transparent and science-based*
- *A regulatory process that allows for efficient and effective continuous improvement*

Editor's Note: Speakers cited are referenced in brackets throughout the article and listed in a box on page 29. Any opinions expressed by the author are his own and not Amgen's. When the author cites from speakers' slides, italics text is used.

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2008 PDA/EMEA Joint Conference

European GMP: Current Issues and Future Developments



18-21 February 2008
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- **Annex 2**
- **Variations**
- **New Guidance**
- **Future of Inspections**
- **And More...**

Most importantly, there will be an extraordinary number of speakers from the EMEA, the European Commission and the national authorities. Rarely have so many officials from so many authorities across Europe committed to present their views and participate in discussions on evolving GMPs. And never has interaction with European inspectors been this convenient.

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Cover art:
QbD, building a new paradigm for quality?
 Artwork
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Editor's Message

One area of contribution I frequently make to the *PDA Letter* is sharing reports on PDA's biggest events with the membership. For instance, the Nov/Dec issue of each year is typically reserved for my reports on the PDA/FDA Joint Regulatory Conference. In this issue, I'm pleased to say that we have a fantastic meeting report on the May 2007 PDA meeting on Quality by Design for biotech products. I'm equally pleased to announce that I am not the author! I wish to thank **Bert Frohlich**, a PDA member with Amgen, for furnishing this very well-written account of the meeting. I think Bert has a really good eye for journalism as he captures many of the most important discussions that took place during the event.

The Quality & Regulatory Snapshot makes its second appearance in this month's issue. PDA's **Bob Dana** deserves a lot of credit for supplying much of the content in this Q&R Snapshot. **Jim Lyda** contributed to it as well. Jim also was instrumental in rounding up the articles in the Europe section of this issue.

In the Science & Technology Snapshot, we are running the first "In Print" snapshot, an excerpt from a newly published PDA-DHI technical book. This month's selection is from *Validation of Analytical Methods for Biopharmaceuticals: A Guide to Risk-Based Validation and Implementation Strategies*, by **Stephan Kraus**, PhD. We look to run the "In Print" regularly in the S&T Snapshot.

Programs & Meetings checks in with an update on their department, which includes a photo of all the people who help deliver PDA's excellent conferences, meetings and workshops.

Finally, **Gail Sherman** explains in her TRI Talk how she and her staff "conquered" Bethesda. 🇺🇸

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PDA Letter Editor

Walter Morris
+1 (301) 656-5900, ext. 148
morris@pda.org

Assistant Editor

Lindsay Donofrio
donofrio@pda.org

Advertising

Cindy Tabb, Sales
+1 (301) 656-5900, ext. 222
tabb@pda.org

PDA Letter Editorial Committee

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PDA Global Headquarters
Bethesda Towers
4350 East West Hwy., Suite 200
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900
Fax: +1 (301) 986-0296
Email: info@pda.org
www.pda.org

PDA Europe
Adalbertstr. 9
16548 Glienicke/Berlin
Germany
Tel: +49 33056 43 6879
Fax: +49 33056 43 6884
Email: petzholdt@pda.org

PDA Training and Research Institute
4350 East West Hwy., Suite 150
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900
Fax: +1 (240) 482-1659
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IPQ—New Member Benefit—Mails in October

PRESIDENT'S MESSAGE



Bob Myers

On behalf of PDA's Board of Directors, I am pleased to announce that the inaugural issue of *International Pharmaceutical Quality*[™], the newest benefit of PDA membership, mailed to members in October. From now on, all PDA members will receive IPQ[™] six times per year—a \$400 value—at no additional charge.

I want to recognize the Board of Directors for making the bold decision to partner with **Bill Paulson** to create *International Pharmaceutical Quality*[™] and to fold the publication into the standard membership benefits package. IPQ[™], along with PDA Technical Reports, the *PDA Journal for Pharmaceutical Science and Technology*, the *PDA Letter*, and discounts to all PDA events and training make membership in PDA a valuable and cost-effective tool for professionals in the pharmaceutical/biopharmaceutical industry around the world.

Please, let us know what you think of *International Pharmaceutical Quality*[™]. Without your support, IPQ[™] would not be possible. For more information on IPQ[™], go to www.ipqpubs.com. In addition, you can contact PDA Managing Editor Walter Morris directly at 301-656-5900, ext. 148, or morris@pda.org with any questions or comments regarding IPQ[™].

I hope you find this new member benefit both useful and valuable. ☺



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www.pdatraining.org/watersystems

DECEMBER 5-6

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The PDA Training and Research Institute will also be conducting the following training course at the Industrial Pharmacy Laboratory of the Institute of Pharmaceutical Technology in Basel, Switzerland:

DECEMBER 4-6

Practical Aspects of Aseptic Processing
www.pdatraining.org/paap

TR-39 Revised Takes Global View

Training on the Document Ongoing

PDA published Technical Report No. 39 (Revised 2007), *Guidance for Temperature-Controlled Medicinal Products: Maintaining the Quality of Temperature-Sensitive Medicinal Products through the Transportation Environment*, updating the 2005 version of the document. The revision broadens the global applicability of the document by harmonizing with both the regulatory requirements of the US Food and Drug Administration (FDA) and the EU's European Medicines Agency (EMA). The document and the training will benefit both manufacturers of temperature-sensitive products and the companies that ship such products.

“Technical Report No. 39 was a landmark document for PDA, as it introduced best practices for controlled temperature shipping to our membership and the industry at large,” says PDA President Bob Myers. “The updated version expands the document's applicability globally by harmonizing with the expectations of EU regulators.”

The rewrite was prepared by the PDA Temperature-Controlled Pharmaceuticals Group—Harmonization Task Force, a panel of experts from the pharmaceutical industry with significant experience manufacturing and shipping temperature-sensitive products. The members of this international group are:

- **Rafik Bishara**, PhD, Eli Lilly and Company (chair)
- **Detlef Dichte**, Eli Lilly and Company
- **Shirley-Ann Feld**, Sanofi-Aventis
- **Janne Grusgaard**, Novo Nordis
- **David Patrick**, Johnson & Johnson
- **Bob SeEVERS**, PhD, Eli Lilly and Company
- **Edward Smith**, PhD, Wyeth
- **David Ulrich**, Abbott Laboratories
- **Wigand Weirich**, PhD, Roche
- **Karl Womastek**, Baxter

Members of the task force will be participating in training workshops and lecture courses in the coming months. Training has taken place already in Berlin and Cork. More workshops are planned in the United States in 2008. Check the PDA website and the *PDA Letter* and the *PDA Connector* for dates. ☞

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A “Sneak Peak” at Upcoming Technical Reports

Rich Levy, PhD, PDA

In the June Science & Technology Snapshot, I wrote about the model PDA developed for generating technical reports during the process of completing Technical Report No. 1. I am pleased to report that we are holding our first Technical Report “Sneak Peak” on Nov. 5.

Five PDA technical reports will be discussed at this meeting by members of the expert Task Forces drafting them:

- Technical Report No. 15, Revised 2008, Validation of Tangential Flow Filtration Systems in Biopharmaceutical Applications
- Technical Report No. 14, Revised 2007, Validation of Column-Based Separation Processes
- Technical Report Draft, Risk Management for Aseptic Processing
- Technical Report No. 3, Revised 2008, Dry Heat Sterilization and Depyrogenation
- Technical Report No. 26, Revised 2007, Sterilizing Filtration of Liquids

We are grateful to our members at Amgen for agreeing to host this conference at their facility in Thousand Oaks, Calif. I look forward to participating in this first TR Sneak Peak and hope to see many PDA members there.

In this month’s Snapshot, we preview a new PDA/DHI book on analytical methods, a team of experts at Johnson & Johnson write about the broadening use of e-beam sterilization technology, Journal Editor Lee Kirsch, PhD, provides the Journal Preview and the 2008 Journal Student Programs are announced. 🍷

Student Programs

PDA Supports Tomorrow’s Pharmaceutical Breakthroughs

Tomorrow’s breakthroughs in the pharmaceutical sciences will be the product of today’s young researchers at pharmaceutical schools across the globe.

Recognizing these researchers’ efforts and the influence of their work, PDA and the *PDA Journal of Pharmaceutical Science and Technology* have established three student scientific programs to promote applied research in areas of study relevant to the scientific foundations of pharmaceutical and biopharmaceutical product development, drug manufacturing and quality assurance technologies.

Two of these programs—the **Annual Graduate Research Symposium** and **Student Poster Sessions**—come together each year at the PDA Annual Meeting and bring students face-to-face with industry and regulatory professionals in formal conference and poster sessions. The Graduate Research Symposium will be hosted as a program session during the 2008 PDA Annual Meeting, and the Student Poster Sessions will be held in the exhibition hall, with presentations hosted throughout the conference.

The Predoctoral Fellowship Program offers doctoral candidates grants of various amounts to assist in their research. In addition to financial support, recipients of the fellowship grants will be given the opportunity to present their work at a distinguished PDA conference held in the United States or internationally.

Each program gives students the opportunity to share their research findings, network with industry leaders and make meaningful career strides. Help support the growth of our industry by encouraging students you know to apply to the 2008 programs today and/or attending a student presentation at the PDA 2008 Annual Meeting.

For more information on the PDA Student Programs and application and eligibility requirements, visit www.pda.org/ssp or contact Iris Rice at +1 (301) 656-5900 ext. 129 or rice@pda.org. 🍷

Journal Preview

Hot topics abound in the fall issue of the *PDA Journal of Pharmaceutical Science and Technology*. The long-awaited third edition of the **M. J. Akers**, PhD and **S. L. Nail's** series (this version with co-author Wendy Saffell-Clemmer) on the *Top Ten Topics in Parenteral Science and Technology* begins this issue. The last version was published ten years ago. The topics reviewed this time include advances in injectable formulation and packaging design, extractables and leachables, new analytical methods for biopolymers, protein aggregation issues, QBD/PAT, manufacturing equipment, isolation technologies and rapid microbial detection methods.

Not surprisingly, the rest of the articles in this issue address some of these very same topics. Two research articles focus on advanced formulation designs to enhance drug dissolution by the manipulation of drug crystallization conditions (*Preparation and Physicochemical and Preclinical Evaluations of Recrystallized Celecoxib* by **S. Mutalk**, et al.) and solid dispersion technology (*In Vivo and In Vitro Evaluation of Solid Dispersion System of Gliclazide:PEG 6000* by **S. Asyarie**, et al.). The role of serum production process variation on endotoxin contamination (*Evolution of Endotoxin Contamination during Production of a*

continued on page 16

In Print

Dealing with Validation Failures

From Validation of Analytical Methods for Biopharmaceuticals: A Guide to Risk-Based Validation and Implementation Strategies, by **Stephan O. Krause**, PhD, Faville, Inc

Most validation scientists do not really talk about how they deal with failed analytical method validation (AMV) or AMV extensions. Ideally, the AMV process should only be a confirmation of the test method capability already known from the analytical method development (AMD) studies. In reality, however, there will always be some AMV studies which did not pass all protocol acceptance criteria, and yes, those we prefer not to discuss. Whether we may admit that we have to deal with these situations, let us simply discuss how we could deal with them.

We should understand that some AMV studies should be expected to fail and therefore this should be planned for when managing time and allocated resources. We should distinguish a validation discrepancy from a

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Technology Trend

Low Energy Electron Beam Applications in Aseptic Filling Operations

Dieter Bachmann, PhD, Cilag,
and Ike Harper, Johnson & Johnson

High-energy electron beams (e-beam) have been used as an effective means of medical product sterilization for many years. The radiation energy generated from low-energy electron beam systems is strong enough to treat the surface of an object, yet low enough that minimal shielding is required to ensure safety when placed in close proximity to personnel. More recently, low-energy e-beam systems have been used to decontaminate the surfaces of presterilized syringe tubs before transferring them into the aseptic filling area where the syringes are filled.

Prefilled syringes have been a popular choice as a convenient and practical dosage form for parenteral drug products for over 30 years. Syringes can be purchased precleaned, sterilized and sealed in a container usually called a "tub." A puncture-resistant pouch covers the tub, and a Tyvek® lid is heat-sealed to the top of the tub, making up the microbial barrier layers for the tub. The syringe supplier sterilizes the syringes and tubs using ethylene oxide, radiation or some other means of terminal sterilization method that results in a sterility assurance level (SAL) of at least 10^{-6} , or less than one viable organism on every 1,000,000 units. The two microbial barrier layers ensure the contents maintain that sterility level until opened.

In order to get the sterile syringes into the aseptic filling area, the syringe tubs must be transferred into the aseptic filling area in a manner that prevents recontamination of the syringes and the filling area. To do this, the outer bag is removed within a clean environment just outside the aseptic filling area. These clean areas are typically Grade C/ISO 8/Class 100,000 environments. Under these conditions, the risk of recontaminating the tub is controlled and minimized, but the tub usually undergoes an additional decontamination treatment before it is transferred into the isolator. Upon successful decontamination of the outer surface, the tub is introduced into the sterile filling area. Once inside, the Tyvek® seal is removed from the tub opening and the syringes are placed onto the filling line for filling.

There are two commonly used methods to decontaminate syringe tubs after removing the outer bag.

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- ▶ Recent solutions to recurring microbiological challenges
- ▶ Practical interpretations of regulatory requirements in aseptic manufacturing

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Technology Trend, continued from page 11

The first option is to simply disinfect the tub surfaces by using a wipe down technique, such as with alcohol wipes. A second option is to use sporicidal gases or a vaporized agent, such as hydrogen peroxide vapor. While these methods have been in practice for many years, they can be limited in terms of effectiveness and efficiency.

The manual-wiping technique can be difficult to prove effective and to demonstrate reproducibility. Lack of consistency in wiping techniques results in a less effective process of reducing bioburden, and variations between operators makes it difficult to show reproducibility. Consequently, a greater risk of recontamination can be expected with the manual method due to more human contact.

Gassing processes using vapor phase hydrogen peroxide, or other gaseous disinfectants, are typically more reproducible and reliable in achieving desired bioburden reduction levels than a manual wipe down method. However, hydrogen peroxide vapor dissipation can be a time-consuming process step, and peroxide residues may remain inside the tubs and syringes after the decontamination process is complete. When manufacturing sensitive parenteral products, high levels of peroxide residues in the syringe can affect the product stability. The most limiting factor of these processes is cycle time, or the time it takes to get a syringe tub into the aseptic filling area. This can be a limiting factor to the overall filling time and capacity. Additionally, both of these processes rely on biological indicators to prove effectiveness, an additional element of uncertainty when proving effectiveness of the process.

Low-energy e-beam radiation is a new alternative as a surface decontamination process. The low-energy e-beam

The bioburden reduction level can be increased or decreased by simply adjusting the e-beam and conveyor settings on the system accordingly.

systems typically comprise of three low-energy e-beam emitters positioned in a tangential (180°) formation to concentrate the e-beams onto a central target, the tub surface. The e-beam system produces ionizing electron beam (beta) radiation energy equivalent to about 100-200 keV, and is capable of penetrating approximately 200 micrometers of a unit density material, i.e., 1gm/cm³. The syringe tubs are conveyed along a pressurized tunnel and decontaminated by electron beams while traveling downstream to the aseptic filling area. The tunnel itself can be decontaminated with vaporized hydrogen peroxide, which may be provided by the generator used to decontaminate the aseptic filling area.

Since the tubs are purchased sterile, the bioburden level on the outer surfaces of the tubs should be extremely low (SAL 10⁻⁶). However, an assessment of the bioburden level on the tub surfaces under worst-case conditions should be performed to determine the theoretical worst-case level of bioburden that may be present. The worst-case conditions should include maximum handling manipulations, maximum hold times without the outer barrier, and maximum environmental monitoring limits. As an example, the estimated bioburden due to recontamination under worst-case conditions may be no more than 10 colony-forming units

(CFU). If a safety factor of 10 were added, the predicted worst-case bioburden level may be 100 CFU. Once the worst-case bioburden level of the surface of the tubs is established, it is important to verify it. This can be done by periodically measuring the bioburden on the tub surfaces after the tubs have been exposed to the worst-case conditions.

According to relevant guidelines and requirements for decontaminating low bioburden materials such as this, a 3-log reduction of bioburden is sufficient, but a higher level is desired for additional assurances. The e-beam system makes it possible to achieve virtually any level of assurance. The bioburden reduction level can be increased or decreased by simply adjusting the e-beam and conveyor settings on the system accordingly.

Establishing the Minimum Dose

The relationship between radiation and bioburden reduction is well-established, so the use of biological indicators is not necessary. The International Organization for Standardization (ISO) provides standards and recommended practices on radiation sterilization of medical devices. ISO document #11137, “Sterilization of health care products – Radiation – Part 2: Establishing the sterilization dose” provides several methods of establishing the sterilization dose for different levels of bioburden reduction. These methods are based on the reduction of the natural bioburden on the medical device(s), not biological indicators, and they are usually applied to high-energy radiation applications.

The same relationship can be proven for low-energy radiation applications. As seen from experimental studies, a dose of 10.6 kilograys (kGy) of low-energy e-beam radiation yields a spore log reduction (SLR) = 5.8 of a highly radiation-resistant microorganism,

i.e., *Bacillus pumilus*, spores with a radiation resistance (D-value) of 1.3 kGy. Upon further extrapolation of this relationship, a dose of 15 kGy would yield an 8-log reduction of this organism. This logic can be applied to establishing the decontamination dose for the low energy e-beam process, which is used to decontaminate much less-resistant microorganisms that would be present on the surface of the tubs.

Once the desired dose is established, it must be accomplished reliably and repeatedly on every tub. In order to achieve the desired dose throughout the run, the equipment parameters of the e-beam system must be set accordingly, i.e., beam current and conveyor speed. This is done by measuring the dose on the surface of the tub at various settings and establishing the relationship between the set points and the delivered dose.

Due to the geometry of the tub, some areas on the surface will receive a higher or lower dose because of the proximity of the tub surfaces to the e-beam emitters as the tubs pass through the tunnel. Following the earlier example, the equipment must be set up to deliver the minimum dose of 15 kGy to the minimum absorbed dose location on the tub surface. This location receives the lowest dose of radiation and thus has the greatest challenge for microbial kill, so as long as this location receives the minimum dose, the tub is decontaminated to the desired level.

“Dose mapping” is the term given to the practice of measuring the absorbed dose across the surfaces of the tubs by using dose meters, or dosimeters. The dose range from the highest to the lowest measured dose on the tub surface represents the “dose distribution” or “dose uniformity” across the tub. The location on the

tub surface that measures the lowest absorbed dose is usually the location that is farthest away from the e-beam emitters. Incidentally, the location on the tub that measures the highest

Once the equipment parameters have been established and validated, they are set for routine production and should only require minimal adjustments over time.

absorbed dose of radiation is usually the part of the tub that comes closest to the e-beam emitter as it passes on the conveyor. For the prefilled syringe tubs, the middle of the front vertical surface and middle of the back vertical surface as the tub passes through the conveyor is typically the minimum dose location(s). The minimum radiation dose must be reached at the lowest absorbed dose location time after time, tub after tub throughout the entire run.

Due to the nature of the process, it is not possible or practical to measure the dose on all surfaces on all of the tubs. Therefore, it is necessary to identify a reference dose location during dose mapping that can be used to extrapolate the dose received at the minimum and maximum dose locations. Routine dose monitoring during production is based on a statistical model developed and verified during validation. The routine dosimeter reading substantiates that the correct equipment parameters were used during production and that the minimum dose was achieved throughout the run.

Establishing the Equipment Settings

Regardless of the manufacturer of the e-beam system and the process mode of the systems, i.e., scanning beam or static energy cloud, the dose will vary across the tub surface, and the lowest absorbed dose location on the surface of the tub is the determining factor for selecting the correct operating settings for the equipment. The following aspects for establishing the equipment parameter settings are taken into account:

- 1) Established relationship between the equipment settings and the dose achieved at those settings and across a range settings
- 2) Dose set point
- 3) Dose distribution across all surfaces of the tub
- 4) Dose range between min and max and reference locations
- 5) Measurements for uncertainties within the dosimetry systems
- 6) Repeatability of process throughout the run and across multiple runs

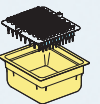
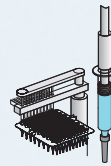
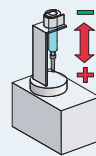
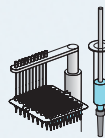
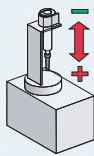
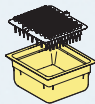
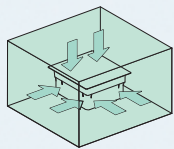
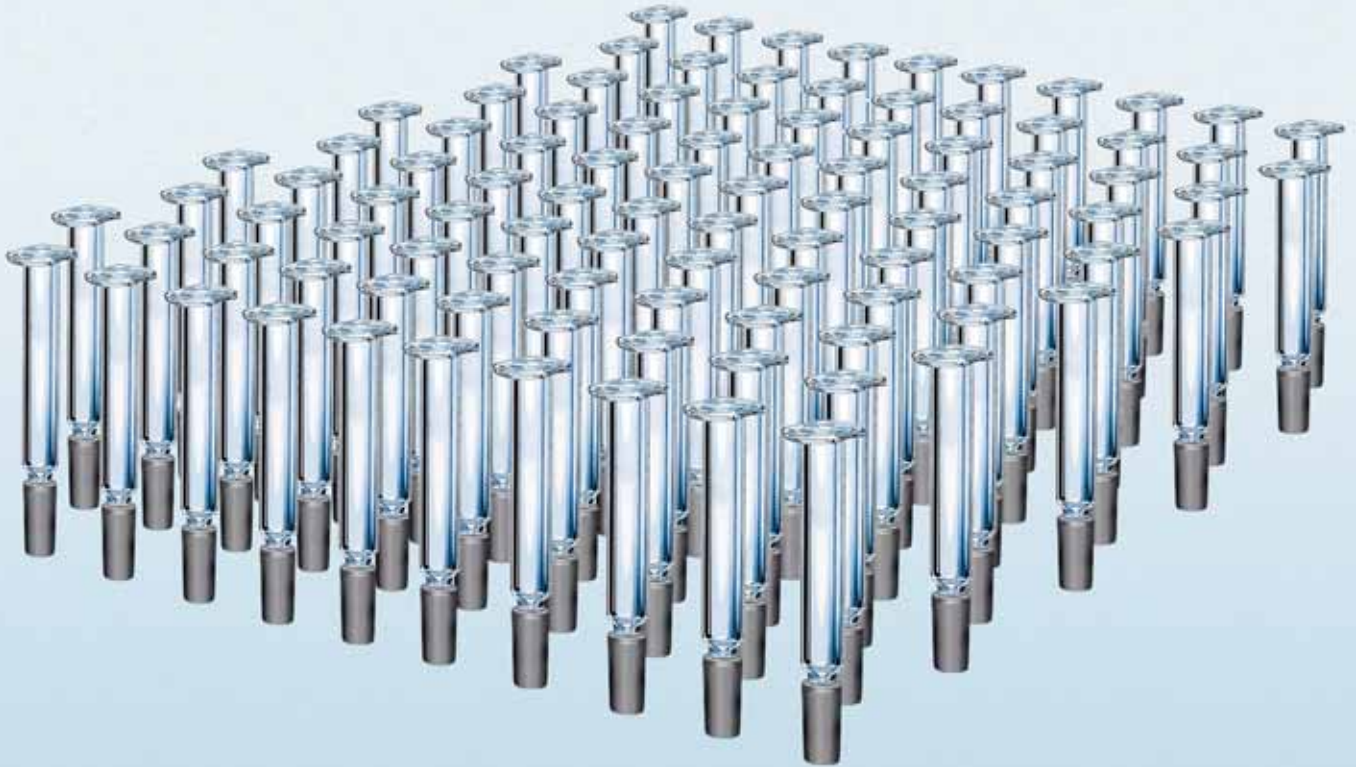
Validation

Once the equipment parameters have been established, validation is required to substantiate the reliability and repeatability of the process. Validation should also test the failure modes of the equipment. These systems are designed to stop if a critical error occurs, such as a tub misfeed. The design of the system should allow for clearance of all tubs on the conveyor system without contaminating the aseptic filling area or the transfer zone between the e-beam and the aseptic filling area. It is important that the equipment is able to detect all system, conveyor and electrical errors. A risk assessment must be performed to determine what action should be taken for each type of error.

Routine Operation and Dose Monitoring

Once the equipment parameters have been established and validated, they ►

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are set for routine production and should only require minimal adjustments over time. In general, dosimeters are used to verify the minimum dose is achieved at the beginning and end of each run by placing dosimeters at the reference location on the first and last tub. The reference dosimeter is used to verify that the dose being received on the tub surface at the lowest dose location meets the preestablished requirement for minimum dose.

Typically, the minimum dose is verified by measuring a reference dosimeter on the first tub, and the filling operations begin. During the run, the e-beam system is monitored by sensors that continuously check the conveyor speed, the power input, the power output and various safety aspects. At the end of the run, a dosimeter is placed on the last tub to verify that the minimum dose was achieved at the end of the run. These dosimeters bracket the run. As a precaution, two dosimeters may be used to substantiate the measurements.

It is necessary to calibrate the dosimetry system regularly to ensure operational readiness and to purchase dosimeters that are traceable to a

national standard laboratory that certifies the dosimeters for use in this type of application. Likewise, it is necessary to place the entire e-beam decontamination system on a preventive maintenance and calibration schedule. Additionally, it is necessary to monitor the tub bioburden on a regular basis to verify that the bioburden does not exceed the preestablished limits and to detect unexpected changes in bioburden levels that may be due to seasonal affects, changes in personnel, changes in the facilities or other influences.

Conclusion

Low-energy e-beam surface decontamination systems are an excellent means to facilitate the continuous transfer of presterilized syringes tubs into an aseptic area. While the e-beam decontamination system can present new technical challenges to the user, such as using dosimetry instead of BI's, many benefits can be realized, such as:

- No vapor residues
- No temperature affects
- Surface treatment only, no impact to tub contents
- Elimination of biological indicators

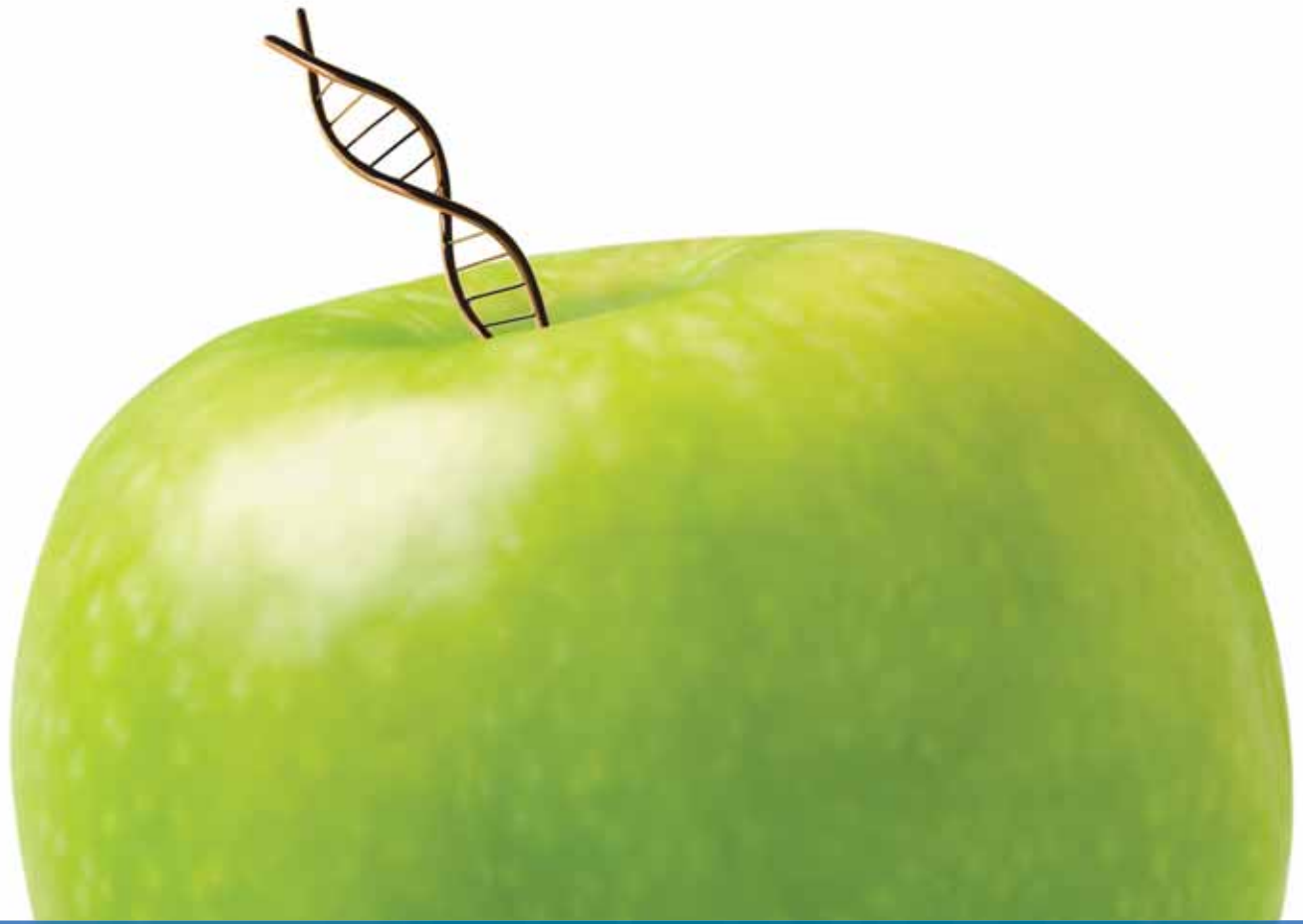
- Modular design
- Quick startup and shut down
- Effective
- Robust
- High capacity
- Control over treatment level

The rate at which the tubs can pass through the system is about 3-5 tubs per minute, corresponding to approximately 300-600 syringes per min, depending on the number of syringes in the tub. The same standard tub can hold many different types of syringes, or other presterilized materials as well. The systems' modular designs fit into virtually any isolator or production line application, so the costs of the systems can vary. Under nearly any configuration, a high rate of throughput can be maintained reliably for the duration of the filling run. These combined benefits make low-energy e-beam decontamination systems an appealing alternative to traditional methods of surface decontamination. 🌍

Journal Preview, continued from page 11

Therapeutic Serum by **H. Massaldi** and **V. Morais**) and the use of polymerase chain reactions for the rapid detection of microbial contamination (*Rapid Diagnostic Method for Quantitative Testing of < 100 microbes in Water* by **A. Walzer**, *et al.*) are the subjects of research articles from Uruguay and Germany, respectively.

This issue also includes a timely and informative review of the role of microbial contamination in recent FDA product recalls (*Microbial Diversity in Pharmaceutical Product Recalls and Environments* by **L. Jimenez**). 🌍



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In Print, continued from page 11

validation failure. It is difficult to put percentages on how many passing AMV studies versus validation failures should be considered appropriate. As discussed, this will somewhat depend on the firm's regulatory and financial standing which may in turn impact the balancing lever between wide and narrow acceptance criteria. For example, passing 100 of the last 100 AMV studies is certainly undesirable, as this suggests that we may run rather meaningless validation studies, and are not challenging the suitability of our processes enough. On the other hand, routinely passing only 50% of all AMV protocols may also be inappropriate because we may have failed to select suitable test methodologies, or may not have sufficiently optimized test methods.

The "Recovery" Mission

Figure 8.1 (page 20) illustrates the recovery process that starts with the observation of a validation failure, i.e., a single AMV protocol acceptance criterion or multiple criteria were not met during the protocol execution. The failure to pass protocol acceptance criteria is shown in the middle of Figure 8.1 and highlighted in grey, to visually represent the fact that we have entered the "grey zone". It is now critical for inspections, compliance, and impact on project completion, to make good decisions. (The author identified and discussed the affected stakeholders in detail in Chapter 4.) Once a validation failure is observed, this must be locked in some form of exception or investigation report (IR). Answers to the following questions will provide the best direction in which to proceed, while keeping stakeholders interests and risks in mind. The answers will then direct us into either the lower loop (inspection/compliance risk) or upper loop (project completion risk). Assuming that we followed the AMV protocol and generated valid test results, meaning no operator error or

test system suitability error occurred, we should now answer the following questions.

- Did we set balanced acceptance criteria?
— *Review protocol acceptance criteria justification(s), specifications, and historical data.*
- Did we lean towards quality or project completion when setting criteria?
— *Re-evaluate risks to patient and firm assessed to set acceptance criteria.*
- Did we fail to pass a critical protocol acceptance criterion (or several) such as intermediate precision when high variability could cause OOS results?
— *Check for criticality and corresponding likelihood of OOS results.*
- Are results generated by this test method critical to assess product safety or product/process quality, or efficacy?
— *Consider production process stage, and impact to safety, quality or efficacy.*
- Were there previous AMV failures (and discrepancies) with this test method?
— *If this is not a new method, review previous AMV(s).*
- Were there any (failing) data sets generated during AMD that were not discussed in the AMD report?
— *Review laboratory notebooks from AMD scientists and (if necessary) conduct interviews with them.*
- What is the predicted release-to-reject ratio or probability for this test method and production process step?
— *(Re-)calculate the predicted OOS probability.*
— *Estimate probabilities for error classes 1A–2B.*
- Has this kind of failure occurred before and what how did we handle this?
— *Count failures versus successful*

completions and review previous recovery processes.

- Were there previous inspection observations for validation processes and/or failures?
— *Review previous regulatory and internal observation notes.*
- What is our current overall compliance standing with regulatory agencies?
— *Review previous commitments of firm.*
— *Evaluate current regulatory expectations such as new OOS Guidance document (CDER/FDA, 2006).*
- What is the impact to this project and connected projects?
— *Review and discuss project timelines with project managers.*
— *Assess the predicted impact (in dollars) to the firm.*

Choosing the Lower Loop

Having assessed all the answers to the questions above, we may decide to go into the lower loop (Figure 8.1). Assuming we need to complete this AMV report because of pressure to complete the project, the lower loop process steps are colored grey as we may only achieve a "pseudo-validated" status once the report is closed. This inspection risk may be tolerated from a business perspective while recognizing the possibility of a potential inspection observation. This AMV completion may be needed to finish a large project that may be vital for the firm's competitiveness, so this option may be selected. At other times, acceptance criteria may have been set too conservatively (narrowly) and re-setting may be justifiable. The firm also may need to consider overall historical and existing compliance status for quality control (QC) operations, since lower loop selections are always inspection and compliance risks, no matter how they are handled and justified. The total number of lower loops, when compared to upper loops, and versus ►

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the proportion of passing validations, needs to be minimal.

Choosing the Upper Loop

Without question, selecting the upper loop is always the better choice when considering (only) the quality of the final test method and the overall validation process. Within this loop there are essentially three levels of how “deep” we look into this failure, and how willing we are to really improve individual test method performance and this will determine the test method performance. Although this may sound strange, we must be willing to improve test method performance and devote resources and allocate time to really implement any improvements.

The first choice to re-execute with the current protocol acceptance criteria based on the identified root cause of error anything but those errors causing validation discrepancies — will be the fastest to resolve. Fixing an “error” will not change or improve anything for test method performance. For example,

spiked proteins were partially adsorbed at or before sample preparation to glass containers, and we concluded that plastic containers should have been used. However, this could be justified simply based on the fact that the originally set requirements for test method suitability are unchanged.

The next box down, “Tightening of Operational Limits”, requires us to run the test method system under more stringent operational limits. These could entail test method standard operating procedures (SOP) limiting the timing brackets for certain reaction steps. Or we could reduce the allowed sample preparation or overall testing time to reduce degradation or other variations that impact on the test results. Another, often used, tightening of operational limits (although not usually identified as such) could be narrowing of the qualification requirements to demonstrate operator proficiency, or excluding the use of particular instruments or critical test reagents. In any case, the tightening

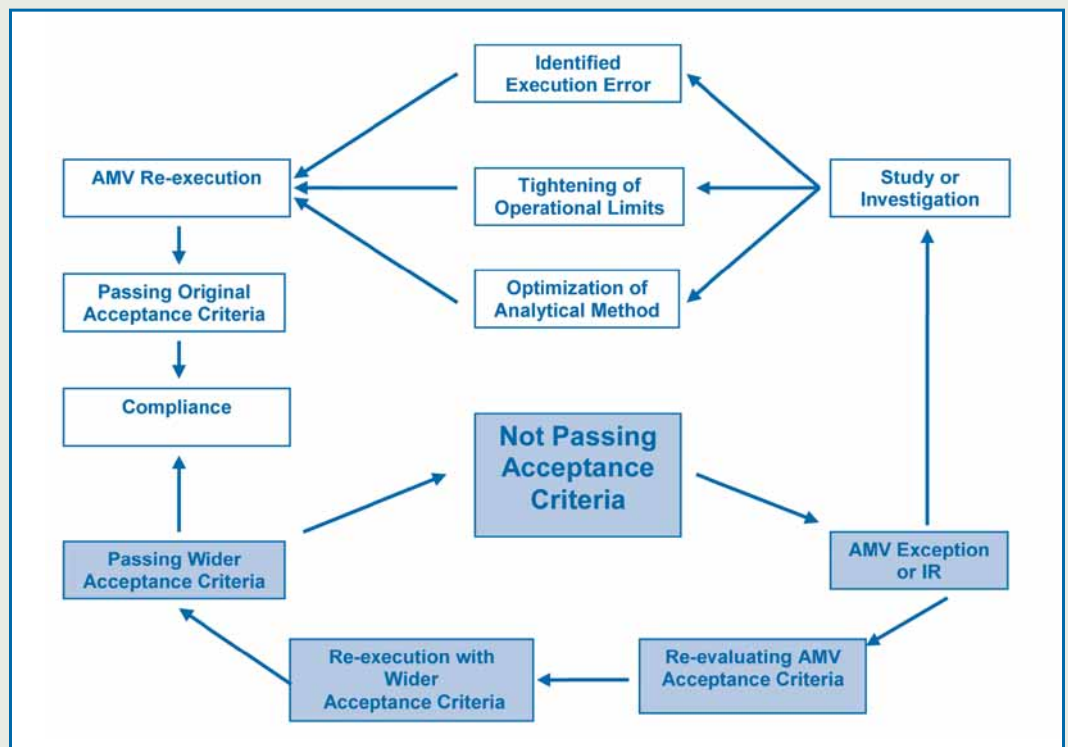
of operational conditions should lead to improved intermediate precision results.

The last and most cumbersome process, to further optimize the test methods, may have the greatest effect on the overall improvement of test method performance. However it may also be the most expensive recovery process—when considering only the short-term business impact—and usually requires a significant time to complete. Because the timely completion of projects is vital for most firms, we must consider all aspects that impact on patient safety, product quality, additional time and costs, along with short- and long-term profits for the firm.

Reference

CDER/FDA (2006). Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production, October.

Figure 8.1
Dealing with AMV Failures



PDA Interest Groups & Leaders

PDA Interest Groups are divided into five sections by subject matter. This aligns them for improved effectiveness, supports increased synergies and provides the opportunity for Interest Group members to play a more active role in Task Forces. The five sections are Quality Systems and Regulatory Affairs, Laboratory and Microbiological Sciences, Pharmaceutical Development, Biotechnological Sciences and Manufacturing Sciences. Any PDA member can join one or more Interest Group by updating their member profile (www.pda.org/pdf/join_IG_instruction.pdf). Please go to www.pda.org/interestgroups for more information.

North American Interest Groups

Section Leader	Frank Kohn, PhD <i>FSK Associates</i>	David Hussong, PhD <i>U.S. FDA</i>	Don Elinski <i>Lachman Consultants</i>	Sandeep Nema, PhD <i>Pfizer Inc.</i>	Robert Dana <i>PDA</i>
Section Title	Biopharmaceutical Sciences	Laboratory and Microbiological Sciences	Manufacturing Sciences	Pharmaceutical Development	Quality Systems and Regulatory Affairs
Related IGs and Group Leaders	<p>Biotechnology <u>Group Leader:</u> Jill A. Myers, PhD <i>BioPro Consulting</i> Email: jmyers@bioproconsulting.com</p> <p>Lyophilization <u>Group Leader:</u> Edward H. Trappler <i>Lyophilization Technology</i> Email: etrappler@lyo-t.com</p> <p>Vaccines <u>Group Leader:</u> Frank S. Kohn, PhD <i>FSK Associates Inc.</i> Email: fsk@iowatelecom.net</p>	<p>Analytical Labs/ Stability <u>Group Leader:</u> Rafik H. Bishara, PhD Email: rafikbishara2@yahoo.com</p> <p>Microbiology/ Environmental Monitoring <u>Group Leader:</u> Jeanne E. Moldenhauer, PhD <i>Excellent Pharma Consulting</i> Email: jeannemoldenhauer@yahoo.com</p> <p>Visual Inspection of Parenterals <u>Group Leader:</u> John G. Shabushnig, PhD <i>Pfizer Inc.</i> Email: john.g.shabushnig@pfizer.com</p>	<p>Facilities and Engineering <u>Group Leader:</u> Christopher J. Smalley, PhD <i>Wyeth Pharma</i> Email: smallec2@wyeth.com</p> <p>Filtration <u>Group Leader:</u> Russell Madsen <i>The Williamsburg Group, LLC</i> Email: madsen@thewilliamsburggroup.com</p> <p>Pharmaceutical Water Systems <u>Group Leader:</u> Theodore H. Meltzer, PhD <i>Capitola Consulting Co.</i> Email: theodorehmeltzer@hotmail.com</p> <p>Sterile Processing <u>Group Leader:</u> Richard M. Johnson <i>Fort Dodge Animal Health</i> Email: johnsor4@fdah.com</p>	<p>Clinical Trial Materials <u>Group Leader:</u> Vince L. Mathews <i>Eli Lilly & Co.</i> Email: vlm@lilly.com</p> <p>Combination Products <u>Group Leader:</u> Michael A. Gross, PhD <i>Chimera Consulting</i> Email: michaelgross@novuscom.net</p> <p>Packaging Science <u>Group Leader:</u> Edward J. Smith, PhD <i>Wyeth Pharmaceuticals</i> Email: smithej@wyeth.com</p> <p>Process Validation <u>Group Leader:</u> Harold S. Baseman <i>ValSource, LLP</i> Email: halbaseman@adelphia.net</p>	<p>Inspection Trends/ Regulatory Affairs <u>Group Leader:</u> Robert L. Dana <i>PDA</i> Email: dana@pda.org</p> <p>Quality Systems <u>Group Leader:</u> David A. Mayorga <i>Global Quality Alliance, LLC</i> Email: david@gqaconsulting.com</p>

European Interest Groups

Section Leader	Roland Guenther <i>Novartis Pharma AG</i> Email: roland.guenther@pharma.novartis.com	Markus Lankers, PhD <i>Rap.ID GmbH</i> Email: markus.lankers@rap-id.com	Roger Seiler <i>Sartorius SA</i> Email: roger.seiler@sartorius.com	D F Chowdhury <i>Aphton BioPharma</i> Email: Fazc@aol.com
Related IGs and Group Leaders	<p>Biotech <u>Group Leader:</u> Roland Guenther <i>Novartis Pharma AG</i> Email: roland.guenther@pharma.novartis.com</p>	<p>Visual Inspection of Parenterals <u>Group Leader:</u> Markus Lankers, PhD <i>Rap.ID GmbH</i> Email: markus.lankers@rap-id.com</p>	<p>Filtration <u>Group Leader:</u> Roger Seiler <i>Sartorius SA</i> Email: roger.seiler@sartorius.com</p> <p>Production and Engineering <u>Group Leader:</u> Philippe Gomez <i>Sartorius SA</i> Email: Philippe.gomez@sartorius.com</p> <p>Prefilled Syringes <u>Group Leader:</u> Thomas Schoenkecht, PhD <i>Bünder Glas GmbH</i> Email: t.schoenkecht@gerresheimer.com</p>	<p>Nanotechnology <u>Group Leader:</u> D F Chowdhury <i>Aphton BioPharma</i> Email: Fazc@aol.com</p> <p>Technology Transfer <u>Group Leaders:</u> Volker Eck, PhD <i>PDA</i> Email: eck@pda.org Zdenka Mrvova <i>Zentiva</i> Email: zdenka.mrvova@zentiva.cz</p>

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QbD: Still in Design? continued from cover

- A pharmaceutical sector that understands its products and the processes, uses risk assessment/mitigation tools and modern effective quality systems, and takes full ownership of the product

The process of QbD does not start with the manufacturing process but from the beginning with drug design and development and clinical study. In fact, there are necessary inputs from product development that are required to subsequently impose QbD on process development and manufacturing. [Cherney]

Although the *desired state* is desirable and achievable, the process will never really be complete if it is to adapt to new conditions and technologies and encourage continuous improvement.

FDA's Outlook

The justification FDA provided for proposing this paradigm shift was in response to increasing cost pressures on both governmental agencies and industry and the escalation of drug prices. Agency representatives depicted the effort as an obligation to society to increase the accessibility of new drugs while maintaining their high quality. If a state of continuous improvement and innovation is to be attained, a new approach will be required to achieve not only greater manufacturing efficiency but also greater efficiency in the overall regulation of the industry. [Woodcock]

When appropriate, FDA is attempting to remove regulatory barriers and encourage more free-form innovation. Having observed that the pharmaceutical manufacturing industry was ossified by the prior environment, the Agency hopes to stimulate the use of the same new scientific methods and technologies that have benefited drug discovery and research in recent years.

FDA also noted that operating companies had been keeping two sets

of books, one set of documents to show the agencies and a more science-based set for themselves that captured their true process understanding. [Woodcock] Thus, FDA would like to encourage an open exchange and change the perception of a rigid regulatory oversight.

The EMEA has a team assigned to QbD submissions that was set up in late 2003.

Although the QbD concept is not new, FDA acknowledged that actual deployment is only just beginning. At present, there are no definitive guidelines available for QbD filings, even for small-molecule drugs, which have been introduced to QbD for some time. Resources have been tight for the Agency; it is only just completing the second part of a guideline for clinical supplies for Phase 1 and has not yet addressed later-stage filings. Thus, the Agency suggested that industry may have to take the first steps and further invest in their manufacturing facilities and process understanding. [Woodcock]

The initiative will require an iterative process and may well increase initial costs of commercialization. Earlier touted to reduce the regulatory burden, FDA indicated that the QbD initiative may better be described as providing greater flexibility in regulatory approaches. [Cherney] It is hoped that the long-term costs of manufacturing and regulation decrease by taking advantage of this flexibility.

FDA also stressed that QbD will have to become an international standard if it is going to take hold. FDA acknowledged the burden on industry,

already having to comply with multiple jurisdictions, and agrees that streamlining is necessary.

The Agency also acknowledged that the concepts and associated flexibility of QbD have not yet reached the inspectional arena. It is still trying to get a consistent approach among inspectors and has embarked on a training program. One class of inspectors has been trained and a second training class is in progress. FDA also spoke of establishment of a Pharmaceutical Inspectorate that would standardize approach and hopefully become an international organization.

EU Outlook

An EMEA representative stated that the regulations and guidelines are still very much in the formative stages. The ICH guidelines have been invoked but remain at a fairly high level. The goal of the guidelines is to: *Develop a harmonised pharmaceutical quality system applicable across the life cycle of the product, emphasizing an integrated approach to quality risk management and science.* [Ho]

Components of the ICH guidelines referred to are the Q8: *Pharmaceutical Development*, Q9: *Quality Risk Management*, and Q10: *Pharmaceutical Quality System* guidelines and attempt to set the groundwork for greater regulatory flexibility.

EMEA has a team assigned to QbD submissions that was set up in late 2003. Currently consisting of five assessors and five inspectors, it is referred to as the Process Analytical Technology (PAT) Team. Even though the PAT terminology is fading in favor of the more general QbD concepts, the EMEA has decided to retain the PAT team description to avoid confusion.

Echoing FDA, this team has not seen much to date in the way of innovative filings or approaches from companies. However, it was also acknowledged

that achieving the desired state will require an iterative process.

Industry Experience and Outlook

Since small molecules are ahead in terms of QbD experience, a case study was presented by a Pfizer representative. Despite Pfizer’s attempts, in a few cases, to file using QbD, the company has not observed the flexibility from the Agency to the extent it expected. However, Pfizer acknowledges a willingness for much more collaboration on the part of the regulators. From Pfizer’s interaction with FDA, there were several lessons learned: [Nosál

1. Since there is no good definition of criticality, a company needs to provide its own clear definition.
2. Provide a reviewer’s guide to the Agency with explanation of documentation structure and definition of terms.
3. Conduct better risk analysis. The FDA did not understand Pfizer’s risk-assessment process and, for example, why some parameters were evaluated and not others.

4. Provide better articulation of control strategy. This includes understanding of design space and description of process-feedback controls and in-process controls.
5. Convince the Agency of robust change control system to take advantage of QbD for post-approval improvements.
6. Conduct process trending on an ongoing basis. This is of interest to FDA.

Other participants also noted the lack of regulatory guidance for QbD and filing content. One person noted that the Q8, Q9 and Q10 guidelines were frustratingly vague. In short, the industry wants to see this flexibility from FDA if it is going to continue to invest in QbD and design space characterization.

Alas, there appears to be no short-term relief from regulatory burden associated with QbD filings. In fact, the workload will increase until the agencies are convinced that the industry truly has a better process understanding and can

leverage this for future improvements.

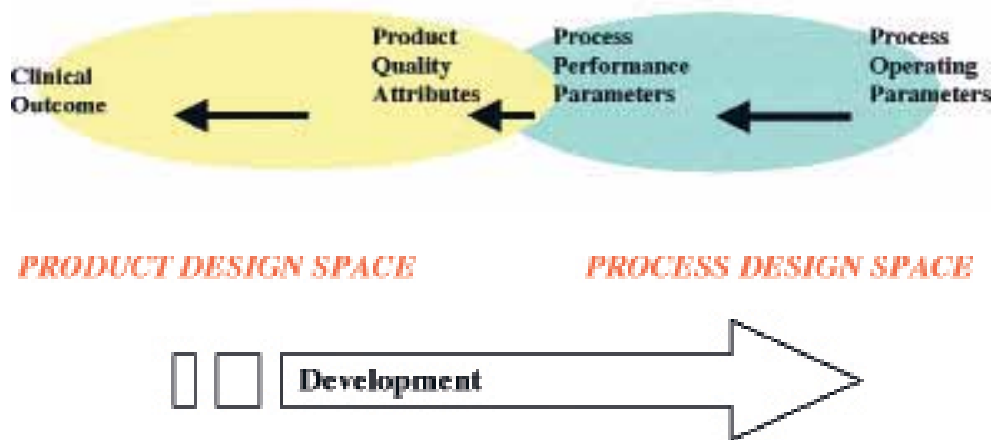
Design Space

The design space concept describes the multidimensional combination and interaction of input variables and output parameters that have been demonstrated to provide a desired objective or quality. Several speakers, including those representing FDA, invoked this concept for both product design (product knowledge) and process design (understanding). As described, [the author’s] interpretation of the relationship is represented by Figure 1 below.

This mathematical concept serves to map inputs to specified outputs. However, the actual development process happens in reverse.

The design space concept appears to be further ahead for process design than for product design in terms of the application of principles. There seems to be general agreement that present clinical study readout is coarse. Therefore, the design-space approach

Figure 1: Author’s depiction of QbD based on discussions at PDA’s QbD workshop.



to process definition is frequently hampered by inadequate information regarding product quality needs, i.e., the deliverables (product specifications) to process development are often vague with respect to the desired product quality attributes. On the clinical side, industry needs to make more use of the literature and experience with similar molecules to better define the product design space. Perhaps more preclinical studies are required to study the effect of product variants and impurities. [Mire-Sluis] A consortium was suggested where such clinical experience and impurity profiles could be shared, but it is unclear what level of participation can be expected.

There was also some confusion around the fact that there are multiple design spaces. FDA stated that its intent to keep the design space definition for the process only and phase out the term for the product design to avoid confusion; [Cherney] however, the concept still applied to the clinical product as well as process environments. This author expressed his opinion that the design space definition was useful for product and process development and that perhaps should be retained for both.

Studying & Documenting Design Space

A number of questions were asked regarding the nature of documentation needed to support the design space. Here, FDA expressed considerable flexibility in allowing the use of prior knowledge. Information from the literature, experience with prior molecules, process and product platforms, and production history can be used to support the design space and to help demonstrate process understanding. [Joneckis] In the spirit of continuous improvement, FDA also acknowledged that the specification of the design space should continually be refined, and that its definition should be captured in a living document. Furthermore, a company is encouraged to continue to accumulate process

Another important aspect of the design space definition includes the characterization of parameter interactions.

understanding post-licensure to build a complete QbD dossier. [Hughes] This statement appeared to be aimed at smaller companies that simply could not be expected to have a fully-characterized process at time of filing. Whether this flexibility would be allowed for new products from larger companies was unclear; however, this approach was certainly encouraged for legacy products.

An important component of the design space definition is the risk analysis that identifies the critical parameters. The rationale behind the criticality of these parameters needs to be documented, and it is acceptable to focus specification of the design space on these critical parameters. This assessment applies to critical product quality attributes as well as critical process parameters (CPPs).

One way of visualizing a critical parameter is where the control space for a given parameter is close to the edge of the design space. Since the presence of a CPP implies risk, it was suggested that critical input parameters could potentially be engineered out of the process. An example given, described the dilution of a titrant stream for post-elution pH adjustment. [Lam]

Another important aspect of the design space definition includes the characterization of parameter interactions. Two parameters may be noncritical separately but critical if both deviate from the set point at the same time.

Justification of the extrapolation of small-scale to large-scale results is also

required if much of the design space was characterized at small scale. Thus, it appears that some sort of scale-down model qualification will need to be available to the regulators.

Where experiments are not possible at small scale, in theory, it is acceptable to explore the design space at large scale. Both the Agency and industry acknowledged that scale-down models do not always adequately represent larger systems, and it is often difficult to model an entire process. While experiments at scale are permissible from the compliance standpoint (as long as the stated bounds of the design space are not exceeded), they represent a business risk if the lot fails to meet specification. [Cherney and Hughes] Such experiments presumably would require a legitimate justification and risk assessment.

Lastly, the documentation of the design space can include a large set of data and many associated reports and documents. A multitiered approach, where a process description document is created as a highest-level summary of the design space, was suggested by [Devine.] (See “QbD Filing Content” page 29.)

Validation

There was some discussion around the impact of QbD on validation. At one point, an audience member proposed a worst-case approach during large-scale validation to exercise the design space. The consensus, however, was that such an approach would be complex and time consuming and that validation really only serves as a verification of the process knowledge gained during process development.

There was also a perception that QbD filings may ultimately obviate validation runs. However, FDA and EMEA still would be uncomfortable with less than three confirmatory runs. Thus, it appears that validation methods at

continued on page 29

North America Events

Please visit www.pda.org for the most up-to-date event, lodging and registration information.

Conferences

October 15-16, 2007

2007 PDA Visual Inspections Workshop
Bethesda, Maryland

October 29-November 2, 2007

PDA's 2nd Annual Global Conference on Pharmaceutical Microbiology
(Conference, Courses and Exhibition)
Bethesda, Maryland

November 1-2, 2007

PDA/FDA Co-sponsored Conference Series on Quality Systems
Bethesda, Maryland

November 6-8, 2007

PDA Extractables/Leachables Forum
Bethesda, Maryland

April 14-18, 2007

PDA 2008 Annual Meeting
(Conference, Courses and Exhibition)
Colorado Springs, Colorado

May 19-23, 2008

2008 PDA Biennial Training Conference
(Conference, Courses and Exhibition)
New Orleans, Louisiana

Training

Lab and Lecture events are held at PDA TRI, Bethesda, Maryland unless otherwise indicated.

Lab Courses

October 1-5, 2007

Rapid Microbiological Methods

October 17-18, 2007

An Introduction to Visual Inspection

October 23-24, 2007

Fundamentals of D, F and z Value Analysis

October 25-26, 2007

Validating a Steam Sterilizer

October 31-November 2, 2007

Advanced Environmental Mycology Identification Workshop

November 13-16, 2007

Validation by Design (R): DoE Basics for PAT Applications

November 14-16, 2007

Developing an Environmental Monitoring Program

November 14-16, 2007

Pharmaceutical Water System Microbiology

December 5-6, 2007

Developing and Validating a Cleaning and Disinfection Program for Controlled Environments

Lecture Courses

October 8-10, 2007

Advanced Pharmaceutical Filtrations and Filters

October 29-31, 2007

Managing Quality Systems

Course Series

October 15-17, 2007

Philadelphia Training Course Series
Philadelphia, Pennsylvania

November 27-29

San Diego Course Series
San Diego, California

Chapters

October 11, 2007

Mountain States Chapter
Quality Systems

November 14, 2007

New England Chapter
Filtration Workshop

November 14, 2007

Puerto Rico Chapter
Cleaning Validation

Europe/Asia-Pacific Events

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October 9-11, 2007

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(Conference and Exhibition)
Berlin, Germany

October 17, 2007

Pharmaceutical Cold Chain Management
(Conference, Courses and Exhibition)
Berlin, Germany

October 25, 2007

Supplier Quality and Global cGMPs
(Conference and Exhibition)
Rome, Italy

November 8, 2007

United Kingdom Chapter
TR-1 Workshop

November 13-15, 2007

European Training Course Series in Berlin
Berlin, Germany

November 15-16, 2007

Cork, Ireland Training Course Series
Cork, Ireland

December 4-6, 2007

Practical Aspects of Aseptic Processing
Basel, Switzerland

December 12-14, 2007

Dublin, Ireland Training Course Series
Dublin, Ireland

February 18-21, 2008

2008 PDA/EMEA Joint Conference
Budapest, Hungary

Asia-Pacific

November 13-14, 2007

Japan Chapter
Chapter Annual Meeting

December 2007

Japan Chapter
Sterilized Product GMP

September Top 10 Bestsellers

bookstore

- 1. Environmental Monitoring: A Comprehensive Handbook, Volume I, Volume II and Protocol CD**
Edited by Jeanne Moldenhauer, PhD
Item No. 17239, PDA Member \$530, Nonmember \$659
- 2. Pharmaceutical Quality Control Microbiology: A Guidebook to the Basics**
By Scott Sutton, PhD
Item No. 17242, PDA Member \$210, Nonmember \$260
- 3. PDA Technical Report 1, Revised 2007, Validation of Moist Heat Sterilization Processes Cycle Design, Development, Qualification and Ongoing Control** *New*
Item No. 01001, PDA Member \$150, Nonmember \$250
- 4. Encyclopedia of Rapid Microbiological Methods, Volume I, II and III**
Edited by Michael J. Miller, PhD
Item No. 17252, PDA Member \$730, Nonmember \$899
- 5. PDA Archive on CD-ROM – PDA Archive Retrieval Index**
Item No. 01101, PDA Member \$395, Nonmember \$590
- 6. Risk Assessment and Risk Management in the Pharmaceutical Industry: Clear and Simple**
By James L. Vesper
Item No. 17219, PDA Member \$235, Nonmember \$289
- 7. Laboratory Validation: A Practitioner's Guide** **20% Off**
Edited by Jeanne Moldenhauer, PhD
Item No. 17201, PDA Member \$295, Nonmember \$369
- 8. PDA Technical Report 39, Revised 2007, Guidance for Temperature-Controlled Medicinal Products: Maintaining the Quality of Temperature-Sensitive Medicinal Products Through the Transportation Environment** *New*
Item No. 01039, PDA Member \$100, Nonmember \$225
- 9. Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2007 - Book & CD-Rom Package**
Item No. 12009, PDA Member \$95, Nonmember \$115
- 10. Microbiology in Pharmaceutical Manufacturing** **40% Off**
Edited by Richard Prince
Item No. 17185, PDA Member \$285, Nonmember \$359

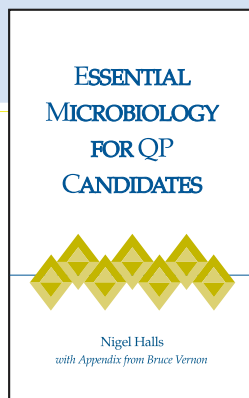
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PDA-DHI Publication

Essential Microbiology for QP Candidates

by Nigel Halls with Appendix from Bruce Vernon

This book has been prepared to address the requirements which are stated in the *Guide to the Knowledge and Practical Experience Required by Qualified Persons in the Pharmaceutical Industry* (the "Study Guide") in relation to pharmaceutical microbiology.

2007
ISBN: 0-933722-18-5

Item No. 17265
Member: \$225, Nonmember: \$279

Two New PDA Publications

Microbiology and Engineering of Sterilization Processes, Twelfth Edition 2007

By Irving J. Pflug, PhD

Item No. 13008
Member: \$225, Nonmember: \$275

Proceedings from the PDA Workshop on Mycoplasma Contamination by Plant Peptones

By Barbara J. Potts, PhD

Item No. 13007
Member: \$250, Nonmember: \$300

www.pda.org/bookstore

QbD: Still in Design? continued from page 25

this point are not much affected by the QbD paradigm shift. FDA also noted that, to date, no novel approaches to validation have been proposed to or observed by the Agency.

QbD Filing Content

Much confusion was expressed regarding what to include in a filing based on QbD concepts. FDA has not seen much from industry so far and is encouraging participation in a pilot program for companies interested in submitting a QbD filing. Such collaborations would allow issues to be addressed during assembly and as case studies for the Agency.

FDA made it very clear that it did not want to, nor had the time to, review very large, data-rich dossiers at the time of filing or even during an inspection. It stressed the need for higher-level summary documents that demonstrate product and process knowledge. Furthermore, the detailed summary should be integrated into the submission and not provided piecemeal. Detailed data and development reports, however, should be available for inspections if needed.

The suggested basic elements of this summary document are:

- Risk analysis including summary of previous knowledge
- Design of studies
- Results
- Conclusions of risk assessment and mitigation actions

To date, the Agency has seen very little in the way of high-level risk assessments for arriving at the design space definition. [Joneckis]

PAT

A presentation was also given on PAT [Koch]. A number of examples were described from other industries where benefits were derived from online, real-time measurements. Extraction of a sample from the process often changes its properties; thus, online measure-

ments offer a clear advantage in that a true measurement is obtained.

A Center for Process Analytical Chemistry (CPAC) initiative is in progress with Exxon Mobil and Dow to develop a new sampling/sensor initiative. A variety of onboard sample handling and analysis devices are available through Swagelok.

Another advantage of PAT is that it reduces the risk of not detecting a parameter deviation. This may even allow the criticality of a process parameter to be reduced. [Lam]

Raw Material Testing

The meeting also covered the subject of analytical profiling of raw materials for discovery and control. [Lanan] Acknowledging that a large fraction of the variation in the biological manufacturing process is often attributed to the raw materials, Biogen Idec has embarked on applying sophisticated multidimensional methods and multivariate analyses to the characterization of raw materials. These methods are nonspecific, but are faster to develop, see a wider set of compounds and, typically, apply to more matrices.


By using techniques such as two-dimensional high-performance liquid chromatography with the use of a diode array, full spectra are collected at multiple retention times. This allows a more complete profiling of media additives and, through principle component analysis, was shown to detect differences between higher- and lower-performing lots.

Going Forward

A number of ideas and initiatives were expressed that represent the next steps for the collective benefit of the industry and the regulatory agencies.

- Standardize terms
- Produce joint publication of guidelines
- Possibly expand PDA Technical

Report No. 42 or write new report as a guideline for QbD

- Pursue international harmonization
- Possibly form a consortium among industry and agency members to share more universal clinical and preclinical experiences around large-molecule drugs and biological process impurities. 

Speakers Cited

The following list includes speakers cited by the author in this report

Barry Cherney, PhD, Deputy Director,
Division of Therapeutic Proteins,
CDER, FDA

Rebecca Devine, PhD,
Biopharmaceutical Regulatory
Consultant

Kowid Ho, PhD, Biologicals/
BioTechnology Unit, Afssaps

Patricia Hughes, Consumer Safety
Officer, Therapeutic Facilities Review
Branch, CDER, FDA

Chris Joneckis, PhD, Senior Advisor
for CMC Issues, CBER, FDA

Mel Koch, PhD, CPAC, University
of Washington

Harry Lam, PhD, Director, Biochemical
Technology, Genentech

Maureen Lanan, PhD, Principal
Scientist, Biogen Idec

Anthony Mire-Sluis, PhD, Executive
Director, Quality, Amgen

Roger Nosal, Executive Director,
Regulatory CMC, Pfizer

Janet Woodcock, MD, Deputy Commis-
sioner for Operations/Chief Medical
Officer, CDER, FDA

This Month's Snapshot

Bob Dana, PDA

Welcome to the second edition of the PDA Quality and Regulatory Snapshot. As **Rich Levy** discussed last month in the inaugural edition, we intend to use this column to bring you news and updates on PDA's activities in the quality and regulatory affairs area, as well as to report on other items of importance in the areas of quality and regulatory affairs.

While we can't rival some of the things going on in TRI for entertainment value (See TRI Talk, p. 46 for the story of the delivery of the new Fedegari Autoclavi autoclave); there's still lots going on in the Quality and Regulatory arena. This issue provides an update on what's happening with some of the Task Forces who are working on various quality/regulatory initiatives, as well as a brief overview of our Regulatory Affairs and Quality Committee. There's a brief update on the goings-on with the Quality Systems Interest Group, and Jim Lyda contributed a summary of a recent meeting held between PDA representatives and the EMEA Inspections Sector for our Regulatory Relations section.

Again, we hope you find this feature useful and an effective means of providing you some information on PDA's activities in the Quality and Regulatory Affairs areas. We welcome your feedback on the content of this Snapshot, as well as your ideas and suggestions for future topics of discussion. Just email your thoughts to us at snapshot@pda.org. Until next month. 🍷

Task Force *Update*

ICH Q10, Pharmaceutical Quality Systems: One benefit to being as far behind as I am is that, at this writing, PDA's comments on the proposed ICH Q10 Guideline entitled *Pharmaceutical Quality Systems* have now been approved by the Board of Directors and submitted to FDA. They will also be submitted to the EMEA; however, logistics still need to be worked out to allow their submission to Japan. If I'd met the intended time line for this column, the comments would have still been a work in process. Our comments were strongly supportive of the basic principles outlined in the guidance, including areas such as life cycle thinking, management responsibility and expectations for escalation as necessary. We did, however, offer some suggestions and recommendations for improvement to the draft guidance, including improved wording for the tables discussing implementation examples, and the annex which discussed opportunities to enhance science and risk based regulatory approaches. The comment transmittal letter and PDA's comments can be seen at the PDA website, www.pda.org/regulatorycomments. The contents of the letter are also reproduced on p. 36 I'd like to thank the PDA volunteer members and staff who worked long and hard to develop and finalize these comments.

EMEA Contents of Batch Release Certificates for IMPs: As reported last month, a PDA task force chaired by **Karen Ginsbury**, PCI Pharmaceutical Consulting, had finalized comments on a proposed EMEA rule on the Batch Release Certificate for Investigational Medicinal Products. The comments were approved by the PDA Board of Directors and submitted to EMEA. The transmittal letter appears on p. 34, and the full letter and comments grid are available at www.pda.org/regulatorycomments.

EMEA Draft Guideline, Monoclonal Antibodies—Production and Control: Another PDA Task Force is currently working to develop comments on a proposed EMEA Guideline entitled *Guideline on Production and Quality Control of Monoclonal antibodies and Related Substances*. This Task Force is being led by **Anita Derks** of Roche, with the support of the European Biotech Interest Group and other PDA volunteers. With a comment due date of November 30, 2007, work on this project is progressing well, and we'll update you on the results in a future issue.

EC GMP Draft Annex 2: Manufacture of Biological Medicinal Products for Human Use: Yet another European proposal is receiving attention from our quality and regulatory colleagues. The European

continued on page 37

Advisory Board *Watch*

RAQC—What and Who Is It?

In reading the above and last month's entries about our comments, you might be wondering how this process works and who provides oversight for it. That's the work of PDA's Regulatory Affairs and Quality Committee (RAQC), led by Committee Chair **Zena Kaufman** (Abbott) and newly named Co-Chair **Steve Mendivil** (Amgen). Congratulations Steve! RAQC is currently composed of fifteen quality and regulatory professionals for the Asia Pacific, European, and the North American regions. Visit the Quality and Regulatory section of the PDA website for a complete listing of RAQC members.

The Committee typically meets 10–2 times a year, either in person or by teleconference, to consider global regulatory issues and evaluate which ones impact PDA and our membership. For those that do, a Task Force is developed and they go about the work of developing PDA comments. These comments are then reviewed and approved by the Committee and ultimately the PDA Board before submission to the appropriate regulatory authorities. Because comment periods, especially in the U.S., tend to be rather short (60–90 days) and time must be left for the review and approval process, the work of the Task Forces is intense and concentrated into a compressed time frame, generally 30–45 days. As you might imagine, this makes for some interesting teleconferences! As of the middle of September, RAQC had developed comments on 5 new regulatory initiatives this year, so the Committee and its Task Forces are keeping busy on that score. Committee members also contribute to the planning process for our various regulatory meetings, including our signature PDA/FDA and PDA/EMEA meetings. Members serve a three year term and can renew once. If you think you would be interested in being considered for RAQC membership, please let Iris or me know. ☺

Interest Group *Briefing*

Quality Systems Interest Group: We'll talk about Interest Groups in more detail in an upcoming issue, but I did want to call attention to the Quality Systems Interest Group, led by Dave Mayorga of GQA Consulting. They are currently in the process of redefining the objectives and expectations of their Interest Group, and recently formed a Steering Committee to help focus the process. You can see what's going on by visiting their Interest Group site on the PDA home page. I'm sure Dave and his Steering Committee would welcome your input. Email your suggestions and thoughts to him at david@gqaconsulting.com. ☺

Regulatory *Relations*

PDA Participates in EMEA GMP & GDP Working Group Interested Parties Meeting and ICH Q10 Briefing for Industry

On September 26, the EMEA Inspections Sector hosted the 2007 "Interested Parties" meeting at the EMEA headquarters in Canary Wharf, London. The interested parties meeting (IPM) is an opportunity for discussion between inspectors and industry representatives on the current GMP topics of interest. Immediately following, the EMEA hosted a briefing for the same audience on an overview of the ICH Q10 step 2 draft.

On the GMP front the IPM addressed the updated work plan for the GMP/GDP working group, a revision to Chapter 5 of the EU GMP guide on raw materials, discussion on atypical actives, and the role of the Qualified Person (QP) for active substances. The major topic of the IPM was the use and evaluation of the EMEA reflection paper on QP discretion in dealing with minor deviations from the marketing authorization (See the September 2007 Quality and Regulatory Snapshot in the PDA Letter, p. 30). This included generally positive reactions from industry on continued use and perhaps codification of the reflection paper into Annex 16 of the GMP guide. A unified industry position was created and presented by EFPIA as part of the discussion.

On the Q10 front, a briefing was given for industry regarding the current status and possible impact of Q10. The briefing was moderated by **Emer Cooke**, head of the Inspections Sector, and included presentations by **Neil Wilkinson**, AstraZeneca (representing EFPIA); **Jacques Morenas**, AFSSAPS, France; and **Ian Thrussell**, Senior Inspector, MHRA, UK. The briefing demonstrated the joint commitment by the regulators and industry to make Q10 a useful and valuable step for both parties, and for the patient.

PDA attendees included **Stephan Roenninger**, Roche; **Peter Reichert**, Novo Nordisk; **Gabriele Gori**, Bausch & Lomb; **Claudia Nardini**, Kedrion; **Peter Gough**, David Begg and Associates; and **Jim Lyda**, PDA.

PDA Submits Results of EMEA QP Discretion Survey

As reported last month, PDA collected survey results on the EMEA Reflection Paper on Quality Person Discretion for Dealing with Minor Deviations. The results have been approved by PDA's Board of Directors and submitted. Turn to page 32 for the complete letter and the survey results. ☺

PDA Submits QP Survey Results

18 September 2007

Mr. David Cockburn
 European Medicines Agency
 Inspections Sector
 7 Westferry Circus
 London E14 4HB
 United Kingdom

Regarding: *Reflection Paper on a Proposed Solution for Dealing with Minor Deviations from the Detail Described in the Marketing Authorisation for Human and Veterinary Medicinal Products (including biological products)*

Doc. Ref. EMEA/INS/GMP/71188/2006, 10 March 2006

Dear Mr. Cockburn:

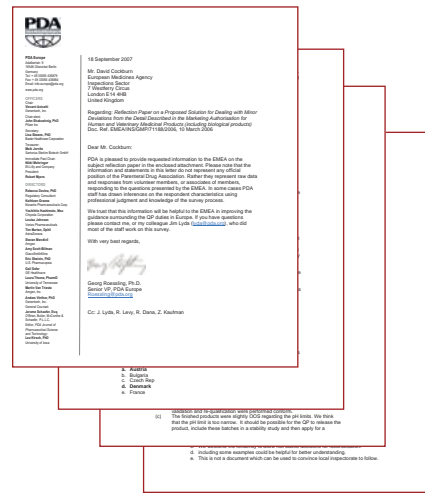
PDA is pleased to provide requested information to the EMEA on the subject reflection paper in the enclosed attachment. Please note that the information and statements in this letter do not represent any official position of the Parenteral Drug Association. Rather they represent raw data and responses from volunteer members, or associates of members, responding to the questions presented by the EMEA. In some cases PDA staff has drawn inferences on the respondent characteristics using professional judgment and knowledge of the survey process.

We trust that this information will be helpful to the EMEA in improving the guidance surrounding the QP duties in Europe. If you have questions please contact me, or my colleague Jim Lyda (lyda@pda.org), who did most of the staff work on this survey.

With very best regards,

Georg Roessling, Ph.D.
 Senior VP, PDA Europe
Roessling@pda.org

Cc: J. Lyda, R. Levy, R. Dana, Z. Kaufman



Survey Responses by EMEA Question

3.1 How many batches failed due to minor deviations for which the reflection paper did not provide solution?

No Response / Not Applicable	0	1-2	3-5	6-10	11-20	21-50	51-100	101+
5	13	2	2	1	1	0	0	0

5. Should the principles in the Reflection Paper be incorporated into Annex 16 of the GMP Guide? (of 23 responses)

- Yes 20 (87%)
- No 3 (13%)

Survey Responses by EMEA Question

1. Did you find the Reflection Paper helpful? (of 23 responses)

- Yes 20 (87%)
- No 3 (13%)

2. How many batches in last year did QPs follow recommendations to certify/release?

No Response / Not Applicable	0	1-2	3-5	6-10	11-20	21-50	51-100	101+
5	9	1	5	2	0	0	1 (60 bat)	1 (150 bat)

PDA INFO ON QP DISCRETION Methodology | Responders | Comments

- This info not official position of PDA
- It is raw responses to verbatim EMEA questions
- Input derived from on-line survey tool
- Invited volunteers for survey from global members
- 47 volunteered to take survey; 24 actually did
- Majority claimed to be QP or QP qualified
- Majority are from Europe
- Most from 'small to medium' size companies
- 'yes/no' answers gave very clear outcome
- Narrative answers conflicting and/or unclear

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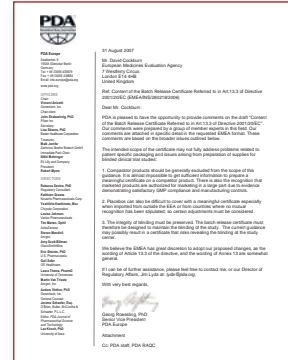
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PDA Comments on EMEA Batch Release Certificate

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

31 August 2007

Mr. David Cockburn
European Medicines Evaluation Agency
7 Westferry Circus
London E14 4HB
United Kingdom



Ref: Content of the Batch Release Certificate Referred to in Art.13.3 of Directive 2001/20/EC (EMEA/INS/280218/2006)

Dear Mr. Cockburn:

PDA is pleased to have the opportunity to provide comments on the draft “Content of the Batch Release Certificate Referred to in Art.13.3 of Directive 2001/20/EC”. Our comments were prepared by a group of member experts in this field. Our comments are attached in specific detail in the requested EMEA format. These comments are based on the broader issues outlined below.

The intended scope of the certificate may not fully address problems related to patient specific packaging and issues arising from preparation of supplies for blinded clinical trial studies:

1. Comparator products should be generally excluded from the scope of this guidance. It is almost impossible to get sufficient information to prepare a meaningful certificate on a competitor product. There is also the recognition that marketed products are authorized for marketing in a large part due to evidence demonstrating satisfactory GMP compliance and manufacturing controls.
2. Placebos can also be difficult to cover with a meaningful certificate especially when imported from outside the EEA or from countries where no mutual recognition has been stipulated; so certain adjustments must be considered.
3. The integrity of blinding must be preserved. The batch release certificate must therefore be designed to maintain the blinding of the study. The current guidance may possibly result in a certificate that risks revealing the blinding at the study center.

We believe the EMEA has great discretion to adopt our proposed changes, as the wording of Article 13.3 of the directive, and the wording of Annex 13 are somewhat general.

If I can be of further assistance, please feel free to contact me, or our Director of Regulatory Affairs, Jim Lyda at: lyda@pda.org.

With very best regards,

Georg Roessling, PhD
Senior Vice President
PDA Europe

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PDA Comments on Q10 Pharmaceutical Quality Systems

October 9, 2007

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, RM 1061
Rockville, MD 20852

**Reference: Draft Guideline entitled *Q10 Pharmaceutical Quality Systems*;
FR Notice July 13, 2007; Vol. 72, No. 134; Docket No. 2007D-0266**

Dear Sir/Madam,

PDA is pleased to offer comments on the Draft Guidance entitled *Q10 Pharmaceutical Quality Systems*, as published in the Federal Register on July 13, 2007. PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological and device manufacturing and quality. Our comments were prepared by a global group of PDA quality system experts and are attached in a spreadsheet with specific detail. PDA appreciates the opportunity to offer comments on this important document and wishes to thank the FDA for the opportunity to do so.

PDA strongly supports the concepts of life cycle thinking that are evident throughout the document and believes that companies embracing these concepts will facilitate the creation, seamless transfer, and maintenance of product and process knowledge. We also salute the articulation of management responsibility as well as escalation expectations—a quality system cannot be successful without the full endorsement and engagement of management. And finally, PDA appreciates that the document facilitates the concepts of continual improvement of the product, processes, and quality systems to assure capable and controlled operations.

Broadly speaking, and to further strengthen the document, we offer the following general comments. More detailed comments and suggestions for rewording are included in the attached spreadsheet which accompanies this letter. For ease of reference, we have attached a Word version of the original Guideline with line numbers added, and have referenced our comments by Section and line number.

1. While PDA enthusiastically endorses the concepts of life cycle thinking, we believe the tables could be improved with more meaningful examples. We have provided detailed comments for the tables in the attached spreadsheet.
2. The document provides commentary on the alignment of quality objectives with a company's strategic plans as well as the development and review of key performance indicators. We strongly support the development of quality objectives but find guidance on the alignment of those objectives to a company's "strategic plans" too prescriptive given the diversity in size and management approaches across the companies to which this guidance will apply. We are proposing the same intent with different language, replacing the words "strategic plans" with "company's corporate strategy and direction". We also find the terminology of "key performance indicators" to be less appropriate than the use of "performance metrics". For many companies key performance indicators are synonymous with financial results.
3. Finally, we have added wording throughout to emphasize the importance of defining roles and responsibilities as well as decision making processes.

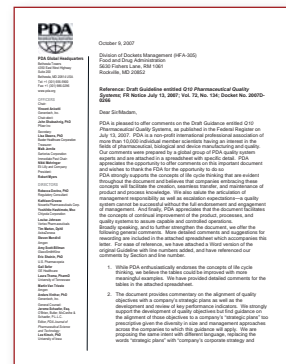
Again, PDA appreciates the opportunity to comment and offers these suggestions for your consideration. We believe that these comments will serve to streamline and strengthen the guidance and will create a document that will better serve the needs of both regulators and industry.

We would welcome the opportunity to participate in a public discussion of these and other comments which FDA may receive on the draft guidance, and would be happy to discuss the details of such a meeting and contribute to the planning process, should you wish to pursue that concept.

If you need further clarification, please do not hesitate to contact me.

Sincerely,

Robert B. Myers
President, PDA



Task Force Update, continued from page 30

Commission has proposed a revision to Annex 2 of the GMP Guide (Manufacture of Biological Medicinal Products for Human Use). Comments on this document are due March 14, 2008, so now would be an excellent time to get involved and volunteer to serve on the Task Force which will develop PDA's comments (new members especially – are you listening!). If you attended the new member breakfast or the breakfast session summarizing the process used to develop PDA's comments, as well as recently submitted comments, you already know something about how this works. I do not mean to exclude veteran members; your expertise would be appreciated as well. Volunteering is fun—hard work, but still fun—and it's a great way to meet other members and expand your networks, as well as contributing to a worthwhile PDA activity. Both BioAB and RAQC are interested in this, so if you are interested in volunteering, contact me (dana@pda.org) or Iris Rice (rice@pda.org).



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Finding Creative Ways to Connect Members: The Southern California Chapter's Corporate Outreach Program

Emily Alesantrino, PDA

Many PDA Chapters span large geographic areas, creating daunting challenges to chapter leaders trying to provide services to their entire membership. The sprawling Southern California Chapter recently formed a “corporate outreach program” to help connect members throughout its large region.

PDA recently spoke to Southern California's Chapter President **Saeed Tafreshi**, Intelitec Corporation, and the new Chapter “Corporate Outreach Coordinator” **Ruchika Raval**, Global Biopharmaceutical Regulations, about the challenges and solutions associated with operating a PDA chapter with a large geographic territory. The Southern California Chapter serves members in three large California counties: Ventura, Los Angeles and San Diego. As a result, the chapter started exploring innovative approaches to best serve the membership.

“From day one we realized there was a big disconnect between our PDA chapter and our members,” said Tafreshi. “So, we started calling people—we've talked to almost every member in our area over the past year.” To deal with the chapter's evident communication obstacles, Raval along with Tafreshi instituted the Corporate Outreach Program. Corporations with a large number of PDA members in the chapter territory are identified and used as communication vehicles for the chapter. Representatives within these targeted corporations are asked to set up an internal board and act as liaisons between the Southern California Chapter and PDA members within their company and/or local community.

“It has been incredibly rewarding,” commented Raval. “We have approached several companies, and



Ruchika Raval and Saeed Tafreshi

we are increasing the database of speakers. Moving forward, we will continue to add corporations. The more companies in the program, the more members our events reach, and their feedback allows us to tailor the events to their needs. It is also rewarding for the volunteers. We all see the need to have local working groups in each area—it helps move the program forward. When corporations appoint their representatives, they see this as part of their employee career development programs.”

Tafreshi added, “The idea was to create a communication system that would last throughout the years—people can come and go, but systems can stay.”

Company representatives support the chapter by opening two-way communication between the chapter members and leaders. Relaying important chapter information and cultivating program ideas with chapter members are the key responsibilities of these volunteers. “Listening to chapter members is extremely important; if there is not a formal vehicle available, set one up,” Raval stated. Because feedback is given directly from chapter members to leaders, targeted and relevant programs can be developed for these members. “This is a practical communication tool, because we realize it is impossible to be in contact with every member,” noted Tafreshi.

The PDA Southern California Chapter has also found some unique ways

to tackle the problem of member outreach. One idea that is currently being explored is to hold an event on a boat or cruise ship. The cruise would pick up and drop off at three locations along the coast, and the meeting would be held out at sea. “What is the difference if members go to a hotel or on a cruise? Either way, we will offer interesting programs and top speakers,” said Tafreshi.

A second idea has already been implemented. Using web-based programming, the Southern California Chapter holds simultaneous meetings in multiple locations. Meeting speakers can physically be located at one chapter location but heard at other meeting sites. For example, a recent talk given by **Jaspreet Sidhu**, PhD, VP, Business Development, Molecular Epidemiology, on microbial testing was heard in both Irvine and Thousand Oaks. A presentation by **Ron Tetzlaff**, PhD, VP, PAREXEL, was heard by members in the cities of San Diego and Irvine and at sites in Ventura County. The advantage of this type of programming is that questions and answers can be asked and answered live.

For a chapter that has members in Los Angeles to San Diego, eliminating the commute is a key factor to more member participation. “By using the technology available, individuals in all locations have the opportunity to ask questions and interact through real-time feed. This option dramatically increases the number of chapter members who can participate in an event,” commented Tafreshi. “We're doing this for the love of the industry, for the love of what we do. You know, we're all professionals and have taken something out of this industry, and this is the opportunity for us to put something back,” said Tafreshi. 🌊

Volunteer Spotlight



Name: Bob Dana

Company: PDA

Title: Vice President, Quality and Regulatory Affairs

Education: BS, Pharmacy, University of Connecticut; Non-degree graduate study program in business administration, Syracuse University

PDA Join Date: 1985

Areas of PDA Volunteerism:

Member of Regulatory Affairs and Quality Committee, Inspection Trends/Regulatory Affairs Interest Group Leader, Quality Systems and Regulatory Affairs Interest Group Section Leader, Instructor for PDA's Training and Research Institute, Speaker and moderator at numerous PDA meetings, Former PDA Director, Past Program Planning Committees: Spring Conference (Chair), Annual Meeting and PDA/FDA, Past member of several PDA task forces, including co-chair of task force responsible for developing PDA comments on May 1996 proposed changes to FDA's GMP regulations

Professional Awards Won:

I received a Distinguished Service Award from PDA in 1998.

Interesting Fact about Yourself:

When I'm not busy with PDA and the weather is nice, which of course we don't have a lot of in Syracuse, I play golf and I fly fish. I tie flies in the winter and I fly fish in the summer, spring and fall.

Of your PDA experiences, which stand out the most?

One of the things I remember more than anything else is the work we did to put together PDA's comments on the proposed GMP regulations in 1996.

Which member benefit do you most look forward to?

The benefits I most look forward to on a repetitive and ongoing basis are the *PDA Letter* and the PDA/FDA conference. I really enjoy looking through the Letter. I typically look through it and read most of the articles in it. I always did read most of the articles in it. The Letter is pretty much a cover to cover experience for me. And for the PDA/FDA conference, I've been going since the meeting began. I've just always

found it to be a really enriching experience. It is great in terms of finding out what is going on in the regulatory world, which is a piece of the world that is important to me and always has been. It is also a great opportunity to meet a lot of the people or "re-meet" a lot of the people I've known over the years with PDA. It's a chance to renew old friendships and make some new ones.

Which PDA event/training course is your favorite?

Of all the repetitive events, the PDA/FDA conference is probably my favorite PDA event. I also think the work PDA's Training and Research Institute has done over the years has really been great work. TRI just celebrated its 10th anniversary. I was involved with the beginning of the TRI experience, certainly in its early stages. I watched it struggle a bit in its early years and then grow to what it has become now. I just think it's a terrific value and benefit, and there is no place like it in the industry that provides the physical facility and resources combined with the hands-on knowledge and education that TRI does. We have such a terrific cadre of instructors, and the new facility is going to be great. TRI is a great place to get involved. Gail Sherman and TRI are always looking for new instructors and new course ideas.

How has PDA benefited you professionally?

PDA has done a lot for me professionally. It certainly has made me a more knowledgeable person. I am much more aware of what is going on in the global arena. So, knowledge and awareness are the key benefits for me. The relationships I've made through my membership are also a very big piece of what I get out of PDA. To me, these relationships are really important. I have met a lot of terrific people throughout my years with PDA. I count a great number of them as personal friends, which has been a very rewarding experience for me. They are all great sources of knowledge as well—they're people I can call on if there is information I am looking for. I can also use them as springboards to sound ideas off of, and I can provide their names to people who are looking for information in areas that I'm just not that familiar with. I think these are the two biggest benefits—the knowledge I've gained and the relationships I've made. Actually, it's probably the other way around—it's really the relationships and friendships I've made and the opportunities I have to keep them going. And then it is how these relationships play into knowledge and awareness for me.

People ask me why I wanted to take a job with PDA after all the years I have worked, and you have to remember I worked in the industry for a lot of years. I always viewed PDA as the primary, absolutely best source of scientific, technical and regulatory information in the industry. I just didn't think anybody else came close to PDA in terms of what it was able to put together, the positions it was able to take, and the knowledge it was able to pass on to its membership, or to the membership and the industry as a whole. So to me, PDA was always the number one organization anywhere in the world. I have been a volunteer member for over 20 years, so when I had the opportunity to come and work here and maybe contribute something, give something back to the organization that has done a lot for me, I thought it was a great opportunity.

PDA Welcomes New Members

Nana Abe, JMS

Colin Abercrombie, Genzyme

Laura Abrams, GlaxoSmithKline

Frank Abbato, DME Alliance

Paula Adams, Anesiva

Michael Adler, F. Hoffmann-La Roche

Arun Agarwal, Becton Dickinson

Maria Ohrner, Octapharma

Daniel Allocco, Precision Pharma Services

Michael Andrew, Medimmune

Wesley Ange, Clarkston Consulting

Hiroaki Arai, Daiichi Sankyo

Jonna Arentoft, Nycomed

Benny Auyeung, Schering-Plough

Jim Axtelle, Insert Therapeutics

I Gusti Putu Bagus Diana Virgo, Kalbe

Sahar Bahrani, Baxter

Sanjay Bajariya, Claris

Deana Baker, Criteria Validation

Sarah Balmer, sanofi pasteur

Jinming Bao, Eastbound Synopharma

Amy Barnard, Medimmune

John Barnes, Genentech

Thomas Barnhart, MedImmune

Megan Barth, Sterigenics

Amy Baumgard, Ben Venue

Roy Behrman, Forest Laboratories

Shirish Belapure, Zydus Cadila

Steve Belikoff, Advanced Medical Optics

Arthur Bergeron, Bristol-Myers Squibb

Alpaben Bhakta, Aderans Research

Soumendu Bhattacharya, Schering-Plough

Christy Bigelow, Emergent BioSolutions

Gabriel Bikah, Merck

Patrick Blacha, Eli Lilly

Michelle Blackwell, GlaxoSmithKline

Derek Blaettler, Genentech

Obed Boateng, Allergan

Bernd Boedecker, Trade & Industrial Inspection Agency

Roberto Guido Bonacchi, Consultant

Lilla Bouilatitene, Sandoz

Chad Boykin, GlaxoSmithKline

Sharon Braithwaite, sanofi pasteur

Megan Brandt, PDL Biopharma

Marilyn Brandt, ImClone

Yael Brenner, Teva

Erin Brewster, Ben Venue

Jeanette Brill, Jerini

Kimberly Buchanan, Merck

June Burge, Wyeth

Kathie Burkett, CSL

James Butler, SGS

Linda Calderbank, TEVA

Johnna Calverase, Novo Nordisk

Douglas Campbell, U.S. FDA

HongHoa Cao, DePuy Spine

Lili Cao, SFDA

Jeff Carey, Novavax

Michael Carlson, Microtest

Daniel Carpenito, Commissioning Agents

Fiona Carroll, GE Healthcare

Bobbie Carter, Arena Pharmaceuticals

Alloin Cecile, GlaxoSmithKline

Krishna Chandran, Sartorius

Sonia Chatellier, bioMerieux

Shaoqiang Chen, JPT Consulting

Yizhen Chen, Shanghai Municipal FDA

Ankita Chitre, Cell Genesys

Choi Yiau Chong, Sihuan Pharmaceutical

Xiuhai Chu, JPT Consulting

John Clarke, Akorn

Nathaniel Clements, Bristol-Myers Squibb

Mark Copeland, Eli Lilly

Brian Corrigan, Wyeth

Joseph Cramer, Hospira

Linda Critelli, Forest Laboratories

Ginamarie Currao, Luitpold

Soren Damkaer, Novo Nordisk

John Davidson, Wyeth

Vonna DeArmond, Imclone

Michele Delaney, Stryker

Paul Derbyshire, Derbyshire Validation

Martin DeStafney, Cryolife

Frederick DeVries, Jr., PAREXEL

Sasa Dizdar, Pliva Croatia

Tara Dougherty, Tengion

Elizabeth Draminski, Emergent BioSolutions

Edward Duffy, Princeton

Anthony Durning, Cardiokine

John Dziuba, Emergent

Fabiola Echegaray, Cetco

Ulf Edberg, Octapharma

Laura Elan, Baxter

Steven Ellers, West Pharmaceutical Services

Björn Elowsson, REXPAC

Karen Emborg, CCURE

Scott Engelking, Watson

Arthur Fabian, SST

Lai Fai, Health Sciences Authority

Barry Fairand, Sterigenics International

Yuming Fang, Shanghai Institute for Food and Drug Control

Thomas Feller, Bristol-Myers Squibb

Adam Fenimore, Alkermes

Niki Fidopiastis, Sterigenics

Kelly Field, Pfizer

Clay Flowers, Northern Lipids

Martha Folmsbee, Pall

Lisa Foster, Sterigenics

Lee Fox, Wyeth

Christina Frey, GlaxoSmithKline

Sheldon Fry, sanofi pasteur

Christine Fuerst, Vetter

Felipe Fukuda, AstraZeneca

Eric Fukumitsu, Genentech

Eran Gabbai, Do-Coop Technologies

Edward Gallagher, CSL Behring

Huijun Gao, Shanghai Municipal FDA

Melissa Garcia, MG Consulting

Gregory Garland, sanofi pasteur

Janet Gent, Pfizer

Carl Gentry, Wyeth

Nancy Giard, Genzyme

- Mick Giles**, Organon
- Indrajit Giri**, Medarex
- Jason Gledhill**, Cell Genensis
- Martin Gohlke**, Dynavax Technologies
- Patricia Gomes**, sanofi pasteur
- Todd Gonitzke**, Accugenix
- Marcos Gonzalez**, Avid Bioservices
- Andrew Graham**, AlphaVax
- Tamara Grisard**, Novartis
- Matthias Gruber**, Roche Diagnostics
- Xiaocheng Gu**, Peking University
- Abaibou Hafid**, bioMerieux
- Shane Haft**, Rocky Mountain Compliance Specialists
- Colleen Hagofsky**, Gerresheimer Buende
- Jennifer Hahn**, Quality Consultant
- Alisa Haller**, West Analytical Services
- Lars Hansen**, Novo Nordisk
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- Ben Harpring**, Eli Lilly
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- Christopher Hill**, CSL
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- Joyce Holland**, Vistakon
- Vivian Horvath**, Ben Venue
- Mary Howe**, Pfizer
- Catherine Hulcio**, sanofi pasteur
- Sung Hung**, Human Genome Sciences
- Desmond Hunt**, USP
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- Susan Hynes**, Bristol-Myers Squibb
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- Nathan Ihle**, Seattle Genetics
- Thomas Ingallinera**, Consultant
- Viorica Iorga**, Wyeth
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- Mikihito Ito**, KIRIN
- Jan Jakobsgaard**, Biogen Idec
- D. Victor Jewell**, SAFC Biosciences
- Tongbo Jiang**, Millipore
- Aniela John**, sanofi pasteur
- Jefferey Jones**, Emergent Biosolutions
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- Bram Jongen**, Helvoet Pharma
- Surekha Karudapuram**, Applied Biosystems
- Mitsunori Katoh**, Dainippon Sumitomo
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- Julie Keeling**, Nabi Biopharm
- Robyne Kelemen**, Cephalon
- Kimberly Kelly-Wintenberg**, Atmospheric Glow Technologies
- William Kentrup**, Wyeth
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- Kandarp Patel**, Baxter
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- Sandy Pei**, JPT Consulting
- Craig Peluso**, Shire
- Todd Perez**, Leica Microsystems
- Carlos Alberto Pinzon Quiroga**, BPM Andina
- Newsha Poursohi**, Genentech
- Jayasri Prabakaran**, Keck Graduate Institute of Applied Life Sciences
- John Price**, Berkshire
- Jessica Pytko**, SAFC Biosciences
- Ma Qinghua**, Watertown Pharmaceutical Equipment
- Karen Quarford**, ZymoGenetics
- Antonio Quinones**, Fluor Daniel Caribbean
- Chris Ramana**, CIBA Vision
- Parvin Rastegar**, Keck Graduate Institute of Applied Life Sciences
- Tom Rebne**, Solvay Pharmaceuticals
- Mathilda Reeves-Jones**, Eli Lilly
- Matthew Ressler**, Enzon Pharmaceuticals
- Ken Rhone**, Emerson Process Management
- Sean Richardson**, Solstice Neurosciences
- Scott Richmond**, Human Genome Sciences
- Mayra Rivera-Ramos**, GlaxoSmithKline
- Rex Roberts**, West Pharmaceutical Services
- Donald Rogers**, Bristol-Myers Squibb
- Tone Rojahn**, GE Healthcare
- Marc Roman**, Biolex Therapeutics
- Michael Rooney**, BioTechLogic
- Joseph Runkle**, West Pharmaceutical Services
- Niesha Russell**, Shire
- Paul Sachtleben**, SciLucent
- Yuka Saika**, Nihon Pharmaceutical
- Sanjay Samudre**, CIBA Vision
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- Susan Shumate**, Organon Teknika
- Ajit Simh**, Arena Pharmaceuticals
- Arlene Simmons**, Biokinetics
- Regina Simmons-Bell**, Human Genome Sciences
- John Sirna**, Apotex
- Marie-Anne Slaney**, Therapeutic Goods Administration Library
- Leonard Smith**, U.S. Army Medical Research Institute of Infectious Diseases
- Ryan Smith**, CIBAVision
- Douglas Smith**, Valitech Compliance
- Jason Snyder**, Diosynth
- Paul Snyder**, Novartis
- Ari Sobel**, West Pharmaceutical Services
- Jeffrey Soderberg**, Mediatech
- Lise-Lotte Soerensen**, Novo Nordisk
- Alan Solomon**, Baxter
- Antonio Souto**, Wyeth
- Alex Spencer**, Ben Venue
- Paula Spencer**, Amgen
- Ramakrishnan Srikumar**, Allergan
- Nicole St. Lawrence**, Microtest
- Kathryn Stein**, MacroGenics
- Dirk Steinhoff**, Institut Straumann
- Marco Stephano**, Sao Paulo University
- Jeffrey Stockman**, General Electric
- Peter Stojnic**, NNE Pharmaplan
- Scott Stratton**, Baxter
- Greg Strickland**, Mentor
- Curtis Strother**, Targanta Therapeutics
- Emily Stump**, PDM Core
- Denise Sturdevant**, Baxter
- Jeffrey Su**, sanofi pasteur
- Nanda Subbarao**, Biologics Consulting Group
- Shuichi Sugie**, Daiichi Sankyo
- Soo Kyung Suh**, Korea FDA
- Fang Suming**, Suzhou Dawnrays Pharmaceutical
- Susmitha Sunkara**, Bayer
- Todd Sunstrom**, Cephalon
- Christian Supina**, Baxter
- Rocco Surace**, Wyeth
- Linette Swayne**, Alkermes
- Chiang Syin**, FDA
- Eiji Takahashi**, Kyowa Hakko Kogyo
- Kazunori Takamoto**, Medtronic
- Christopher Tam**, Sepracor
- ChinBin Tan**, Millipore
- Tohru Tanami**, Taisho Pharmaceuticals
- Minhao Tang**, Shanghai Municipal FDA
- Constance Taylor**, Merck
- Matthew Tench**, Ben Venue
- Marianne Thompson**, Alexion Pharmaceuticals
- Timothy Thompson**, Eisai
- Paul Thompson**, Bausch & Lomb
- Stacey Thompson**, Baxter
- Anders Thorn**, Novo Nordisk

If your information appears inaccurate in this list, please visit www.pda.org to update your profile or email changes to info@pda.org.

Chapter Contacts

The following is a list of the PDA Chapters, organized by the regions of the world in which they are located. Included are the Chapter name, the area(s) served, the Chapter contact person and his or her email address. Where applicable, the Chapter's website is listed. More information on PDA Chapters is available at www.pda.org/chapters.

Asia-Pacific

Australia Chapter

Contact: Anna Corke

Email:

acorke@medicaldev.com

India Chapter

Contact: Darshan Makhey, PhD

Email:

dmakhey@hotmail.com

Japan Chapter

Contact: Katsuhide Terada, PhD

Email: terada@phar.toho-u.ac.jp

www.j-pda.jp

Korea Chapter

Contact: Woo-Hyun Paik, PhD

Email: whpaik@hitel.net

Southeast Asia Chapter

Contact: K. P. P. Prasad, PhD

Email: prasad.kpp@pfizer.com

Taiwan Chapter

Contact: Shin-Yi Hsu

Email: shinyi.hsu@otsuka.com.tw

www.pdatc.org.tw

Europe

Central Europe Chapter

Contact: Andreas Wenng, PhD

Email:

andreas.wenng@chemengineering.com

France Chapter

Contact: Jean-Louis Saubion, PhD

Email: ufch@wanadoo.fr

Ireland Chapter

Contact: Frank Hallinan

Email: hallinf@wyeth.com

Israel Chapter

Contact: Raphael Bar, PhD

Email: rbar@pharmos.com

Italy Chapter

Contact: Stefano Maccio, PhD

Email: stefano.maccio@ctpsystem.com

www.pda-it.org

United Kingdom

Contact: Siegfried Schmitt, PhD

Email: siegfried.schmitt@parexel.com

North America

Canada Chapter

Contact: Patrick Bronsard

Email: patrick.bronsard@snclavalin.com

www.pdacanada.org

Capital Area Chapter

Areas Served: MD, DC, VA, WV

Contact: Allen Burgenson

Email:

allen.burgenson@lonza.com

www.pdacapitalchapter.org

Delaware Valley Chapter

Areas Served: DE, NJ, PA

Contact: Art Vellutato, Jr.

Email: artjr@sterile.com

www.pdadv.org

Metro Chapter

Areas Served: NJ, NY

Contact: Nate Manco

Email: natemanco@optonline.net

www.pdametro.org

Midwest Chapter

Areas Served: IL, IN, OH, WI, IA, MN

Contact: Madhu Ahluwalia

Email: madhu@cgxp.com

www.pdamidwest.org

Mountain States Chapter

Areas Served: CO, WY, UT, ID, NE, KS, OK, MT

Contact: Sara Hendricks

Email: scarry@att.net

New England Chapter

Areas Served: MA, CT, RI, NH, VT, ME

Contact: Louis Zaczekiewicz

Email: lzaczekiewicz@hyaluron.com

Puerto Rico

Contact: Manuel Melendez

Email: manuelm@amgen.com

Southeast Chapter

Areas Served: NC, SC, TN, VA, FL, GA

Contact: Patrick Sabourin

Email: psabourin@clarkstonconsulting.com

Southern California Chapter

Areas Served: Southern California

Contact: Saeed Tafreshi

Email:

saeedtafreshi@intelitecorporation.com

www.pdasc.org

West Coast Chapter

Areas Served: Northern California

Contact: John Ferreira

Email: jferreira@banzigersystems.com

www.wccpda.org

Programming Department Offers a Full Lineup of Conferences

The PDA Programs and Registrations Services Department is as busy as ever this autumn. We have just completed one of the most successful PDA/FDA Joint Regulatory Conferences to date in time to move on to the Visual Inspection Forum (Oct. 15-16), the 2nd Annual Global Conference on Pharmaceutical Microbiology (Oct. 29-31), and the Extractables/Leachables Forum (Nov. 6-8).

New this year is the PDA/FDA Co-Sponsored Conference Series on Quality Systems. This is an international conference series with meetings taking place in Bethesda, Md. (Nov. 1-2), Dublin, Ireland (Dec. 10-11), Beijing, China (Apr. 21-23) and Shanghai, China (Apr. 24-25).

We are very excited to share the experiences of expert professionals with the global community.

2008 is shaping up to be just as busy and exciting. To highlight a few events, PDA's 2008 Annual Meeting will be held at the beautiful Broadmoor Hotel and Resort in Colorado Springs,



(Left to right) Shyla Fuentes (Customer Service), Nikki Nasabzadeh (Assistant Director, Programs & Meetings), Leslie Edmonds (Coordinator, Programs & Meetings), Luis Castro (Senior Coordinator, Programs), Christina Bogyo (Senior Manager, Programs & Meetings), Jason Brown (Senior Coordinator, Programs), Paula Pagano (Assistant Manager, Programs & Web Seminars), Patresa Day (Assistant Manager, Registration & Customer Services), and Wanda Neal-Ballard (Vice President, Programs & Registration Services)

Colorado, Apr. 14-18. Through this meeting, PDA is committed to bringing the membership the latest information on science and technology innovations. For the first time, PDA is featuring celebrity keynote addresses from **Linda Armstrong Kelly**, the mother of Tour de France

Champion **Lance Armstrong**, as well **Shelley Morrison**, the actress who played Rosario on **the NBC series *Will and Grace***. Both speakers will provide insight on their struggles when diagnosed and while coping with breast cancer and the role the pharmaceutical industry played in their recoveries.

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FILAMATIC



PDA is proud of its decision to bring the Biennial Training Conference (May 19-23) back to New Orleans in 2008, which was previously cancelled due to the Hurricane Katrina. In addition to offering best practices in training, PDA volunteers plan to assist in this city's economic recovery. More information on this effort will be included in upcoming issues of the *PDA Letter* and in the conference materials.

To best serve you, the Programs and Registration Services Department works in teams on each conference. There is a liaison to each program planning committee as well as a speaker manager and a dedicated registration person. In addition, the department designates an assistant director to oversee all conference logistics.

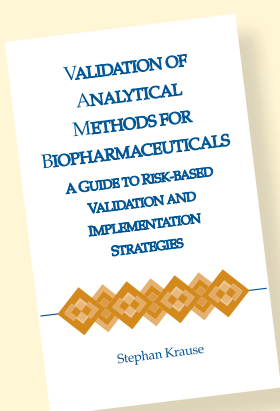
New innovations in registration help PDA deliver excellent customer service to conference/event attendees. A newly implemented "no call goes



The Programs and Meetings Department thanks Katey Webber, our valuable summer intern, for all her help, especially with the PDA/ FDA Joint Regulatory Conference

unanswered" policy requires that every call is answered by a customer service specialist. Over the next few months, PDA will implement a new event/registration management system and ask for your comments. This system will take the department to the next level, and the membership will surely benefit and see immediate results.

For more details on conferences and the web seminar program and for the department's contact information, please visit www.pda.org. The Programs and Registration Services Department is here to ensure your best PDA experience. ☺



What Other PDA Members Think of *Validation of Analytical Methods for Biopharmaceuticals: A Guide to Risk-Based Validation and Implementation Strategies*

"The book contains many new practical tips, tools, and case studies that will validation scientists and management to make good risk-based decisions during planning, execution, and post-implementation changes for all projects.

This book is therefore centered on what "sufficient performance" and "suitable for use" really mean for analytical methods. You will also learn what risk really means when it comes to analytical methods. How can we measure risk and how can we control this risk using well-designed validation studies.

Currently, regulatory guidelines provide only basic guidance for analytical method validation. Dr. Krause's work builds on these basic regulatory guidance documents and provides several detailed validation practices, discussions, and case studies on the best-possible strategies to assist readers to make good decisions.

After reading this book, I felt a bright light focused on many of the items that I once considered hidden in a black box. I encourage validation scientist, quality and regulatory managers to read this thought provoking book to better understand how to effectively monitor your production processes and quality of your products. It will also allow you to prepare quicker and more robust regulatory filings.

I hope you enjoy the work in this book as much as I have."

Martin VanTrieste
VP Quality, Commercial Operations

Bethesda—We Came, We Saw, We Conquered!

Gail Sherman, PDA

TRI TALK

TRI has officially and ceremoniously opened its doors in Bethesda, Md. While we moved to our new location on July 2, we did not receive full occupancy until August 20, when the last inspector walked out as our “Aseptic Processing Training Program” students were walking in. We were holding our collective breath, knowing all the while that it would be just fine. To date, we have successfully run three laboratory courses—the “Environmental Mycology Identification Workshop,” “Downstream Processing: Separations, Purifications and Virus Removal” and of course the “Aseptic Processing Training Program” (all 10 days of it!).

I won't tell you that the move went off without a hitch. As a matter of fact, the day we were scheduled to move from Baltimore to Bethesda, we learned that our movers forgot to schedule us. Fortunately, we were lucky to end up with a great evening crew who packed almost everything into the trucks for delivery to Bethesda the next day, or so we thought. A few weeks later we actually learned that we had left some equipment on the loading dock in Baltimore!


Our biggest challenge to date was getting the Fedegari Autoclavi autoclave in place. It was one of the hottest days in July—a Friday to be exact. We had been waiting patiently for our new autoclave to arrive from Italy, along with a Fedegari technician who had come all the way from Italy to assist with the installation. Around 9:00 that morning, a truck pulled up in front of the building and the driver informed us that she had a crate weighing about 1,700 kilograms (3,740 pounds). The truck didn't have a liftgate and or a pallet jack, and we definitely didn't have enough arms to budge that amount of weight. We called our shipper, and he showed up with another truck—still no liftgate or pallet jack. Around 3:00 that afternoon, we rented a forklift and a flatbed truck and managed to get the 1700 kilo crate to the ground. However, we couldn't get the crate the additional 75 feet into our space. So, we spent the next three hours uncrating and dismantling what we could (thanks to PDA staff **Frank Sarlo, Feng Chen, Bob Collier and Jason Brown**) and trying to find movers or riggers who could move the bulk of the machine into place. Of course, no one could do anything until morning. As night came, we wrapped the remaining piece of equipment in blankets and bags, hired a security guard and called it a night. The next morning, armed with forklift and movers, the autoclave was finally moved into its permanent home. Now we are waiting for another piece of equipment—crated weight 800 kilos. This one will be a snap as long as we can get it off the truck!

As an aside, I want to thank our friends and colleagues at the University of Maryland Biotechnology Institute for performing the autoclaving for our first Aseptic Processing course for us at their facility since our autoclave wasn't functioning yet.

I could tell you many other stories, probably best told over a glass of wine. The challenges were many, but the TRI staff accepted them head on and never gave up. I think TRI's **James Wamsley** moved his cot into the office for the duration, and I'll sure be happy to have a weekend at home one day soon! We still have some arranging and rearranging to do, but things are falling nicely into place. It's amazing how everything somehow works out.

We dedicated the facility on September 26, just over 10 years after the original TRI was dedicated in Baltimore. We look forward to another successful 10 years and more in Bethesda.

Before I call it quits for this month, I'd like to remind you that we have two very important training programs coming up in Europe over the next few months. We will be conducting training on the newly revised Technical Report No. 39, *Guidance for Temperature-Controlled Medicinal Products*, with the authors as instructors in Berlin (Oct. 15-16) and Cork (Nov. 15-16). Also in Cork, we will be offering a training program on the revised Technical Report No. 1, *Validation of Moist Heat Sterilization Processes*. Experts who were key to the revision of this report, including PDA President **Bob Myers**, will facilitate the program. Please join us for these very important and new training programs.

Next month we will run a photo spread of the new TRI from the groundbreaking to the dedication a true work in progress! 

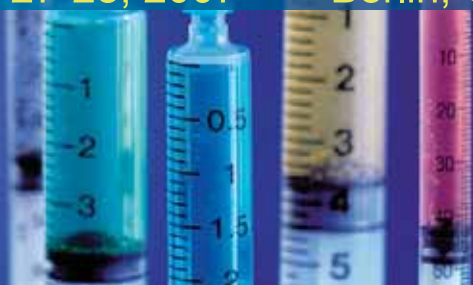


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Upcoming Event

Regulatory Expectations: Modern Sterile Manufacturing

Johann Kurz, Austrian Federal Ministry of Health,
Family and Youth, and Volker Eck, PDA

Sterile manufacturing is one of the most critical aspects of pharmaceutical production. For any individual in an industry or regulatory setting to judge with competence such manufacturing operations, many years of experience in this sophisticated area are needed. Sterile manufacturing, particularly aseptic production, is also a challenge for regulatory bodies and inspectorates enforcing legislation that might not fit the practical challenges.

The core issues of filling and capping will be featured topics of discussion during upcoming presentations at the Modern Aseptic Production conference in Södertälje, Stockholm, Sweden, Nov. 7-8. EU GMP Annex 1 is the regulatory basis for sterile manufacturing. The evolution of Annex 1 has been the result of many discussions leading to a prolonged consideration by the EMEA of input from the industry, scientific associations like PDA and individuals who specialize in sterile manufacturing. The version of Annex 1 recently adopted by the GMP working party at the EMEA will be discussed at this conference. The changes in the Annex, their interpretation, and the impact on a modern aseptic production will be reviewed with practical examples of sterile manufacturing sites.

Interestingly, the EMEA has published a report on GMP deficiencies observed in the decade from 1995 to 2005.

In evaluating this document (*Good Manufacturing Practice: An analysis of regulatory inspection findings in the centralised procedure*), there are several interesting aspects worth noting when looking closer at the 9,465 observations listed.

Chapter 4.3 ("Comparison of deficiencies in the manufacture of sterile products versus nonsterile") of

Table 8

	Non-Sterile	Sterile
Number of inspections	186	249
Number of critical deficiencies	33 (0.88%)	160 (2.77%)
Number of major deficiencies	251 (6.72%)	752 (13.00%)
Number of other significant deficiencies	3451 (92.40%)	4872 (84.23%)
Total deficiencies	3735	5784
Average deficiencies per inspection	20	23

Table 8 is a comparison of the deficiencies found from 1995 to 2005 between manufacture of sterile vs. nonsterile medicinal products.

Critical

Ranking	Category of GMP Deficiency	Number	Incidence (%)
2	Contamination, microbiological – potential for	20	10.4
7	Personnel issues: Hygiene/Clothing	11	5.7
8	Environmental control	10	5.2
10	Sterility assurance	8	4.1
11	Environmental monitoring	7	3.6
	Total	56/193	29.0

Major

Ranking	Category of GMP Deficiency	Number	Incidence (%)
1	Contamination, microbiological – potential for	112	11.2
6	Sterility assurance	53	5.3
15	Environmental monitoring	25	2.5
16	Personnel issues: Hygiene/Clothing	25	2.5
n/l	Environmental control	n/l	n/l
	Total	215/989	21.7

n/l: not listed

Critical

Ranking	Category of GMP Deficiency	Number	Incidence (%)
1	Design and maintenance of premises	31	16.1
3	Contamination, chemical/physical – potential for	17	8.8
12	Design and maintenance of equipment	6	3.1
n/l	Equipment validation	n/l	n/l
	Total	54/193	28.0

n/l: not listed

Major

Ranking	Category of GMP Deficiency	Number	Incidence (%)
4	Design and maintenance of premises	59	6.0
9	Equipment validation	43	4.3
10	Design and maintenance of equipment	36	3.6
13	Contamination, chemical/physical – potential for	33	3.3
	Total	171/989	17.3

Chapters and People

Susanne Keitel Named New Director of EDQM

Susanne Keitel, PhD, was recently appointed Director of the European Directorate of the Quality of Medicines & HealthCare (EDQM). EDQM is the European organization best known for publishing and administering the European Pharmacopoeia (PhEur). Keitel joins the EDQM after more than 20 years of international experience in the regulatory and pharmaceutical sectors.

Keitel served as Head of EU, International Affairs at Germany's Federal Institute for Drugs and Medical Devices (BfArM) from 2005 until her recent appointment. BfArM reviews the proof of efficacy, safety and adequate pharmaceutical quality of finished medicinal products. As a member of the Joint CHMP/CVMP Quality Working Party (QWP) since 1998, she was elected Vice-Chair of this group early in 2005. She has been a member of the EMEA Paediatric Working Party, representing QWP,



Susanne Keitel, PhD

and has been actively involved in the International Conference on Harmonisation (ICH), where she acted as the EU topic leader for the ICH guidelines on stability testing and pharmaceutical development. Earlier in her career she worked for Schering in Berlin.

Both PDA and Keitel look forward to the continued partnership between the EDQM and PDA. Keitel said, "I feel PDA and the EDQM have a very positive relationship and very good working interactions. PDA frequently shares its scientific

knowledge and expertise with the EDQM and takes an active interest in the work of the PhEur. I would like to highlight the comments PDA provided to the PhEur chapter on rapid microbiological methods. In addition, PDA regularly invites the EDQM to participate in its conferences, scientific committees and annual meetings. These opportunities create a platform for scientific discussions on important EDQM work."

PDA congratulates Keitel on her new position and hopes to further its relationship with EDQM under her management, which begins in October. Keitel commented, "I am committed to continuing and strengthening this valuable interaction between PDA and the EDQM and am very much looking forward to our future collaboration." 🌐

the report states the following: Table 8 makes a comparison between manufacturers of sterile products vs. nonsterile products. The average numbers of deficiencies observed in each category of these manufacturers were similar (20 for nonsterile vs. 23 for sterile). However, the deficiencies are distributed in a different manner, showing more higher-risk deficiencies (critical and major) for manufacturers of sterile products. This may be explained by the higher complexity of the sterile processes. Table 8 is presented with this article.

This data gives evidence to the statement made earlier that maintaining

sterile manufacturing facilities and up-to-date processes is critical. Evaluation of the data shows the obvious impact of microbiological risks, environmental monitoring and control, sterility assurance and personal hygiene.

Facility design and maintenance show a similar high incidence in the deficiencies reports. This indicates that keeping facilities up to the expectations and managing them accordingly poses a big challenge for the industry.

In conclusion, it might be more than coincidence that the percentages of critical (Sterility: 29.0%; Facility: 28.0%) and major (Sterility 21.7%; Facility: 17.3%) observations of both

aspects are very similar. Thus it can be interpreted that if the facilities have problems, these problems cause issues in sterile manufacturing areas.

The program for the PDA conference on Modern Aseptic Production illustrates that not only facility design, but also microbiology issues are areas for inspection and audit attention. As part of the conference, participants will have the opportunity to visit an AstraZeneca production facility to better understand the reciprocal dependence of sterility assurance and facility design. 🌐

Conference Report

Technology Transfer Today Highlights

Jim Lyda, PDA

PDA hosted its Technology Transfer Today conference in Basel on September 12-13. The attendees were greeted with a direct and useful survey of the status of site-to-site technology transfer in today's environment.

Special recognition is in order for two of the presentations. First, the team from F. Hoffmann-La Roche, **Hans Groeger**, PhD, **Juergen Nelis** and **Cristina Sanchez de Ulloa**, presented a full, integrated session on their project to transfer almost 500 products—chemical, biotech and galenical—in the next few years. It was a stunning presentation that demonstrated the value of effective planning and execution of a project of this size. (See related diagram extracted from their presentation.)




Tech Transfer Speakers (l-r): Juergen Nelis, Cristina Sanchez de Ulloa, Bernd Boedecker and Hans Groeger

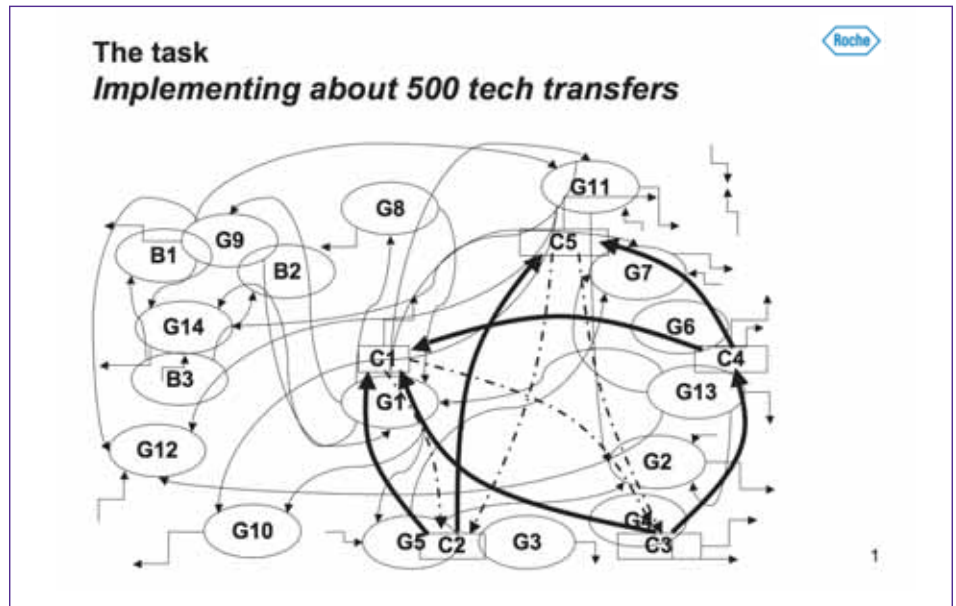


Tech Transfer Speakers (l-r): Philipp Goepel, Volker Eck, Claudia Nardini, Peter Smith and Jim Lyda, Siegfried Schmitt

On the regulatory side, GMP Inspector **Bernd Boedecker**, Gesundheitslicher Verbraucherschutz, who has recently joined the inspectorate after more than 20 years in the industrial pharmaceutical sector, gave a very detailed and

inclusive talk on an inspectors view of tech transfers.

PDA thanks all the presenters and speakers for their time and dedication (see photos below). 



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2008 PDA ANNUAL MEETING

Science Driven Manufacturing:
The Application of Emerging Technologies

THE
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April 14-18, 2008

Colorado Springs, Colorado

Conference | April 14-16, 2008

Exhibition | April 14-15, 2008

Career Fair | April 14-15, 2008

Courses | April 17-18, 2008

The PDA Annual Meeting is the one meeting each year dedicated to advancing the careers of pharmaceutical and biopharmaceutical professionals by focusing program content on science and technology innovation, offering extensive formal and informal networking opportunities and providing a forum to contribute to and influence the advancement of science and regulation in the industry.

Highlights of this year's conference program include:

- The patient point-of-view and how you and your organization may have contributed to their well-being and/or recovery
- Novel manufacturing technologies that enhance patient safety
- New contaminants implications, detection and exclusion

Complementing the conference are PDA Training and Research Institute (PDA TRI) training courses, an exhibition featuring today's leading pharmaceutical and biopharmaceutical companies, PDA's 4th Annual Career Fair and enhanced networking opportunities.



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