



September 2004

ELECTION BALLOT for 2005 Board of Directors enclosed with this issue!

Please return your completed ballot to PDA by October 29.

An Equipment Suppliers View of PAT, p. 12

VP's Message: Revised TR#32 Now Available

Expansion of Document's Scope Now in the Works

This month, I am pleased to announce the availability of revised PDA Technical Report #32, *Auditing Suppliers of Providing Computer Products and Services for Regulated Pharmaceutical Operations*.

Following four years of application by certified industry auditors, the PDA Industrial Advisory Board and the PDA Audit Repository Center (ARC) decided to refine the document so that it reflects the best auditing practices used today.

All PDA members will receive a CD-ROM of the

technical report with the September/October 2004 issue of the *PDA Journal of Pharmaceutical Science and Technology*. The report is available in the Adobe Portable Document Format (pdf) for ease of use.

I want to recognize the hard work of Harvey Greenawalt, President, Audit Repository Center, for his role in leading the revision effort.

Subject Matter Expert Volunteers Needed

While working on the revision of TR-32, the PDA Industrial Advisory Board has decided to expand the

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Gail Sherman Joins PDA!

Senior CBER Trainer Takes Helm of PDA Training and Research Institute, Career-long Learning Programs

PDA welcomes Gail H. Sherman as the association's new Vice President of Education and Director of the PDA Training and Research Institute.

Gail brings to PDA over 20 years of professional training experience with the U.S. Department of Health and Human Services, the last 13 years of which came with the U.S. FDA Center for Biologics and Research (CBER). As a senior manager with CBER, Ms. Sherman led teams of scientific, public affairs and education specialists to develop curriculums and standard operating procedures on a variety of challenging scientific and technical subjects.

During her last seven years with CBER, Gail served as the Director of the Division of Manufacturers Assistance and Training, where she was responsible for managing both internal training programs and external outreach to industry.

Gail created valuable and successful courses for industry professionals at all levels of experience. She designed and developed various technical training

programs for CBER's review and inspection staff and leadership programs for senior managers. Her programs had to meet the needs and engage professionals with bachelors degrees, doctoral degrees and medical degrees.

One of Gail's more significant accomplishments was the creation of a CBER reviewer training program, which became a key education tool for the

continues on page 7

PAC Guide for Sterile Drugs?

by Glenn Wright, Eli Lilly and Company, PDA Science Advisory Board

Does the industry need a post approval change guidance specific for sterile products? That has

been an open question for the past several years.

What is the right answer, or even more fundamentally, is there a right answer? My experience with this question, and I have been

continues on page 24

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Important Dates...

- **September 7-8—PDA-BFS Joint Workshop on Blow/Fill/Seal Processing**, Sulzbach-Laufen, Germany
- **September 14—PDA UK and Ireland Chapter Presents: "The Training Process,"** Horley, UK
- **September 20-24—2004 PDA/FDA Joint Reg. Conf., Courses & Tabletop Exhibits: The New Guidances**, Omni Shoreham Hotel, Washington, D.C.
- **October 6-7—PDA and PDA Central Europe Chapter Present: "Hands On" Visual Inspection Problem Solving**, Berlin, Germany
- **October 18-19—PDA and PDA Central Europe Chapter Present: Pre-Filled Syringes: New Tips and Strategies**, Hanover, Germany

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Directors

Gautam Maitra, *Europe*
Wanda Neal, Programs and Meetings

PDA Global Headquarters

3 Bethesda Metro Center, Suite 1500
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900 Fax: +1 (301) 986-0296
E-mail: info@pda.org
Web site: www.pda.org

PDA European Headquarters

287 Avenue Louise
BE-1050 Brussels
Belgium
Tel: +32-2-643-2045 Fax: +32-2-645-2671

PDA Office of European Director

R-1059.747 Postfach
Schwarzwaldalle 215
CH-4002 Basel
Switzerland
Tel: +41 61 321 56 30 Fax: +41 61 321 83 48
E-mail: maitra@pda.org

PDA Training and Research Institute

c/o UMBC Technology Center
1450 S. Rolling Road
Baltimore, MD 21227 USA
Tel: +1 (410) 455-5800 Fax: +1 (410) 455-5802
E-mail: info-tri@pda.org

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Neal G. Koller
PDA President

President's Message

Autumn Brings Strong PDA Science & Regulatory Events to Europe

I am excited to discuss and recognize the hard work of the PDA Chapters, PDA Interest Groups and members in Europe, as well as our European and U.S. staff, for developing and delivering a series of strong science, technology and regulatory career-long learning programs for the pharmaceutical and biopharmaceutical communities during the second half of 2004.

With the PDA/FDA Joint Regulatory Conference serving as PDA's main second-half event, the programs discussed below will provide individual and hands-on career-long learning opportunities in locations convenient to our members working in Europe, and easy access for those outside Europe. The lineup reflects the full scope of PDA educational offerings including, conferences and Interest Group meetings, and, for the first time in Europe, Training and Research Institute laboratory courses.

The schedule begins with the PDA Training and Research Institute (TRI): TRI is bringing a hands-on Blow/Fill/Seal (BFS) laboratory course to Europe to meet the requests of our European members. TRI, in cooperation with the Pharmaceutical BFS International Operators Association, have developed a course on BFS processing to be held September 7-8, in Sulzbach-Laufen, Germany, that consists of lecture, discussion, facility tour and hands-on training. Attendees will benefit from this unique opportunity to visit Sulzbach-Laufen facilities of Holopack Verpackungstechnik GmbH and Kocher-Plastik GmbH for hands-on work with BFS equipment.

The next event is cosponsored by PDA and the PDA UK & Ireland Chapter Training Special Interest Group and takes place on September 14, at the Holiday Inn Gatwick Airport in Horley, UK. "The Training Process" is a one-day workshop that will provide a comprehensive overview of PDA's draft document, "Best Training Practice." Delegates also will discuss plans for another PDA training document, tentatively titled, "Training Performance Measurement & ROI." This workshop is a follow-on meeting by the Training Special Interest Group, which held its first open meeting in September 2003.

Germany is the site of the next event: "PDA Scientific Forum on Visual Inspection," October 6-7. Cosponsored by PDA and the PDA Central Europe Chapter, this event will provide new insight and recommendations for this vital step in the production of safe and effective drug products. The workshop includes a review of the results from the Interest Group's visual inspection survey and expert advice from an international group of senior industrial managers. PDA Board of Directors member and Visual Inspection Interest Group leader John Shabushnig, PhD (Pfizer Inc.), joins Markus Langers, PhD (rap.ID

GmbH), as co-chairs of the forum. PDA Director and Treasurer Georg Roesling, PhD (Schering AG), deserves special recognition for his hard work on the arrangements for this conference.

PDA and the Central Europe Chapter also will host a two-day seminar for experts from global companies to discuss their strategies for manufacturing pre-filled syringe drug products, October 18-19, in Hanover, Germany. New manufacturing equipment, outsourcing and self-injection devices are among the topics to be addressed. This seminar features hands-on instruction on practical aspects of visual inspection and a tour of Bunder Glas GmbH's world-class pre-filled syringe manufacturing facility in Hanover. I hope all those who attend take advantage of the opportunity to tour this remarkable facility.

PDA and the European Branch of the PDA Biotechnology Interest Group are offering a two-day workshop in Rome, graciously hosted by the PDA Italy Chapter, on viral safety and TSE risks, also October 18-19. With technologies, standards and regulatory expectations constantly evolving in these critical areas, this workshop promises to provide delegates the tools they need to assure their processes and procedures are state-of-the-art and compliant. This workshop builds on and is an update to the 2003 PDA/EMEA Viral Safety Congress in Langen, Germany, and an authoritative in-between update opportunity before the upcoming 2005 PDA-FDA-EMEA Viral Safety Conference, May 16-18, in Bethesda, Maryland.

October ends on a great regulatory note in Barcelona where PDA together with the PDA Spain Chapter is hosting a workshop on the FDA risk-based cGMP initiative (October 25). FDA's groundbreaking revision to the cGMPs is closely followed by biopharmaceutical and pharmaceutical professionals around the world. This one-day event is the perfect opportunity for PDA members in Europe to get the latest information on new and changing regulations and to improve their knowledge and skills to enhance success.

For the first time, PDA TRI is holding a 3-day hands-on "Practical Aseptic of Aseptic Processing" laboratory course based on our well-respected and attended PDA 2-week aseptic processing course, currently taught only at the PDA TRI facility in Baltimore, Maryland. This 3-day laboratory course will introduce participants to critical aspects of the complete 2-week course, including hands-on training with a production equipment in a cleanroom environment located on the University of Basel campus. This new course, held for the first time in Europe, will be taught November 17-19, in Basel, Switzerland.

Wrapping up the second half of 2004 PDA career-long learning opportunities in Europe is an important

The European Fall Line-Up:

PDA-BFS Joint Workshop on Blow/Fill/Seal Processing
Sept. 7- 8
Sulzbach-Laufen, Germany

2nd Open Meeting: "The Training Process"
Sept. 14
Horley, UK

"Hands On" Visual Inspection Problem Solving
Oct. 6-7
Berlin, Germany

Pre-filled Syringes: New Tips and Strategies
Oct. 18-19
Hanover, Germany

Viral Safety and TSE Risks
Oct. 18-19
Rome, Italy

Gail Sherman, from cover

regulated industry. The training is offered to the CBER review staff in a format composed of lecture and interactive case study discussion, often on issues that integrate the regulatory processes with specific scientific issues. Under her direction, the program was delivered to the regulated industry as a course called *CBER 101 for the Industry*. It was also made available to the public via an open meeting called *CT Product Development*. Gail led this effort to offer the course to industry in order to “open the black box that is FDA,” by providing industry the opportunity to interact with CBER experts on issues related to the drug approval and review processes.

Under Gail’s supervision, CBER scientific, public affairs and training staff developed a variety of internal standard operating procedures (SOPs) for the center, as well as curriculums for topical training courses. Recent SOPs developed by Gail and her staff outlined steps for responding to technical manufacturing and principal investigator inquiries and outreach requests.

The latest curriculum developed by Gail and her staff dealt with the many regulatory changes precipitated by the Medical Device User Fee and Modernization Act and FDA’s various quality system initiatives. At her time of departure in July,

CBER management was reviewing a proposed “regulatory site review training program” which, if approved, will facilitate the participation of CBER review staff in industry on-site training.

Gail served as a liaison to several trade associations to discuss workshop opportunities, provided leadership on program committees, and served as a speaker, moderator and/or session chair for several of these meetings.

PDA has benefited from Gail’s efforts. She lent her expertise to PDA planning committees for the 2002 and 2004 PDA Training Conferences, the 2000 PDA/FDA Team Biologics Update Workshop, and the 1999 PDA/FDA Joint Regulatory Conference. The PDA Training Conference is on the long list of industry meetings at which Gail has presented over the years. Gail’s strong abilities and qualifications have earned her many awards and honors—including the 2002 PDA Trainer’s Choice Award for a multimedia presentation. ■

PDA Thanks Bob Mello

Bob Mello, PhD, is returning to the pharmaceutical/biopharmaceutical industry after more than a year-and-a-half of serving as PDA’s VP of Education and Director of the PDA Training and Research Institute (TRI).

Under Bob’s steady hand, TRI significantly expanded its laboratory course and lecture series offerings and the number of pharmaceutical/biopharmaceutical professionals served both nationally and internationally. Several lecture series set new PDA attendance records (2003 San Diego and Boston), and, at TRI, donations of much needed equipment and services increased during his tenure.

A highlight of Bob’s tenure was the TRI training program for the Italian Inspectorate in 2003. Bob led a cadre of dedicated faculty and the TRI staff to develop, manage and deliver this important service to help the Italian health authorities improve the skill sets of their regulatory inspectors.

Bob anticipates remaining an active PDA member. He has served PDA as a member of the Board of Directors, as the chair of the Industry Advisory Board for the Audit Repository Center, as president and treasurer of the Capital Area Chapter, as a member of the Regulatory Affairs and Quality Committee and as a leader on program planning committees and task groups.

Bob’s initial plans are to return to consulting in Quality Systems, Aseptic Processing Compliance and Contract Manufacturing a path he was on prior to joining PDA’s staff in 2002. PDA will always be grateful for his dedicated service and looks forward to his continued participation in the years to come. ■

Complying with FDA’s New cGMP’s for the 21st Century Using Risk/Science-Based Validation
Oct. 25
Barcelona, Spain,

PDA-TRI Laboratory Course: Practical Aspects of Aseptic Processing
Nov. 17-19
Basel, Switzerland

New Success Factors for Bio/Pharmaceuticals/Manufacturing in Europe
Dec. 6-7
Paris, France

Go to www.pda.org for more information on these events.

President’s Message, from page 6

new 2-day meeting on successful biopharmaceutical/pharmaceutical manufacturing in Europe, sponsored by PDA together with the PDA France Chapter. This very valuable event is the first congress assembled by the PDA France Chapter. With six months experience operating in the expanded EU, professionals in the communities around the world need access to the most current information in order to better plan their product development and manufacturing strategies. This two-day forum in Paris (Dec. 6-7) features leaders from industry and European health authorities who will discuss risk-based management approaches, clinical trials in the newly enlarged EU and the latest GMP revisions.

We would like to thank all the members involved with the PDA Chapters and Interest Groups who have worked so hard to develop these remarkable career-long learning opportunities in the second half of 2004 in Europe. We would also like to extend a special thanks to the new staff at the PDA European Office in Brussels who wasted no time getting involved in facilitating these events.

I encourage all PDA members to visit the PDA Web site (www.pda.org) to learn more about these events and to register online. With workshops like these, the last four months of 2004 promise to offer valuable science, technology and regulatory updates for all of us to better perform on the job and advance our organizations. ■



George A. Robertson
VP, Science & Technology

VPs Message: TR#32 Now Available, from cover

scope of the auditing procedure to other services and products commonly used in the production of medicinal products. As a start, we are looking for volunteers with technical or auditing expertise to contribute in the following areas:

- Clinical Research Organizations
- Packaging
- Excipients
- Part 11
- Contract Manufacturers
- Sterile Filters and Filtration

Interested members should contact me at robertson@pda.org for details. Please specify what your area of expertise is and your qualifications. The PDA Industrial Advisory Board would like to have a Task Force assembled by October. Subject matter expert volunteers are not obligated to be, or to be qualified as TR-32 auditors.

About Technical Report 32

Since many PDA members may not come in to contact with the processes encompassed in TR-32, I thought it helpful to review what the auditing process described in the document is.

TR-32 was developed by PDA in response to the U.S. FDA's appeal to the regulated industry to standardize the auditing process for suppliers of computer products and services and establish a global repository for sharing audit information. The issues that concerned FDA included:

- **Uncertainty:** Without an objective standard for all suppliers to follow, the obvious dilemma is that a supplier can never be reasonably certain that they are in compliance.
- **Inconsistency:** Unless the objective standard is applied uniformly, from company to company, it is fair to say that not all companies are being treated alike. Some companies are more in compliance, while others are less compliant.
- **Redundancy:** Because a supplier is often

requested to submit to audits by a number of client manufacturers, a global repository makes sense since it would avoid a duplicative process.

PDA Technical Report No. 32 defines a six-step process for performing such an audit. Each of the steps represents a collection of activities to be accomplished by qualified auditors, manufacturers, and suppliers.

1. Audit initiation, including defining scope and objectives

2. Preparation and pre-work, including information acquisition, tailoring audit criteria, team selection and scheduling.

3. Conduct audit, execution of the audit *per plan* and dealing with contingencies.

4. Observations and Reporting, document and verify results.


5. Decision, the focus in the analysis by the end user.

6. Follow-up and closeout, process is formally closed out and information gathered to prepare for surveillance.

The TR-32 process also includes auditor training at the PDA Training and Research Institute. Auditors are qualified by completion of the course and by demonstrating documented competency in the areas they are going to review. This process is contained in TR-32 as well.

PDA Industrial Advisory Board

PDA has established the Industry Advisory Board (IAB) to periodically review and approve changes to the process model and data collection tools described in PDA Technical Report #32. The IAB also monitors auditor qualification and re-qualification requirements and provides oversight of the Audit Repository Center (ARC) to ensure that the process remains current with respect to changing technology and regulatory environments, to periodically analyze ARC's registration history, promotional efforts, and service performance, and furnish ARC with suggestions, if any, for improvement. ■



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ASTM Committee E55 on PAT: A Supplier's Perspective

by Ian Clegg, PhD, ABB Process Solutions

The pharmaceutical industry is subject to a number of pressures, although the overriding drivers remain the research, development and marketing of new therapies and the maintenance of the highest quality standards at point of use. Both these factors are in the direct interest of all stakeholders, i.e., manufacturers, consumers and industry regulators. The R&D groups within the industry concentrate on the development and assessment of new chemical entities (NCEs) and dosage forms, that is, on the delivery of new products, since this ensures that new medicines will become available with associated high profit potential and that the industry will grow.

A direct consequence of the emphasis on NCEs and new product forms has meant that manufacturing, as a whole, was not considered a critical core competence or tool for competitive advantage. Manufacturing assessments are widely practiced in industry in general and there are many standard metrics that allow performance to be compared and contrasted between the various industrial sectors (an assessment produced by ABB Process Solutions is shown in Table 1). Although there is no doubt that pharmaceutical manufacturing processes are able to produce products to specification, these metrics show that manufacturing performance and therefore cost effectiveness lag behind those of other sectors.

There are many potential reasons for these differences in performance but one example is

the differences in the regime that ensures that appropriate product quality is achieved. Within the pharmaceutical industry, the existing quality regime in manufacturing is based upon a process of control whereby raw materials, intermediate products and final products are all typically subjected to an extensive range of clearly defined and closely monitored analytical and physical tests. If a material being tested conforms to a pre-determined standard value then it is deemed fit for purpose and processing can continue or product can be released for sale. This regime is traditional practice for the industry and it seems intuitively reasonable, i.e., there are clear checks and balances at all the critical stages during manufacture.

However, in terms of effective use of capital assets, this approach to the control of quality does confer significant disadvantages—compromising capacity, cycle time and cost—and is clearly out of step with other manufacturing sectors such as semiconductor and aerospace. In these other sectors, product quality is assured through the operation of robust and well-understood processes. Such processes can be relied upon to produce high-quality products quickly and in a cost-effective manner; they have a minimum amount of quality control testing and the overriding emphasis is based on thorough understanding of the manufacturing process embodied in process control mechanisms that are inherently repeatable.

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Key Performance Indicators	Pharmaceutical Industry Now	A Winning Pharmaceutical Plant	A World-Class Manufacturing Plant
Stock Turn	3 to 5	14	50
OTIF	60% to 80%	94.4%	99.6%
RFT	85% to 95%	96.0%	99.4%
CpK	1 to 2	35	32
OEE	30%	74%	92%
Cycle Time (Hours)	720	48	8
Added Value Per Employee		£500k	£500k

Where:
 Stock turn is a measure of how fast a business turns over its stock.
 OTIF is on time in full, a measure of the capability of the process to produce product when required.
 RFT is the process capability and relates the variability in product to the specification limits.
 OEE is overall equipment effectiveness the percentage of time for which process equipment is adding value.

PAT

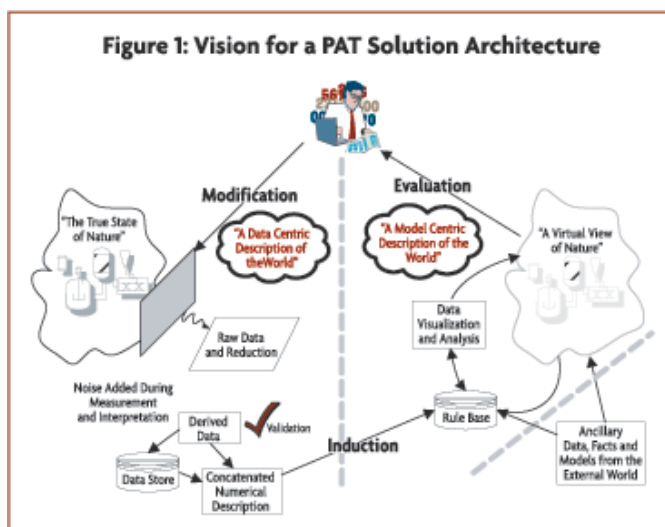
There are several ways in which this existing position within pharmaceuticals might be improved, although one of the more prominent ones is the application of process analytical technology; this has been the subject of a significant amount of coverage in the technical and trade press in recent months. With PAT-based systems, the parameters that affect the process are monitored, their effect on the process understood, and their influence controlled. PAT systems allow the quality of the products to be assured by enabling highly repeatable and inherently stable processes with immediate indication of non-conformance. In terms of the manufacturing metrics described here, PAT would enable improvements to be made, for example CpK (process capability) would be increased and cycle time radically decreased.

PAT is the direct subject of the recently formed ASTM Committee E55 which has approximately 140 members drawn from pharmaceutical manufacturers, suppliers, regulators, as well as academics and consultants.

A Misnomer

In some ways, the acronym PAT is misleading. Although this initiative is based on analytical science and measurement technology, it also includes other important tools (see Table 2). The “problem” word in PAT is analytical because this implies complete reliance on the analytical aspects of process technologies. It is true that the analytical measurement method is important, as this gives the primary data view into the process and can provide unique insights into absolute process behaviors, stability and dynamics. Indeed, if suppliers fail to provide a wide range of reliable, robust and validated measurement techniques that are able to perform properly under realistic process conditions, then this will inevitably limit the rate of deployment of measurement technologies and the associated improved process understanding within the industry. It is, however, comforting to reflect on the fact that the provision of the analytical measurement system is a reliable and fairly well-proven aspect of the PAT initiative, for example, the substantial number of instruments (predominantly based on near-infrared spectroscopy) that have already been installed within the

Figure 1: Vision for a PAT Solution Architecture



industry.

Unfortunately, it is also true that the analytical measurement is of limited value to manufacturing (although the value of improved understanding in R&D and scale-up cannot be underestimated) unless it works in concert with other procedures and systems. For it is only after the transition has been achieved from raw data through to information and ultimately to knowledge that true value accrues to the user of PAT-based systems.

A view of the ultimate objectives of PAT is shown in Figure 1. In the left hand side of this figure is a data-centric description of the “world” (i.e., the process under examination), and the right hand side is a model-centric view of the same world. This diagram describes a situation where processes are developed and a virtuous cycle is set up, whereby data from a PAT system is induced into a model-centric view; the results are then evaluated and modifications are subsequently made to the PAT system (or its data treatment sequence) and further sets of results are induced into the model.

In this way, there is a continuous improvement in the overall data set available to

TABLE 2: THE PAT TOOLBOX

- ▶ Design of Experiments (DoE) to generate the maximum amount of relevant data.
- ▶ Measurements to gather in real time, process data describing critical to quality attributes.
- ▶ Chemometrics, which are used to translate multi-variate data into physical and chemical characteristics.
- ▶ Data Modeling/Mining to drive out casual relationships and critical to quality attributes.
- ▶ Process Modeling to translate data and information into mathematical and empirical models.
- ▶ Product and Process Design and Optimization Strategies
- ▶ Risk Based Inspection regimes and methods for demonstrating control of the critical attributes.
- ▶ Information Management tools, including advanced data visualization.

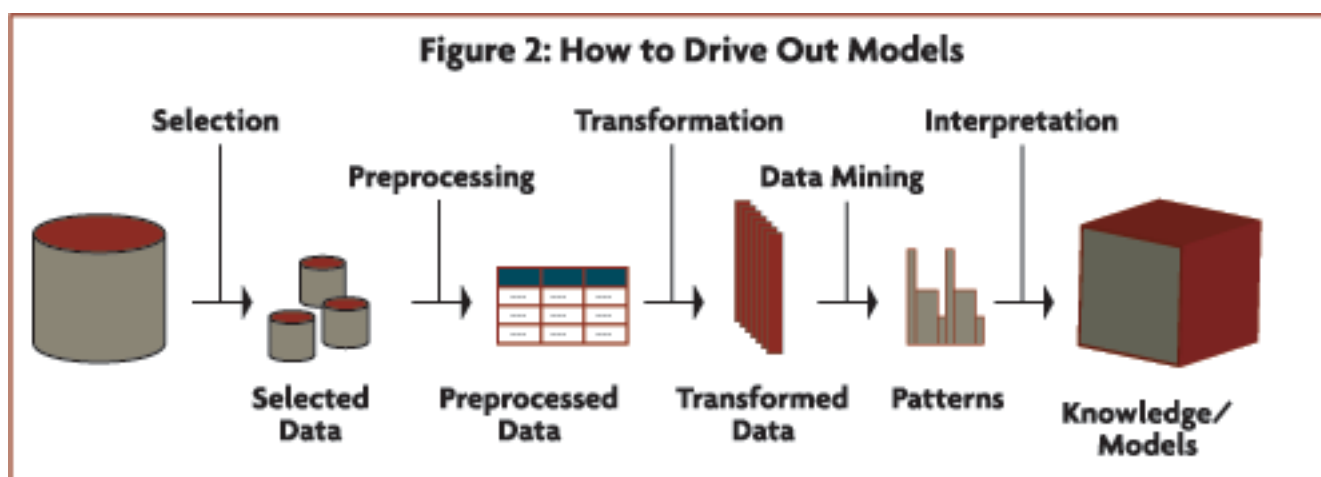
the assessor of the system and the degree of understanding of the system increases as a direct result. Here, the “system” may be as simple as a small unit operation or as complex as a large manufacturing unit with multiple, integrated stages. Once the model-centric view of the process is complete and in full accordance with that process, and it has been validated as such, then this is the ultimate realization of PAT. In such a situation, the interaction between all significant process variables are known and constraints can be applied to them; product quality can be assured through good design practice and appropriate control of the process.

A Complex Process

Of course, the transitions between data,

advantages. For example, the cost of ownership is lowered, the data/information set is easier to deal with, and this will increase the rate at which the models can be developed and validated. This, in turn, lowers the cost to the manufacturer.

As an example, Figure 3 shows part of a production process and the data flows from left to right, i.e., from the process vessels to the manufacturing execution system. Attached to the process equipment are the analytical techniques that are at the core of the PAT initiative. However, it can be seen from this diagram that a series of data treatment steps, information management layers and control action functions are required. For example, the analytical equipment generally produce spectral data; these can be thought of as arrays of numbers that encode the chemical and



information and knowledge takes some time to achieve; it is generally a complex process typically requiring input from a variety of technical disciplines, because these manufacturing processes often include many subtleties and incorporate many detailed interactions.

As an example, a typical data flow is shown in Figure 2. Here, raw data is obtained using an instrument (or more likely, a series of instruments) and is mathematically treated and then transformed to generate a process model. The term model can (and does) cover many things, including chemometrics to examine the analytical information, fluid dynamics to simulate particle flows, and dynamic simulations to describe the effects of changing behaviors of process, materials and equipment.

The basic components required for PAT, such as measurement devices and model methods, are widely used in other industries and are available for application in the pharmaceutical industry. Of course, they will need adaptation to be fully compliant with the prevailing regulatory regime, although the key is to be able to deploy them in a highly integrated manner. Integration is important since it confers a number of important

physical information in the samples that are being analyzed. These arrays need to be mathematically treated in some way (using a range of techniques that fall under the umbrella term of chemometrics) in order to produce derived data, and they also need to be communicated effectively and stored properly within a process information management system (PIMS).

Although chemometric software programs are available, generally they were developed specifically for use in the laboratory environment (where they are still mainly deployed) and their extension to the manufacturing arena has proven to be difficult. This is not to say that they cannot be transferred, but rather that they must be adapted and this will inevitably take time to achieve before being accepted by a new set of personnel that inhabit the process arena. Even something seemingly as simple to source as PIMS is difficult in a PAT regime because most of these systems currently available have no concept of storing data as arrays of information; they are simply not designed to handle the complexity and the volume of data. Data mining techniques are also required to uncover the hidden interactions between the data and batch control records are

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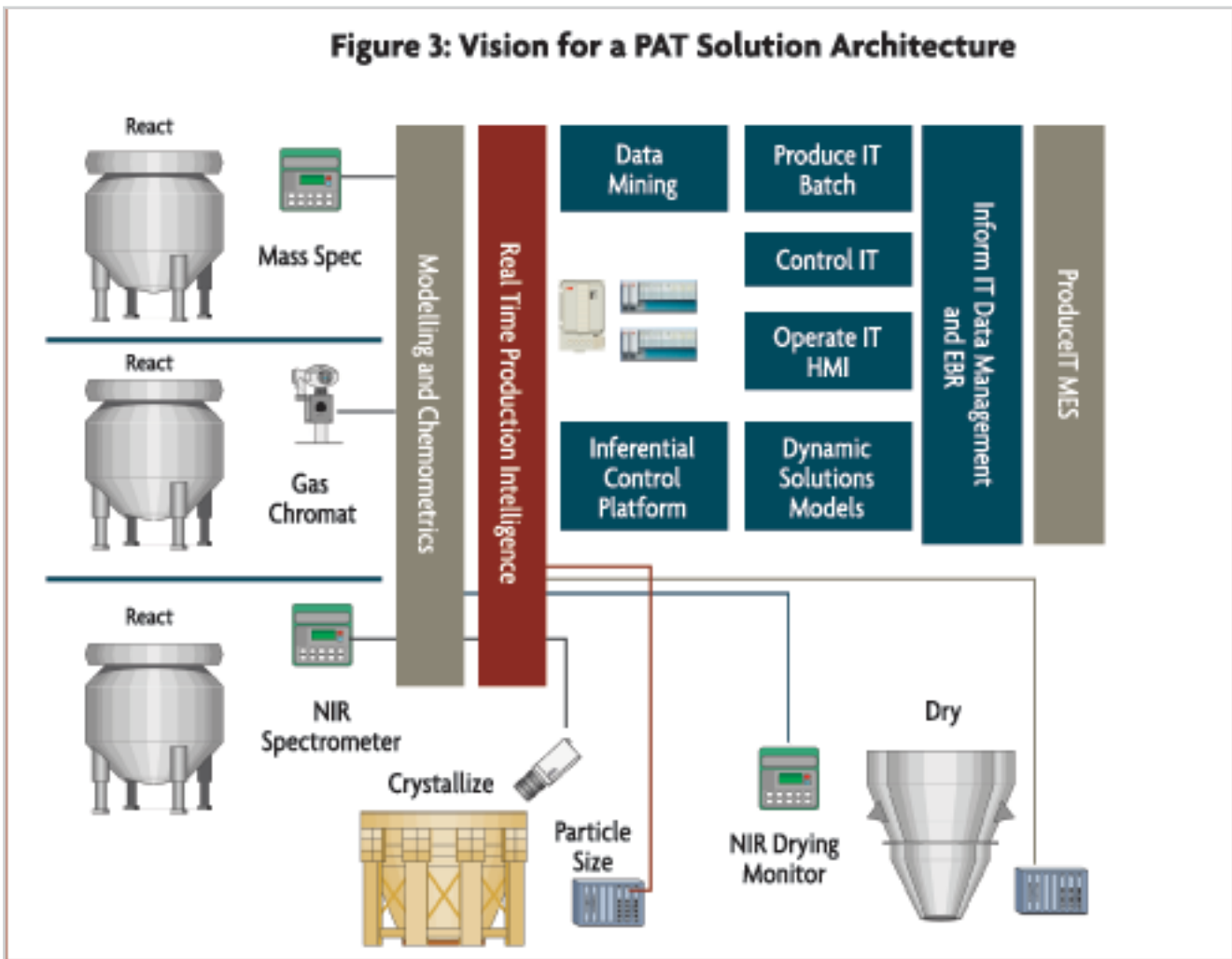
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Figure 3: Vision for a PAT Solution Architecture



required. Static and dynamic models also play a part and must be available. Control systems must also be provided, these may have actions that are taken manually (open loop) or automatically (closed loop), although the latter option is unlikely given the infancy of the PAT initiative. Of course, this whole array would need to be orchestrated, typically by a manufacturing execution system.

So in order for the full potential of PAT to be realized, manufacturers must supply a range of products and services that underpin the initiative

and that include all of its detailed technology facets. Users may choose to deploy individual components and integrate themselves, but an important option is that the components should be available as an integrated suite. This minimizes the complexity of systems, their maintenance and extension while maximizing the benefit from integrating information from diverse physical processes, geographical locations, manufacturing sources and lifecycle stages. ■

Ian Clegg currently holds a senior consultancy position with ABB Process Solutions in the UK, and is a member at large of the Executive Subcommittee of ASTM Committee E55 on Pharmaceutical Application of PAT. He has nearly 20 years experience in designing, developing and commissioning measurement systems for application on a range of chemical and pharmaceutical plants.



Victoria Ann Dedrick
VP, Quality and
Regulatory Affairs

Vice President's Message

Busy Summer Means Valuable Future Programs

Summer may be a slow time for many people, but at PDA it has been a time of accelerated action as we plan and execute the 2004 PDA/FDA Joint Regulatory Conference, September 20-22 in Washington, D.C. To ensure that the program content for the "New Guidances" is exceptional, PDA and the program planning committee has been working very closely with the U.S. FDA and the agency experts who have driven the risk-based cGMP initiative. With FDA anticipating the announcement of numerous new guidances and implementation initiatives just prior to the meeting, we are looking forward to one of the best joint regulatory conferences to date.

FDA Center for Drug Evaluation and Research (CDER) Office of Compliance (OOC) Director David Horowitz, JD—the keynote speaker at the conference—recently commented that FDA will make a "major announcement" regarding the cGMP initiative in September and that the "initiative is not over; much more work to be done."

These same sentiments were echoed at a Newsmaker Luncheon held by Acting-FDA Commissioner, Lester Crawford, DVM, PhD, at the Washington Press Club on August 2, 2004, which PDA President Neal Koller, Senior Editor Walter Morris and I attended. Dr. Crawford stated that the cGMP initiative will be completed "on time" this autumn and announcements regarding the implementation process will be made.

Dr. Crawford also stated, "FDA will announce the National Critical Path Opportunities List which will pinpoint those areas of product development that could benefit most from innovative approaches and emerging technologies. This will enable us to rally our partners in government, industry and academia to build the path to innovation in these key areas." He went on to say, "Cutting-edge applied science and a crosscutting approach are essential to fostering a more modern health care system. Equally important to modernizing this system is the introduction of best practices in product manufacturing."

CDER OOC Division of Manufacturing & Product Quality Director Joseph Famulare recently outlined specific achievements the agency anticipates announcing on or around September 15, including: a notification of a rule change to the cGMPs; the availability of a draft guidance on quality systems; and the availability of the *final* "Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing." All of these accomplishments will be discussed at the joint regulatory conference, as well as other advances in the initiative made throughout 2004.

In recognition of the interest PDA members have in the long-awaited aseptic processing guidance, PDA has dedicated the closing plenary session of the joint regulatory conference to it. Both FDA and industry's point of view regarding the document will be presented. It should be a very exciting and interactive session with lots of take-home information and a great way to conclude the conference.

The closing plenary session of the joint regulatory conference is just the beginning of PDA's plans for helping to facilitate the implementation of this landmark guidance. PDA is developing a series of two-day forums that will partner PDA's scientific and technical expertise in the area of aseptic processing with FDA's topic leaders to provide a step-by-step and side-by-side comparison of the new guidance to the original 1987 FDA aseptic processing guideline and to current international guidances available from the health authorities in the EU and Japan and other sources. Speakers also will identify gray areas of the final guidance and areas not covered. FDA and industry experts will clarify these important issues and offer solutions to meet these challenges in the practice.

These aseptic processing forums will be cosponsored with FDA and will be incorporated into the agency's planned training program for its field inspectors. They will launch in mid-January 2005.

Another important feature of the forums will be an executive manufacturing panel. This group will provide specific insight into the direct impacts the new guidance will have on various aspects of the manufacturing process such as: line design; line utilization; shift scheduling; personnel skills and training; media fill acceptance criteria; increased monitoring frequency and requirements; types and scope of environmental monitoring investigations; and product costs.

These forums will represent an exciting opportunity for everyone engaged in the activity of producing sterile drug products by aseptic processes to rapidly learn and apply the recommendations in the new guidance across their company.

Again, it has been an exciting summer for us at PDA; I look forward to seeing all of you at the PDA/FDA Joint Regulatory Conference here in Washington, D.C., in a few weeks.

Please plan to take advantage of the PDA aseptic processing forums so you get your manufacturing, quality and regulatory processes up to speed as quickly, efficiently and cost effectively as possible.

See you at Capitol Steps.... ■

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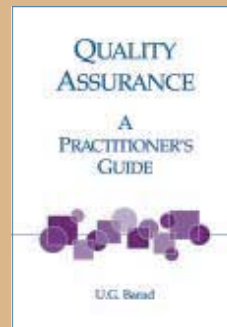
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<p>2004</p> <p>September</p> <p>15 PDA Audio Conference: Update to PDA TR#32: Auditing of Suppliers Providing Computer Products and Services for Regulated Pharmaceutical Operations</p> <p>20-24 2004 PDA/FDA Joint Reg. Conf., Courses & Tabletop Exhibits: <i>The New Guidances</i> Omni Shoreham Hotel, Washington, D.C.</p> <p>2005</p> <p>February/March</p> <p>28-3 PDA International Congress, Courses & Exhibitions Rome, Italy</p>	<p>April</p> <p>4-8 PDA Annual Meeting, Courses and Exhibitions Hyatt Regency, Chicago, Illinois</p> <p>May</p> <p>16-18 PDA, FDA & EMEA Viral & TSE Safety Conference Hyatt Regency, Bethesda, Maryland</p> <p>September</p> <p>12-16 2005 PDA/FDA Joint Reg. Conf., Courses & Tabletop Exhibits Washington, D.C.</p> <p>October</p> <p>10-11 Taormina Conference Taormina, Italy</p>
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<p>September</p> <p>15 Canada Preparation for Equipment Qualification Toronto, Canada</p> <p>29 Delaware Valley Aseptic Processing Malvern, Pennsylvania</p> <p>29 Capital Area Real Compliance and How to Achieve It Gaithersburg, Maryland</p> <p>October</p> <p>1 New England Workshop on Combination Product Development Cambridge, Massachusetts</p> <p>6 Southern California Management Controls/FDA Inspection Planning Huntington Beach, Calif.</p> <p>6-7 Central Europe "Hands On" Visual Inspection Problem Solving Berlin, Germany</p> <p>18-19 Italy TSE & Viral Safety: Regulatory Expectations & Industry Practices Rome, Italy</p> <p>18-19 Central Europe The Universe of Pre-filled Syringes Hanover, Germany</p> <p>19 Israel Seminar: Process Validation Tel Aviv, Israel</p> <p>20 Southeast Annual Fall Meeting Research Triangle Park, North Carolina</p>	<p>25 Spain Complying with FDA's New cGMPs of the 21st Century Using Risk/Science-Based Validation Barcelona, Spain</p> <p>27 UK & Ireland Biotechnology Conference OSI Pharmaceuticals Oxford, England</p> <p>November</p> <p>9-10 Japan Japan Chapter Annual Meeting Tokyo, Japan</p> <p>17-19 Central Europe Aseptic Processing Course Basel, Switzerland</p> <p>17 Delaware Valley Environmental Monitoring Malvern, PA</p> <p>19 Metro Current Compliance Trends Clark, NJ</p> <p>19 Midwest Rapid Microbiology Techniques and PAT Northbrook, IL</p> <p>December</p> <p>6-7 France Bio/Pharmaceuticals Manufacturing in Europe Paris, France</p> <p>8 New England Dinner Seminar on PAT Cambridge, MA</p> <p>27 Israel Annual Meeting Tel Aviv, Israel</p>
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4-8 Aseptic Processing Training Prgm: Week 1

14-15 Fundamentals of D, F, and z Value Analysis

18-22 Rapid Microbiological Methods

25-27 Designing, Operating, and Controlling High Purity Water Sys. for Regulatory Compliance

November

1-5 Aseptic Processing Training Prgm.: Week 2

11-12 Developing and Validating Cleaning & Disinfection Prgms. for Controlled Envsn.

15-17 Cleaning Validation

17-19 Practical Aspects of Aseptic Processing
University of Basel
Basel, Switzerland

18-19 Remediation of Existing Computer Systems

December

2-3 Environmental Mycology Identification Workshop

6-7 What You Need to Know to Select Adequate Thermal Validation Equipment

Laboratory Courses -- 2005

February

7-11 Aseptic Processing Training Prgm: Week 1

24-25 Environmental Mycology I.D. Workshop

March

14-18 Aseptic Processing Training Prgm.: Week 2

22-23 Validating a Steam Sterilizer

April

18-22 Aseptic Processing Training Prgm.: Week 1

May

16-20 Aseptic Processing Training Prgm.: Week 2

June

2-3 Environmental Mycology I.D. Workshop

August

22-26 Aseptic Processing Training Prgm.: Week 1

September

7-9 Adv. Environmental Mycology I.D. Workshop

19-23 Aseptic Processing Training Prgm.: Week 2

October

17-21 Aseptic Processing Training Prgm.: Week 1

25-26 Validating a Steam Sterilizer

November

14-18 Aseptic Processing Training Prgm.: Week 2

December

1-2 Environmental Mycology I.D. Workshop

Lecture Courses

October

26-27 21st Century cGMPs: A Risk/Science-Based Approach to Validation
PDA-TRI, Baltimore, Maryland

December

6-7 Computer Products Supplier Auditing Process Model: Auditor Training

Course Series

September

20-24 2004 PDA/FDA Joint Reg. Conference, Courses and Tabletop Exhibits
Washington, DC

Change Control & Documentation

Auditing Pharmaceutical Microbiology Laboratories

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October

18-20 Boston, Massachusetts

Analytical Problem Solving for CAPA Sys.

Design and Validation of a Cleaning & Disinfection Prgm

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FDA's New cGMP Questions and Answers Guidance

"Regulatory Briefs" will return next month.

As part of the U.S. FDA's cGMP initiative, and to help FDA achieve greater transparency with cGMP policy, the agency has developed a question and answer resource on cGMPs. The goal is to provide timely answers to questions about the meaning and application of cGMPs for human, animal, and biological drugs, and to share these widely. These questions and answers generally clarify statements of existing requirements or policy, and as such, are considered Level 2 guidance. The Center for Drug Evaluation and Research, Center for Veterinary Medicine, Center for Biologics Evaluation and Research and Office of Regulatory Affairs are cosponsoring the Q&A. The Q&A guidance is available on FDA's Web site, and a link to the page is available on PDA's regulatory news archive page (www.pda.org/regulatory/RegNewsArchive.html).

The guidance is organized by cGMP topic area. Topics currently addressed are: equipment; control of components and drug containers and closures; production and process controls; packaging and labeling controls; laboratory controls; and records and reports. Each answer includes references to the cGMPs and, in some cases, other sources. An FDA contact name is provided with each answer.

Below, the "production and process controls" section of the guidance is reproduced.

Production and Process Controls

1. Do the CGMPs require a firm to retain the equipment status identification labels with the batch record or other file? Assuming each major piece of equipment has a unique "Cleaning and Use Log" that is adequately retained, is it acceptable to discard these 'quick reference' equipment labels?

The CGMP regulations for finished pharmaceuticals require the retention of cleaning and use logs for non-dedicated equipment, but no similar requirement exists for retaining what are intended to be "quick reference" or temporary status labels. Examples of these kinds of status labels include "mixing lot ###"; "clean, ready for use as of d/M/y"; "not clean." We see no value in the retention of such labels in addition to the required equipment log or batch record documentation. The labels serve a valuable, temporary purpose of positively identifying the current status of equipment and the material under process. Any status label should be correct, legible, readily visible, and associated with the correct piece of equipment. The information on the temporary status label should correspond with the information recorded in the equipment cleaning and use log, or the previous batch record for non-dedicated equipment.

Labels are merely one way to display temporary status information about a piece of equipment. It is considered acceptable practice to display temporary equipment status information on dry-erase boards or chalkboards. And it would be appropriate for an FDA investigator to verify that the information on a temporary status label is consistent with the log.

References:

- 21 CFR 211.182: Equipment cleaning and use log
- 21 CFR 211.105: Equipment identification

Contact for further information: Brian Hasselbalch, CDER, hasselbalchb@cder.fda.gov

2. Can containers, closures, and packaging materials be sampled for receipt examination in the warehouse?

Yes. Generally, we believe that sampling in a typical drug manufacturing facility warehouse would not represent a risk to the container/closure or affect the integrity of the sample results. But whether the act of collecting a sample in the warehouse violates the CGMPs requirement that containers "be opened, sampled, and sealed in a manner designed to prevent contamination of their contents..." will depend on the purported quality characteristics of the material under sample and the warehouse environment. For container/closures purporting to be sterile or depyrogenated, sampling should be under conditions equivalent to the purported quality of the material: a warehouse environment would not suffice (see 211.94 and 211.113(b)). This is to preserve the fitness for use of the remaining container/closures as well as ensure sample integrity, if they are to be examined for microbial contamination. At a minimum, any sampling should be performed in a manner to limit exposure to the environment during and after the time samples are removed (i.e., wiping outside surfaces, limiting time that the original package is open, and



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properly resealing original package). Well-written and followed procedures are the critical elements.

Note that the CGMPs at 211.84 permit a manufacturer to release for use a shipment of containers/closures based on the supplier's certificate of analysis and a visual identification of the containers/closures. Once a supplier's reliability has been established by validation of their test results, a manufacturer could perform the visual examination entirely in the warehouse.

References:

- 21 CFR 211.84: Testing and approval or rejection of components, drug product containers, and closures
- 21 CFR 211.94: Drug product containers and closures
- 21 CFR 211.113(b): Control of microbiological contamination
- 21 CFR 211.122: Materials examination and usage criteria

Contact for further information: Anthony Charity, CDER, charitya@fda.hhs.gov

3. A firm has multiple media fill failures. They conducted their media fills using TSB (tryptic soy broth) prepared by filtration through 0.2 micron sterilizing filter. Investigation did not show any obvious causes. What could be the source of contamination?

A firm recently had multiple media fill failures. The media fill runs, simulating the filling process during production, were conducted inside an isolator. The firm used TSB (non-sterile bulk powder) from a commercial source, and prepared the sterile solution by filtering through a 0.2 micron sterilizing filter. An investigation was launched to trace the source of contamination. The investigation was not successful in isolating or recovering the contaminating organism using conventional microbiological techniques, including the use of selective (e.g., blood agar) and nonselective (e.g., TSB and tryptic soy agar) media, and examination under a microscope. The contaminant was eventually identified to be *Acholeplasma*

laidlawii by using 16S rRNA gene sequence. The firm subsequently conducted studies to confirm the presence of *Acholeplasma laidlawii* in the lot of TSB used. Therefore, it was not a contaminant from the process, but from the media source.

Acholeplasma laidlawii belongs to an order of mycoplasma. Mycoplasma contain only a cell membrane and have no cell wall. They are not susceptible to beta-lactams and do not take up Gram stain. Individual organisms are pleomorphic (assume various shape from cocci to rods to filaments), varying in size from 0.2 to 0.3 microns or smaller. It has been shown that *Acholeplasma laidlawii* is capable of penetrating a 0.2 micron filter, but is retained by a 0.1 micron filter (see Sundaram, et al.). *Acholeplasma laidlawii* is known to be associated with animal-derived material, and microbiological media is often from animal sources. Environmental monitoring of mycoplasma requires selective media (PPLO broth or agar).

Resolution: For now, this firm has decided to filter prepared TSB, for use in media fills, through a 0.1 micron filter (note: we do not expect or require firms to routinely use 0.1 micron filters for media preparation). In the future, the firm will use sterile, irradiated TSB when it becomes available from a commercial supplier. (Firm's autoclave is too small to permit processing of TSB for media fills, so this was not a viable option.) The firm will continue monitoring for mycoplasma and has revalidated their cleaning procedure to verify its removal. In this case, a thorough investigation by the firm led to a determination of the cause of the failure and an appropriate corrective action.



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- "Validation Master Plan", by Trevor Deeks (Item No. 17195 Price: US\$ 80 member/US\$ 109 nonmember)
- Richard Shepherd training CD's – Discount on all titles by Richard Shepherd.
- "The Essence of GMPs" by U.G. Barad (Item no. 17203 Price: US\$ 185 member/US\$ 229 nonmember) – WINNER, 2003 PDA/DHI Technical Books Distinguished Author award.
- "Rapid Analytical Microbiology" by Wayne P. Olson (Item no. 17184 Price: US\$ 195 member/US\$ 239 nonmember)

Enter the promotion code SEPT04 on the order form or in the "Special Delivery Request" field online.

References:

- 21 CFR 211.113: Control of microbiological contamination
- 21 CFR 211.72: Filters
- 21 CFR 211.84(d)(6): Testing and approval or rejection of components, drug product container, and closures
- Sundaram, S., Eisenhuth, J., Howard, G., Brandwein, H. "Application of membrane filtration for removal of diminutive bioburden organisms in pharmaceutical products and processes." *PDA J. Pharm. Sci. Technol.* 1999 Jul-Aug; 53(4): 186-201.
- Kong, F., James, G., Gordon, S., Zekynski, A., Gilbert, G.L. "Species-specific PCR for identification of common contaminant mollicutes in cell culture." *Appl. Environ. Microbiol.* 2001 Jul; 67(7): 3195-200.
- Murray, P., Baron, E., Pfaller, M., Tenover, F., Tenover, R. *Manual of Clinical Microbiology* ASM Press, Sixth Edition.

Contact for further information: Brenda Uratani, CDER, uratanib@fda.hhs.gov

4. Some products, such as transdermal patches, are made using manufacturing processes with higher in-process material reject rates than for other products and processes. Is this okay?

Maybe. It depends on the cause and consistency of the reject rate. Many transdermal patch manufacturing processes produce more waste (i.e., lower yield from theoretical) than other pharmaceutical processes. This should not of itself be a concern. The waste is usually due to the cumulative effect of roll splicing, line start-ups and stoppages, roll-stock changes, and perhaps higher rates of in-process sampling. This is most pronounced for processes involving lamination of rolls of various component layers. Roll-stock defects detected during adhesive coating of the roll, for example, can often only be rejected from the roll after final fabrication/lamination of the entire patch, which contributes to the final process waste stream.

We expect that validated and well-controlled processes will achieve fairly consistent waste amounts batch-to-batch. Waste in excess of the normal operating rates may need (see 211.192) to be evaluated to determine cause (e.g., due to increase in sampling or higher than normal component defects... or both) and the consequences on product quality assessed. We've seen a small number of cases where unusually high intra-batch rejects/losses were due to excessive component quality variability and poorly developed processes.

References:

- 21 CFR 211.100: Written procedures; deviations
- 21 CFR 211.103: Calculation of yield
- 21 CFR 211.110: Sampling and testing of in-process materials and drug products
- 21 CFR 211.192: Production record review

Contact for further information: Brian Hasselbalch, CDER, hasselbalchb@fda.hhs.gov ■

Glenn Wright, Director, Manufacturing Science and Technology, Eli Lilly and Company, is speaking during the “21st Century: Post-Approval Change” session of the 2004 PDA/FDA Joint Regulatory Conference, Sept. 20-22. For more information, go to www.pda.org/pdafda2004.

asking it a lot lately, leads me to believe the response varies based on the role an individual has within the agency or industry and their past experiences with post-approval change.

Over the past decade the FDA has increased its efforts at clarifying the reporting of manufacturing change, but there remains a growing desire to more clearly understand the landscape of how and when to report change. Historically, decisions about making a change in the manufacturing process, in some cases, could be impacted based on the time required for approval. New movement within FDA (e.g. Comparability Protocols) has signaled a willingness to explore new alternatives that encourage companies to make changes by allowing more rapid implementation. These regulatory innovations recognize the benefits of updating methods (i.e. FDA's Process Analytical Technology initiative) while weighing the risk of change.

Post-approval guidance developed for others areas, such as BACPAC I (for intermediates in drug substance synthesis) and SUPAC-IR/MR (for immediate release and modified release solid oral dosage forms), are viewed as invaluable by most industry members. They remove many of the common questions regarding the level of reporting required for specific changes and allow for more accurate evaluations of the reporting expectations. When you review these guidances you find a clear link with risk management. The higher the risk to product quality the greater the reporting required, the lower the risk to product quality the lower the reporting required.

When we think of sterile products, there are a number of areas that would seem to benefit from specific post-approval change guidance. A few areas where added guidance would appear to be helpful include:

- Changes in the facility layout
- Changes in manufacturing hold times
- Changes in in-process controls
- Changes in sterilizer loading patterns
- Changes in environmental monitoring
- Changes in batch sizes
- Changes in bioburden control strategy
- Changes in manufacturing sites
- Changes in the sterile filtration process
- Changes that bring older application files up to date

If one reaches a conclusion that guidance in this area would be useful, what process could be used in its creation? The FDA could develop the initial draft for comment; PQRI could be used to bring together members from the FDA, industry, and academia to provide recommendation to FDA on guidance content; or industry could prepare a draft and submit it under the FDA's Good Guidance Practices regulation for FDA's consideration. I certainly don't have the answers, not that there is one correct answer, on which model would be most appropriate. I do feel however, that additional guidance would be helpful.

At some point in the future it might even be asked if a global post approval guidance for change should be considered, linked possibly in some manner to the ICH Common Technical Document. But that is a much larger question. Whatever the conclusions eventually reached, or not reached, it makes for great discussion. ■

PDA Annual Conference 2005: A Return to PDA Tradition

The world we live in is a continuous evolution of old processes. Change is made recognizing the immediate impact but the long-term effect is not always fully known. The idea is to make better our environment and how we fit into it, and sometimes the result is positive and a new path is created to explore and develop. At other times the new path may not encourage exploration, and the end realization is that the best place to be is where you came from.

The latter is where PDA finds itself. With a renewed sense of purpose and dedication to the organization's mission, the 2005 PDA Annual Meeting will return to providing access to information, education and training in pharmaceutical and biopharmaceutical technology, both domestically and internationally. Chicago, Illinois, an important "hub" of the pharmaceutical industry and home to a growing biotech community, is where PDA will reestablish this position, April 4-8, 2005 at the Hyatt Regency Chicago.

Relying exclusively on PDA resources and membership support, the 2005 PDA Annual Meeting will reintroduce to the membership PDA core meeting values, tailored educational sessions addressing current and pending regulatory processes backed with scientifically sound information, and abundant networking opportunities.

PDA's guarantee is that the 2005 PDA Annual Meeting will return to the membership a spirit of tradition that has sustained the organization for more than 58 years.

Continue to check www.pda.org for updates on program information. PDA is considering papers for the Annual Meeting until September 30, 2004.

By Deborah Stokes, Programs & Meetings Manager

PDA's "New Innovative Technologies" Exhibition™ Program

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Please contact Nahid Kiani at Kiani@pda.org for more details.

PDA Chapter Focus: A Successful First Year

March 30, 2004 marked the commencement of the PDA Chapter of Puerto Rico's "Information Sharing Forum," held in the Wyeth – Carolina facilities. Approximately 50 people benefited from a thorough presentation of the organization and the Chapter initiatives. Bob Mello, PhD, former PDA Vice President, Education, opened the event with a presentation of the PDA organization, which was followed by a presentation from the Puerto Rico Chapter.

The presentations focused on the importance of the Chapter within the Puerto Rico Pharmaceutical Industry, the benefits of becoming a member; the vision, mission and objectives of the Chapter. Since that time, Silma Bladuell, Puerto Rico Chapter President (SCI Associate Director, Wyeth), has seen much activity in response to the Chapter's requests – despite many employment shifts within the Chapter affecting PDA members and Chapter officers alike.

"Many people are moving from one company

to another, but this is nothing new," said Bladuell. "The Chapter will remain focused on supplying the information needed within the area and I don't see that really ever changing."

Chapter Secretary Eliezer Hernández (Quality Assurance Specialist, Pfizer) recognizes area changes in industry affecting the Chapter and event planning because he himself faces a new corporate culture.

"This year, there have been many mergers, acquisitions, consolidations of operations. Along with these come a lot of changes in strategies," said Hernández.

"I think that attendance at meetings and trainings has been affected. In my particular case, I always had opportunity to attend at least one conference per year, but since the acquisition of Pharmacia by Pfizer, I have not had the opportunity to attend any of them."

The pharmaceutical industry in Puerto Rico represents the most important sector on the island, with the presence of 14 top pharmaceutical companies worldwide, and accounts to more than 43 percent share of the island's net income. The Puerto Rico Chapter aspires to help the island become the pharmaceutical industry center of excellence providing a forum to share ideas, experiences and knowledge to the pharmaceutical community.

"The Puerto Rico Chapter is committed to advance the pharmaceutical, biopharmaceutical, medical devices and health care technology through Puerto Rico, the Caribbean Region and Latin America by promoting scientifically and practical technical information as well as education for industry, university, regulatory agencies and public and private industrial development organizations," said Hernández. "This is [the Chapter's] goal and it is difficult to get most people involved."

Hernández offers this advice to new Chapter officers: "Don't get disappointed and use all the means possible for getting results."

"On occasions we have used the e-mail almost like a chat meeting (we should consider a chat meeting in the near future) and we have also used teleconferences...and don't count on having a lot of support from your boss."

Other Puerto Rico Chapter officers include: Chapter President-Elect Jorge Ros (General Manager, Janssen), Treasurer James Feshold (Director, Packaging and Material Center, Wyeth) and Chapter Representative Faris Yany (President, ISS Corp). ■

By KiKi Coffman, Chapter Coordinator

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Promoting PDA from Within: Members Make A Difference

Members often contact the PDA Membership and Chapters department inquiring how they can aid PDA with their limited time and resources. While there are many ways to volunteer at PDA, one of the most time-efficient and simple means to improve PDA is to promote membership to colleagues and friends.

In order to support the ever-growing needs of PDA and its members, our membership must grow. PDA is the members' association and an increasing membership not only gives us the resources to strengthen our valuable career-long learning programs, new members expand the breadth of expertise within our association, which can result in the development of new and different types of technical programs, courses, reports and books to the benefit of all members.

Member referral is one way to recruit new blood, and to that end, PDA's Chapters are on the frontline of our outreach efforts. Just within the last month, PDA welcomed a surge of new members thanks to the determined focus of the volunteer leaders of the PDA Japan Chapter, whose efforts boosted PDA membership in Japan from 473 to 609. The Japan Chapter's success was the result of a focused campaign to contact colleagues whose membership had lapsed and an collaborative outreach effort with PDA Headquarters to recruit first-time members.

Japan Chapter representative Kunio Kawamura (Executive Advisor, Otsuka Pharmaceutical Co.) credited Chapter leaders Yoshihito Hashimoto (Engineering Consultant, Chiyoda Corp.), Taiichi Mizuta, PhD (Manager, Denka Seiken, Co.), and Hiroshi Harada (Quality Assurance, Denka Seiken, Co.), for the recruitment success. Mr. Kawamura noted that the Chapter is not resting on its laurels. "I think we still have to continue our effort," he said.

continues on page 28

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Promoting PDA From Within, from cover

In recent months, other PDA Chapters have addressed the need to expand the membership by evaluating data from Chapter membership reports to identify members whose membership will lapse in the coming months and the largest corporate components of their membership. They are identifying the largest companies within their geographic regions and comparing that information with their current membership data to see if there is a disparity between the current and potential company representation by members. Chapters can request these Chapter membership reports at any time from the Chapter Coordinator at PDA.

The effects of one Chapter purposefully addressing the challenge of a declining membership carried a huge downstream effect on PDA's overall membership numbers. The Japan Chapter's efforts made a difference, and with further cooperative efforts between the PDA Chapters, individual members and PDA

headquarters, membership has the potential to increase significantly within a short amount of time.

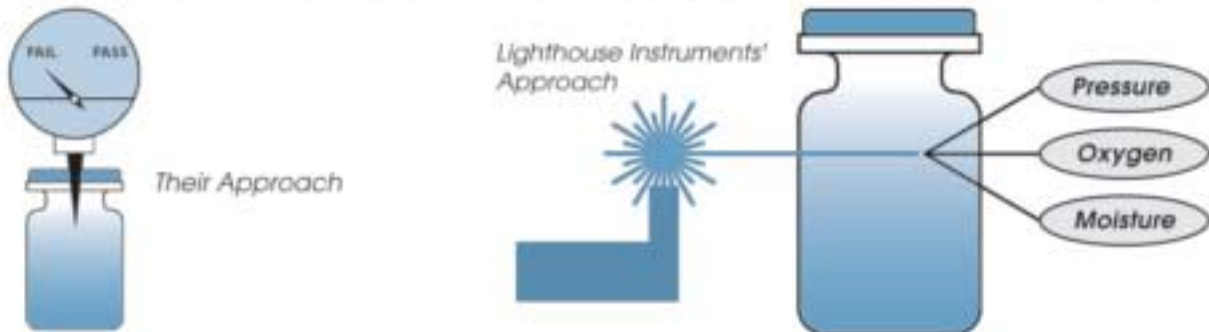
Of course, under the PDA Chapter Points Program, Chapters can receive awards for promoting membership. However, Chapters are expected to help strengthen the association through member recruitment at all times.

By bringing in new members, we help to build a bigger, better and stronger association. Any member can post a flyer on a community bulletin board or inform his or her human resources department about training opportunities at PDA. Simply elaborating on positive personal experiences as a PDA member can influence a colleague's decision to join.

For more information about increasing membership or the PDA Chapter Points Program, please contact KiKi Coffman, Chapter Coordinator, at coffman@pda.org. ■

By KiKi Coffman, Chapter Coordinator

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PDA Chapter Contacts

The following is a list of the PDA Chapters, organized by the area of the world they are located. Included in the list are the Chapter name, the area(s) served, the chapter contact person, their affiliation and their e-mail address. Where applicable, the Chapter's Web site is listed. More information on the Chapters and the volunteer members who lead them is available at www.pda.org/chapters/index.html.

Asia Pacific

Australia Chapter

Contact: Ken Dibble
Millipore Australia
E-mail: ken_dibble@millipore.com

India Chapter

Contact: Darshan Makhey, Ph.D.
Nicholas Piramal India Limited
E-mail: dmakhey@nicholaspiramal.co.in

Japan Chapter

Contact: Hiroshi Harada
E-mail: hharada@bcasj.or.jp
Web site: <http://www.j-pda.jp/index.html>

Korea Chapter

Contact: Jun Yeon Park
E-mail: jun_yeon_park@pall.com

Southeast Asia Chapter

Contact: K. P. P. Prasad, Ph.D.
Pfizer Asia Pacific Pte Ltd
E-mail: prasad.kpp@pfizer.com

Taiwan Chapter

Contact: Tuan-Tuan Su
E-mail: pdatc@ms17.hinet.net

Europe

Central Europe Chapter

Contact: Erich Sturzenegger, Ph.D.
Novartis Pharma AG
E-mail: erich.sturzenegger@pharma.novartis.com

France Chapter

Contact: Phillippe Gomez
Sartorius Corporation
E-mail: philippe.gomez@sartorius.com

Italy Chapter

Contact: Vincenzo Baselli
Pall Italia
E-mail: vincenzo_baselli@europe.pall.com
Web site: <http://www.pda-it.org>

Prague Chapter

Contact: Zdenka Mrvova
Léciva A.S.
E-mail: zdenka.mrvova@zentiva.cz

Spain Chapter

Contact: Jordi Botet, Ph.D.
STE Compliance Services
E-mail: jbotet@stegroup.com

United Kingdom and Ireland Chapter

Contact: John Moys
Sartorius
E-mail: john.moys@sartorius.com

Middle East

Israel Chapter

Contact: Karen S. Ginsbury
PCI-Pharmaceutical Consulting Israel Ltd.
E-mail: kstaylor@netvision.net.il

North America

Canada Chapter

Contact: Hein Wick
HWMR, Ltd.
E-mail: hwick@hwmr.ca

Capital Area Chapter

Areas Served: MD, DC, VA, WV
Contact: Barry A. Friedman, Ph.D.
Cambrex Bio Science Baltimore, Inc.
E-mail: barry.friedman@ cambrex.com
Web site: www.pdacapitalchapter.org

Delaware Valley Chapter

Areas Served: DE, NJ, PA
Contact: Art Vellutato, Jr.
Veltek Associates, Inc.
E-mail: artjr@sterile.com
Web site: www.pdadv.org

Metro Chapter

Areas Served: NJ, NY
Contact: Nate Manco
Sandoz
E-mail: nate.manco@gx.novartis.com

Midwest Chapter

Areas Served: IL, IN, OH, WI, IA, MN
Contact: Amy Gotham
Northview Labs
E-mail: PDAMidwest@comcast.net

Mountain States Chapter

Areas Served: CO, WY, UT, ID, NE, KS, OK, MT
Contact: Jeff Beste
Pendelton Resources
E-mail: cmdjeff@aol.com
Web site: www.mspsda.org

New England Chapter

Areas Served: MA, CT, RI, NH, VT, ME
Contact: Mark A. Staples, Ph.D.
MicroCHIPS
E-mail: mstaples@mchips.com

Puerto Rico Chapter

Contact: Silma Bladuell
Wyeth Lederle, Inc.
E-mail: bladues@wyeth.com

Southeast Chapter

Areas Served: NC, SC, TN, VA, FL, GA
Contact: Lisa Eklund
Hospira, Inc.
E-mail: lisa.eklund@fresenius-kabi.com
Web site: www.pdase.org

Southern California Chapter

Areas Served: Southern California
Contact: John Spoden
Allergan
E-mail: spoden_john@allergan.com
Web site: <http://www.pda.org/chapters/Website-SoCal/SoCal-index.html>

West Coast Chapter

Areas Served: Northern California
Contact: Randall Tedder
IconNova
E-mail: randall@iconnova.com

PDA Interest Groups & Leaders

The following is a list of PDA Interest Groups (IGs). Starting in 2004, PDA began establishing "Branches" of each IG in the various regions of the world served by PDA. The list below includes the IG's name and contact information for each IG's leader, including the leader's affiliation and his or her e-mail address. Contact information for a "Branch" leader is included where applicable. More detailed information on PDA's Interest Groups and contact information is available on the PDA Web site at: www.pda.org/science/IGs.html.

Biotechnology

Frank Matarrese
Chiron Corporation
E-mail: frank_matarrese@chiron.com

European Branch

Roland Günther
Novartis
E-mail: roland.guenther@pharma.novartis.com

Computer Systems

Barbara L. Meserve
Acculogix, Inc.
E-mail: bmeserve@acculogix-usa.com

Drug-Device

Delivery Systems

Raymond A. Pritchard
Alkermes, Inc.
E-mail: ray.pritchard@alkermes.com

European Branch

Alexander Schlicker, Ph.D.
Hoffmann La Roche Ltd;
E-mail: Alexandra.schlicker@roche.com

Georgios Imanidis, Ph.D.
Pharmaceutical Technology
E-mail: georgios.imanidis@unibas.ch

Filtration

Jack Cole
Jack Cole Associates
E-mail: jvcole@aol.com

European Branch

Roger Seiler
Sartorius
E-mail: roger.seiler@sartorius.com

GMP Purchasing

Nancy M. Kochevar
Amgen, Inc.
E-mail: nancyk@amgen.com

Inspection Trends/ Regulatory Affairs

Robert L. Dana
Elkhorn Associates Inc.
E-mail: elkhornassoc1@aol.com

Isolation Technology

Dimitri P. Wirchansky
Jacobs Engineering Group, Inc.
E-mail: dimitri.wirchansky@jacobs.com

Lyophilization

Edward H. Trappler
Lyophilization Technology
E-mail: etrappler@lyo-t.com

Microbiology/ Environmental Monitoring

Jeanne E. Moldenhauer, Ph.D.
Vectech Pharmaceutical
Consulting, Inc.
E-mail: jeannemoldenhauer@yahoo.com

Nanotechnology

D. F. Chowdhury
Aphton Corporation
E-mail: fazc@aol.com

Ophthalmics

Chris Danford
Alcon Laboratories Inc.
E-mail: chris.danford@alconlabs.com

Packaging Science

Edward J. Smith, Ph.D.
Wyeth Pharmaceuticals
E-mail: smithej@wyeth.com

Pharmaceutical Water

Theodore H. Meltzer, Ph.D.
Capitola Consulting Co.
E-mail: theodoreheltzer@hotmail.com

Production and Engineering

Frank Bing
Consultant
E-mail: frankbingjr@aol.com

Quality Assurance/ Quality Control

Don E. Elinski
Eli Lilly & Company
E-mail: elinski@aol.com

Stability

Rafik H. Bishara, Ph.D.
Eli Lilly & Company
E-mail: rhb@lilly.com

Training

Thomas W. Wilkin, Ed.D.
Schering-Plough Corp.
E-mail: thomas.wilkin@spcorp.com

Vaccines

Frank S. Kohn, Ph.D.
FSK Associate
E-mail: fsk@lowatelecom.net

Validation

Bohdan M. Ferenc
Qualification Services
E-mail: biferenc@aol.com

Visual Inspection of Parenterals

John G. Shabushnig, Ph.D.
Pfizer Inc.
E-mail: john.g.shabushnig@pfizer.com

European Branch

Markus Lankers, Ph.D.
APSYS GmbH
E-mail: markus.lankers@apsys.de



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If your order totals: *Add:*
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 US\$75.01–US\$150 US\$9.95
 US\$150.01–US\$250 US\$11.95
 US\$250.01 or more US\$13.95

Subtotal _____
 Shipping & Handling _____
 5% Tax _____
 (Maryland residents only)
TOTAL _____

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A. By **Credit Card** (VISA, MasterCard/EuroCard, American Express, Diners Club), clearly indicating account number and expiration date and billing address. **Proceed to Item 4 below.**

B. By **Bankers' Draft/Check** forwarded together with the order form PAYABLE IN US DOLLARS ONLY to:

PDA, Inc., P.O. Box 79465, Baltimore MD 21279-0465

C. **Wire Transfer Payments**/By bank-to-bank transfer to: (required if paying in foreign currency; Contact Janny Chua at +1 (301) 656-5900 ext. 133 or chua@pda.org for quotes in various currencies.)

UBS AG Basel Swift Code: **UBSWCH33HAN**

Account number (please specify correct account number for currency being remitted):

- CHF: Account No. 292-568-280-03Z
- EUR: Account No. 292-568-280-68L
- GBP: Account No. 292-568-280-69R
- USD: Account No. 292-568-280-70P
- YEN: Account No. 292-568-280-71K

Bank Address:

UBS AG Basel
 Postfach
 Aeschenplatz 6
 4002 Basel, Switzerland

Wire Transfer Confirmation: _____

(insert your confirmation of receipt by UBS Bank here.)

4. Please check the appropriate box: Charge: MasterCard/EuroCard VISA AmEx Diners Club

Account Number: _____ Exp. Date: _____

Name (exactly as on card): _____

Signature: _____ Date: _____

Billing Address: _____ **Federal Tax I.D. #52-1906152**

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PDA USE:
 Date: _____ Check: _____ Amount: _____ Account: _____



PDA Training and Research Institute Registration Form

R
LTR 09/04

1. Please type or print your name, address and affiliation.

Preferred Address: Business Home

Mr. Ms. Dr. First Name _____ Middle Initial _____ Last Name _____

Job Title _____ Membership Number _____

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City _____ State/Province _____ ZIP+4/Postal Code _____

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 :

2.

Course Title/Course No.	Date	Current Member	Join PDA and Attend Course	Attend Course Only; Do Not Join PDA	Government/Health Authority Employee *

* You must be an employee of an official government agency or health authority to qualify for this rate. TOTAL _____

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B. By Bankers' Draft/Check forwarded together with the registration form PAYABLE IN US DOLLARS ONLY to:

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Please mark here to request a PROFORMA INVOICE from PDA to process your company payment.¹

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UBS AG Basel Swift Code: UBSWCH2H40M

Account number (please specify correct account number for currency being remitted):

- CHF: Account No. 292-568-280-02T
- EUR: Account No. 292-568-280-64B
- GBP: Account No. 292-568-280-65E
- USD: Account No. 292-568-280-66M
- YEN: Account No. 292-568-280-67C

Please reference code: 2-2-2000

Bank Address:
 UBS AG Basel
 Postfach
 Aeschenplatz 6
 4002 Basel, Switzerland

Currency conversions available at:
 : www.forex.com/
 : forex_market_commentary.html :
 :

Wire Transfer Confirmation: _____
(insert your confirmation of receipt by UBS Bank here.)

4. Please check the appropriate box: Charge: MasterCard/EuroCard VISA AmEx Diners Club

Account Number: _____ Exp. Date: _____

Name (exactly as on card): _____

Signature: _____ Date: _____

Billing Address: _____

Federal Tax I.D. #52-1906152

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Overview

Visual inspection continues to be an important step in producing high-quality injectable products. PDA has organized this forum to provide the most current information that you can use immediately on-the-job:

- Inspection methods and equipment
- Practical experience implementing inspection methods
- Foreign material identification and control
- Compendial requirements and regulatory trends
- Validation of visual inspection methods
- Process optimization

Co-chairs: *Markus Lankers, PhD, rap.ID GmbH, Berlin*
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Professionals working in the pharmaceutical and biopharmaceutical communities:

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 - In-depth case studies
 - Address your specific visual inspection issues - work with presenters and delegates to effectively resolve them
 - Delegates are encouraged to share their visual inspections experiences, please contact: markus.lankers@rapid.com

6-7 October 2004

Berlin, Germany



Venue

Hilton Berlin
Mohrenstrasse 30
10117 Berlin
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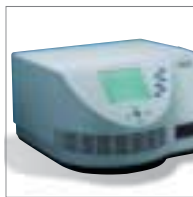
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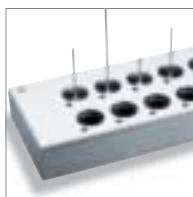
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Key experts and industry leaders will provide **valuable tips** and **proven strategies** to help you benefit from this dynamic market.

- ✓ Contract Filling
- ✓ Syringe Accessories
- ✓ Self Injection
- ✓ Syringe Processing

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Manufacturing

Senior Managers
Middle Managers
Entrance Level

New Information You Can Use Immediately:

- Clear knowledge about outsourcing opportunities for stability tests and commercial quantities
- Better planning tools for efficient processing of syringe accessories
- Fast, efficient processing strategies for pre-filled syringes as a primary container for self injection devices
- Latest news and updates on high- and low-volume processing equipment

A Valuable 2 Days for...

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- Successfully apply quality assurance requirements for aseptic filling, inspection and packaging of pre-filled syringes
- Immediate tips for the production of pharmaceutical rubber accessories
- Current GMP updates on the manufacturing of self-injection devices
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A Valuable 2 Days for...

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PLUS: Tour the Bänder Glas GmbH facility and see world-class manufacturing processes of pre-filled syringes first-hand!

18-19 October 2004

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