People • Science • Regulation

PDA Letter

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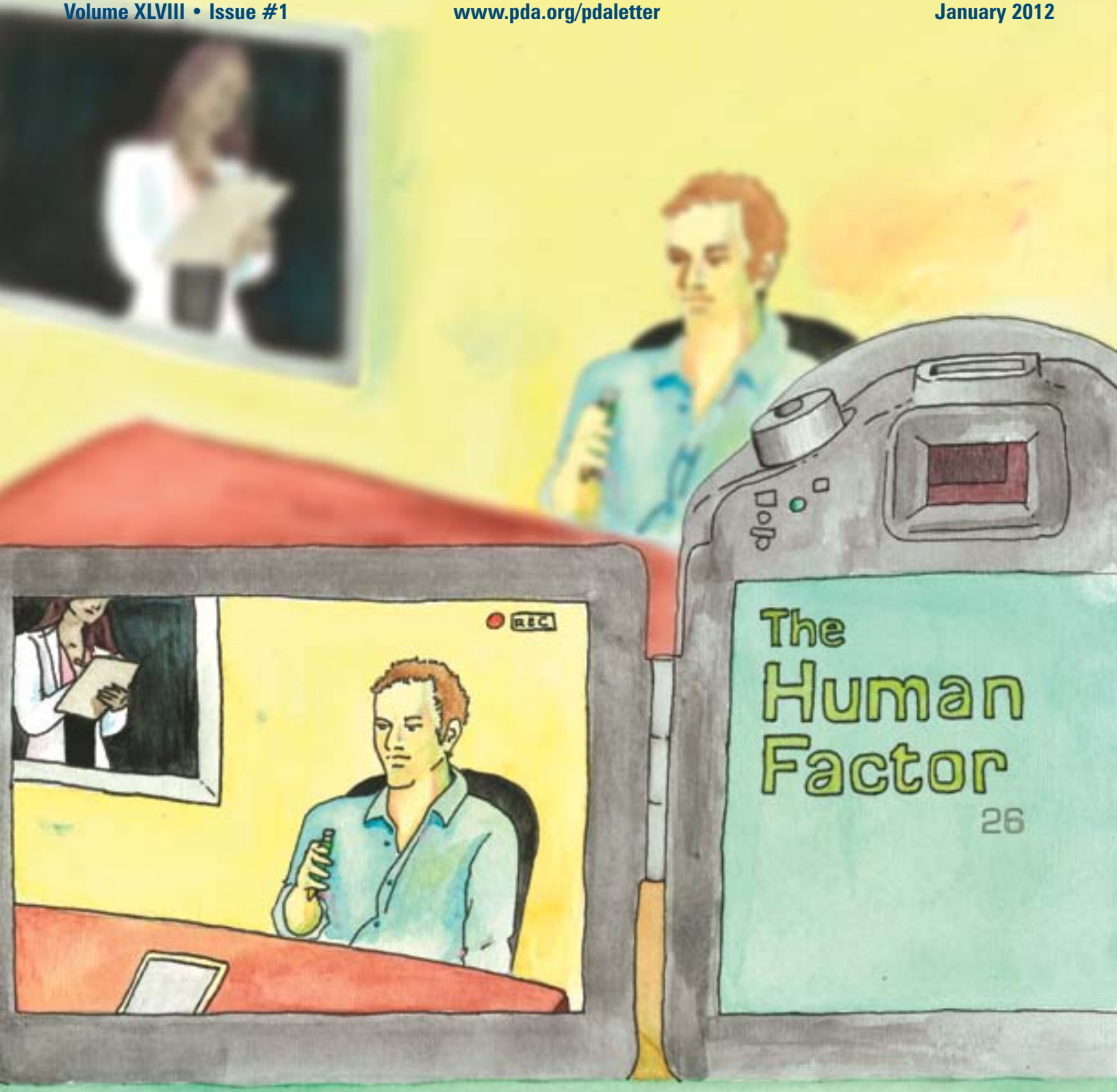

Conference Brochure Just Posted Online!

The Parenteral Drug Association presents...

2012 PDA ANNUAL MEETING

April 16-18, 2012

JW MARRIOTT DESERT RIDGE RESORT • PHOENIX, ARIZONA

The 2012 PDA Annual Meeting is the meeting place this April. The distinguished Program Planning Committee, made up of your peers, is hard at work to bring you ***the best*** content in the industry. They know what you are concerned about, what you want to hear and who you want to hear it from.

The Best Content in the Industry

Conference Highlights Include:

- **Two Great Opening Plenary Topics:**
  - **Future Benefits for Patients: From Discovery to Commercial Products, Cellular and Gene Therapies**, David Shanahan, President, *Mary Crowley Research Center* and President, CEO and Founder, *Gradalis*
  - **The Future of Personalized Medicine – Challenges Ahead**, Ted Love, MD, Executive Vice President, R&D and Technical Operations, *Onyx Pharmaceuticals*
- **Plenary Session Two:**
  - **The Future of the Biopharmaceutical Industry**, David Urdal, Chief Scientific Officer, *Dendreon*
  - **The Future of the Biopharmaceutical Regulatory Perspective**, *FDA Representative Invited*
- **Student Call for Posters – Abstracts Due February 6, 2012**
- **Closing Plenary Topics:**
  - **Manufacturing Opportunities and Challenges in the Next 10-20 Years**, Matt Croughan, Professor, *Keck Graduate Institute of Applied Life Sciences*
  - **Emerging Regulatory Expectations**, Emily Shacter, PhD, Chief, Laboratory of Biochemistry, *CDER, FDA*
- NEW: Breakfast Sessions on: Career Development Strategies and the Quality and Regulatory Job Market Outlook 2012
- Networking Receptions & Events like the 6th Annual PDA Golf Tournament at the Wildfire Golf Club & the PDA 6th Annual Walk/Run *(benefiting the Phoenix Children's Hospital)*
- Post-Conference Workshop: PDA Single Use Systems Workshop on April 18-19
- PDA's Training and Research Institute (PDA TRI) will be offering eight courses on April 19-20
- **Hotel activities for the entire family!**

Register now and save up to $400

www.pda.org/annual2012

EXHIBITION: April 16-17 | **CAREER FAIR:** April 16-17
POST-CONFERENCE WORKSHOP: April 18-19 | **COURSES:** April 19-20

PARENTERAL DRUG ASSOCIATION TRAINING AND RESEARCH INSTITUTE (PDA TRI)

Aseptic Processing Training Program

2012 Schedule:

Session 1:
Week 1: Janu
Week 2: [illegible]-10
Se[illegible]
[illegible]arch 5-9
[illegible] 2: March 26-30

SOLD OUT

Session 3:
Week 1: May 14-18
Week 2: June 4-8

Session 4:
Week 1: August 20-24
Week 2: September 10-14

Session 5:
Week 1: October 15-19
Week 2: November 5-9

The most comprehensive program in the preparation of sterile parenteral products

This two week comprehensive training program, taught by 20 industry leading experts in their fields, with over 300 years of combined experience, will give you and your personnel the training and information needed to properly evaluate and improve your aseptic processes to ensure sterile products. This program provides the perfect balance of hands-on laboratory and lecture training, equipping you with tools and actual experience you can bring home and apply immediately on the job.

For more information contact:
James Wamsley, Senior Manager, Laboratory Education
Tel: +1 (301) 656-5900 ext. 137 | E-mail: wamsley@pda.org

Location:
PDA Training and Research Institute
4350 East West Highway, Suite 150, Bethesda, MD 20814
Tel: +1 (301) 656-5900 | Fax: +1 (301) 986-1093

Benefits of Attending

- Learn to relate and incorporate each component of aseptic processing into one operation for an overall improved process and finished product
- Understand the theory and practice behind personnel gowning and aseptic technique qualification to minimize risk of product contamination by personnel
- Use proper environmental monitoring techniques combined with a good cleaning and disinfection program to avoid common sources of contamination in your facility
- Learn to incorporate proper documentation practices into your aseptic processing program to facilitate regulatory compliance

Learning Objectives

Upon completion of this course, you will be able to:

- Demonstrate an increased proficiency of techniques and skills relating to aseptic processing
- Evaluate and improve current aseptic processing procedures at your facility
- Limit risk for manual product contamination with airflow visualization studies
- Evaluate your environmental monitoring program to collect appropriate data, identify and interpret trends
- Incorporate proper gowning principles into a complete personnel qualification program
- Describe the importance of filter integrity testing when filtering water, gases, or proteinaceous solutions

SPACE IS LIMITED - REGISTER NOW:
www.pda.org/2012aseptic

PDA Letter

Volume XLVIII • Issue #1 www.pda.org/pdaletter

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Cover Art Illustrated by Katja Yount

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Features

2012 Board of Directors

PDA is pleased to announce the results of the 2012 Board of Directors and Officers election.

Executive Committee

Congratulations to **Anders Vinther**, PhD, VP, Head Quality Biologics, Genentech, who assumes the role of PDA Chair for the 2012-2014 cycle.

Harold Baseman, Principal and Chief Operating Officer, ValSource, has been elected as the Chair-Elect.

Steven Mendivil, Executive Director, Corporate Quality External Affairs, Amgen, has been elected as Secretary.

Rebecca Devine, PhD, Regulatory Consultant, was elected to the position of Treasurer.

Maik Jornitz, Senior Vice President, Marketing Bioprocess Sartorius Stedim North America, moves into the Immediate Past Chair position for the next two years.

Chair
Anders Vinther, PhD
Genentech

Chair-elect
Hal Baseman
ValSource

PDA would like to thank **John Shabushnig,** Sr. Manager/Team Leader, Quality Systems & Technical Services, Pfizer, for serving as PDA Chair in 2008-2009 and as Immediate Past Chair from 2010-2011.

Secretary
Steven Mendivil
Amgen

Treasurer
Rebecca Devine, PhD
Regulatory Consultant

Immediate Past Chair
Maik Jornitz
Sartorius Stedim Biotech

Directors

PDA congratulates and welcomes two new Directors: **Ursula Busse**, PhD, Head of Project Office for Biopharmaceutical Operations, Novartis and **John Finkbohner**, PhD, Senior Director, Regulatory Affairs, MedImmune.

Reelected to the Board were **Chris Smalley**, PhD, Associate Director, BioSterile Validation, Merck, and **Junko Sasaki**, Quality Assurance Principal, Dainippon Sumitomo Pharma. Co.

PDA thanks **Amy Scott-Billman**, Head, Worldwide Regulatory Strategy, Cancer Immunotherapeutics, GlaxoSmithKline, for her service to PDA and its Board.

Ursula Busse
Novartis

Jette Christensen
Novo Nordisk

John Finkbohner
MedImmune

Gabriele Gori
Novartis

Zena G. Kaufman
Abbott Laboratories

Michael Sadowski
Baxter Healthcare

Junko Sasaki
Dainippan Sumitomo Pharma

Sue Schniepp
OSO BioPharmaceuticals

Lisa Skeens, PhD
Baxter Healthcare

Christopher Smalley
Merck

Martin VanTrieste
Amgen

Glenn Wright
Eli Lilly and Company

Stay Up-to-Date with the PDA Newsbrief

Are you always up-to-date with news in the parenteral drug industry? The *PDA Newsbrief* is a highly informative e-news brief that delivers the most relevant content to your inbox each and every week. Sign up today! Just enter your email address at multibriefs.com/optin.php?PDA

Interested in viewing previous issues of the *PDA Newsbrief?* Visit our complete archive: multibriefs.com/briefs/PDA

You may also use the archive to search for news on a particular topic of interest and explore our most popular past articles.

Suppliers: Start reaching the inboxes of your target market year-round with the *PDA Newsbrief*! Visit our media kit at multibriefs.com/briefs/PDA/mediakit.pdf.

Register for the Annual Meeting Before Feb. 3 and Save

The *2012 PDA Annual Meeting* is just around the corner! Join us in Phoenix, Ariz. for the 66th PDA Annual Meeting from April 16-18. Register before **February 3** and save up to $400!

This year's meeting will focus on the keystone of our industry: the manufacturing of quality products. Immediately following the conference, the *PDA Single Use Systems Workshop* will be hosted on April 18-19. Register for both the conference and workshop and save up to **$550**.

To view the brochures that have just been posted for both events and to register visit: www.pdaannualmeeting.org.

Volunteer

Brendan Cahill, Associate Director, Quality Operations, Pfizer

PDA Join Date: September 2006

Interesting fact about yourself: I used to work as a tractor driver to help pay my way through college.

Why did you join PDA? I was interested in joining an organization that could connect me with others in the industry with whom I could share and discuss the latest trends, hot topics and challenges. It also brought the added advantage of access to PDA publications and events at members' rates.

Of your PDA volunteer experiences, which have you enjoyed the most? I have enjoyed being involved in organizing and running local PDA events in Ireland. I always get great satisfaction when an event is successful and attendee feedback is positive.

How has volunteering in PDA benefited you professionally? It has opened up new channels in terms of being able to benchmark or contact other members, and this has helped me bring a broader industry perspective back to my own place of work.

Which PDA conference/training course is your favorite? I particularly enjoy the joint PDA/EMA conferences. It's a great event for bringing together the industry and the regulators to present and discuss the latest developments.

What would you say to somebody considering PDA membership? Go for it! You will learn something new, and you will gain a wider insight into the industry as a whole. You will also have the opportunity to become involved with your local PDA Chapter, and perhaps even volunteer to help with local events or become a chapter committee member.

2010 Honor Awards Recipients

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

The Service Appreciation Award

The Service Appreciation Award is presented annually for special acts, contributions or services that have contributed to the success and strength of PDA. The 2011 Service Appreciation Award recipients are:

Raphy Bar, PhD, BR Consulting

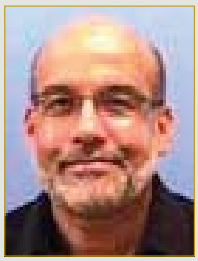
Gerard Boudreault, Drug Development Resources

Colman Casey, PhD, University College Cork

Michele Creech, Talecris Biotherapeutics

Véronique Davoust, Pfizer

Lothar Hartmann, PhD, F. Hoffmann – La Roche



Manuel Melendez, Amgen

Lara Soltis, ITW Texwipe

Laura Thoma, University of Tennessee

Member Volunteer Opportunities

Volunteers Needed for Prefilled Syringe Technical Report

Ron Forster, PhD, Amgen

The new PDA Prefilled Syringe User Requirements for Biotechnology Applications Task Force chaired by **Ron Forster,** PhD, Executive Director, Product and Process Engineering, Amgen, is seeking core and subteam members to work on a technical report.

The main objective of this document is to establish a set of scientific methods that biotech product manufacturers can use to develop user requirements* for prefilled syringe products that have a 1 ml long prefilled syringe. User requirements include critical attributes of the syringe components themselves, the assembled syringe system and the final filled syringe product. Attributes unique to the pharmaceutical product itself are excluded from consideration.

Individuals who work for NDA or BLA holder companies that develop biotech products in prefilled syringes are encouraged to apply for core team membership. Core team members are expected to actively participate in regular teleconferences and assume specific actionable responsibilities (including those of the subteams) for team deliverables.

The nature of the main deliverable of the task force will be discussed and agreed upon by the team. It is expected that the team will establish a common set of user requirements and best practice scientific approaches for evaluating these requirements.

In early 2012, the first meeting of the core team is expected to take place within a month after the membership selection is completed. Once the framework of the TR has been set by the core team, several subteams will be formed to execute and complete the agreed upon plans.

The outcome of this initial effort will be collated into a working draft document. The draft will then be reviewed by an expanded team made up of about 20 companies. Suppliers are welcome to join.

The final draft of the document will be incorporated into a PDA technical report, which will be published in early 2013. This task force will also generate training materials to support the technical report, which may be used in PDA training activities.

Interested individuals should submit the CVs of their representatives to **Iris Rice,** Manager, Scientific and Regulatory Affairs, PDA at rice@pda.org.

The email should clearly state the name of the person and their preference for joining either the core team or subteam. If you are applying for the core team role, please be a leader in your firm's prefilled syringe functional area. Subteam roles should be filled by those who are subject matter experts. We expect such division of effort will greatly facilitate progress of this task force.

Speaker and Poster Opportunities

Committees for Prefilled Syringes Conference and PDA Annual Meeting are seeking submissions

See pages 10 and 25 for more details.

The Universe of Pre-filled Syringes and Injection Devices

October 15-17, 2012 | Red Rock Resort and Spa | Las Vegas, Nevada

CALL FOR ABSTRACTS / CASE STUDIES

The 2012 Pre-filled Syringe Program Planning Committee invites you to submit a scientific abstract for presentation at PDA's 2012 Universe of Pre-filled Syringes and Injection Devices. The theme of this year's conference is: ***Integrating the Unmet Market Needs: Bringing it All Together for Tomorrow's Success.***

Suggested topics include, but are not limited to:

- **Advances in Primary Container/ Prefilled Syringe Technology:**
  - Analytical Characterization Methods
  - Quality Improvements
  - Protein/Syringe Interactions
  - New Materials/Injector Technologies
  - Multiple Chamber Injector
  - Safety Devices
  - Autoinjectors and Add-ons
- **Factors Influencing the Selection and Development of Delivery Devices:**
  - Human Factors
  - End User Needs and Perspectives
  - Interaction between Device and Syringe
  - Regulatory Filing Process
  - Impact of Drug Characteristics
- **Case Studies: Market and Regulatory**
  - Global Market Trends
    - Asia Market
    - Europe Market
    - Latin America Market
    - North America Market
  - Regulatory and Clinical Strategies
  - Combination Products
- **Case Studies: Manufacturing**
  - Vial to Pre-filled Syringe Conversion
  - Integration of PAT and Q8
  - Manufacturing Technologies Based on Disposable Processing Units
  - Material Selection
  - Stability Study Strategies
  - Aseptic Processing and Final Packaging Best Practices
  - Tech Transfer Best Practices
  - Contract Manufacturing Best Practices
  - Clinical Trails with Prefilled Syringes
  - Release Testing
    - Incoming Components
  - Microbial Control
  - Quality Agreements

Abstracts must be received by March 30, 2012 for consideration.
Pleas visit **www.pda.org/prefilled2012** to submit your abstract.

Case studies are particularly desired. Commercial abstracts featuring promotion of products and services will not be considered. After June 1, 2012, you will be advised in writing of the status of your abstract. PDA will provide one complimentary registration per podium presentation. Additional presenters and all poster presenters are required to pay appropriate conference registration fees. All presenters are responsible for their own travel and lodging, with the exception of health authority speakers.

QUESTIONS?

Contact PDA:
Leon D. Lewis
Manager
Programs and Web Seminars
Tel: +1 (301) 656-5900 ext. 149
Fax: +1 (301) 986-0296
Email: lewis@pda.org

ALL ABSTRACTS WILL BE REVIEWED

All submitted abstracts will be reviewed by the Program Planning Committee for inclusion as a podium presentation or for poster presentation.

ATTENTION EXHIBITORS

PDA is seeking vendors who provide excellent products/services in support of this conference. Space is limited and is on a first-come, first-service basis. To reserve your space, please contact David Hall at hall@pda.org or +1 (301) 656-5900 ext.160.

www.pda.org/prefilled2012

PDA's History for Sale

The History of PDA: 65 Years of Connecting People, Science and Regulation® is now available for purchase! This 232-page book provides details on the growth of PDA activities in the 15 years since its Golden Anniversary in 1996. Longtime PDA member and now President, **Richard M. Johnson** had the vision and the initiative to create this 65th Anniversary Book in order to capture and commemorate the explosive growth of PDA's activities.

To buy the free online version, visit tinyurl.com/pdahistory.

To purchase the hard copy, visit tinyurl.com/pdahistory bookstore.

Membership Department Thanks Survey Participants

We would like to thank all participants of the 2011 PDA Membership Satisfaction Survey for giving us one of our highest feedback rates ever! The information from the survey will give us an opportunity to improve our services, benefits and products.

Our ultimate goal is to create greater value for you, our members.

We would also like to congratulate **Wade Johnston,** PhD, Principal Microbiologist, CIBA Vision Corporation, for winning the iPad 2 that was raffled off in conjunction with the survey.

PDA's 6th Annual Global Conference on Pharmaceutical Microbiology

Opening Remarks

(l-r) Lynne Ensor, U.S. FDA; Daniel Y.C. Fung, Kansas State University; Edward Tidswell, Baxter Healthcare

Ask the Regulators Panel Discussion

(l-r) Bryan S. Riley, U.S. FDA; Renee Blosser, U.S. FDA; Thomas J. Arista, U.S. FDA; Dennis E. Guilfoyle, U.S. FDA

Preservation Challanges for Non-Sterile Multi-Dose Products

(l-r) David Steinberg, Steinberg & Associates; Philip Geis, Proctor & Gamble; Jean Porracchia, Johnson & Johnson; Steven Schnittger, Estee Lauder Companies

Applications of Risk Assessment in the Microbiology Laboratory

(l-r) Lawrence Lin, Baxter Healthcare; Sophia Nguyen, Baxter Healthcare; Amy McDaniel, Pfizer; Rhonda Ezell, Qualitest Pharmaceuticals; James M. Payne, bioMérieux

Challenges in Radiation Sterilization of Pharmaceuticals and Medical Devices

(l-r) Betty Howard, Steris Isomedix Services; Kalavati Suvarna, U.S. FDA; Joyce Hansen, J.M. Hansen & Associates Consulting; Patrick Weixel, U.S. FDA

Impact of Objectionable Microorganisms on the Industry and on Patient Safety

(l-r) James J. Leyden, Penn Medicine; Judith Noble-Wang, CDC; Jean Porracchia, Johnson & Johnson; Amy McDaniel, Pfizer; Anthony Cundell, Merck Sharp & Dohme

Container Closure Integrity

(l-r) Destry Sillivan, U.S. FDA; Dana Guazzo, RxPAX;
Scott V.W. Sutton, The Microbiology Network; Donald Singer, GlaxoSmithKline;
Anthony Marchesano, GlaxoSmithKline

Microbiological Issues Associated with Reconstitution, Administration, and Holding of Products

(l-r) Cheryl Moser, Merck Sharp & Dohme Corporation; John W. Metcalfe, U.S. FDA;
Rudolf R. Eggers, WHO; Edward Tidswell, Baxter Healthcare

Poster Exhibit

The Universe of Pre-Filled Syringes and Injection Devices

(l-r) Uwe Rothhaar, Schott; Paolo Golfetto, Nuova Ompi; Paolo Magiagalli, BD Medical; Thomas Bühler, Bausch + Ströbel; Thomas Schönknecht, Schott; Rob Swift, Amgen

Steven Kaufman, SHL Group

(l-r) Frank Lehle, Vetter Pharma Fertigung; Klaus Ullherr, Bosch Packaging Systems; Jörg Lümkemann, F. Hoffmann-La Roche

(l-r) Jörg Zimmermann,Vetter Pharma Fertigung; Nagarajan Thyagarajapuram, Eli Lilly; Antoine Alarcon, Sanofi Pasteur; Thomas Schönknecht, Schott; Mathias Romacker, Amgen; Gerhard Mayer, Sensile Medical; Jörg Sielemann, F. Hoffmann-La Roche; Georg Roessling, PDA

Fun & Networking

European Cold Chain Conference

(l-r) Belén Escribano Romero, AEMPS; Riekert Bruinink, Health Care Inspectorate, Netherlands; Katrin Nodop, EMA; Mohamed Refaat, Egyptian Ministry of Health; Miriam Kaplan,Ministry of Health, Israel

Please Welcome the Following Industry Leaders to the PDA Community

Zsoldos Agnes, Ceva-Phylayia

Scott Allan, Teva Pharmaceuticals

Stephane Allard, IMA Life

Paola Amore, Praxair España

Philip Archambault, Elpro Services

Vani Battar, MedImmune

John Paul Bevel, Teva Animal Health

Fabrice Bonacci, A. Raymondlife

Robert Byrne, Genzyme

Alberto Carazo, Gadea Biopharma

Salvador Cassany Pou, The Ministry of Health, Social Policy and Equality

Carlos Castro Izaguirre, Bayer HealthCare

David Cate, Genentech

Rupert China, Elekta

Astrid Claus, Ferring Pharmaceuticals

Mario Contorni, Novartis Vaccines and Diagnostics

Misha Cook, Lonza

Dominic DeMuro, Pfizer

Emanuel Dilberto, Campbell University

Matthew Doherty, Lantheus Medical Imaging

Gabriella Dowling, Pfizer

Carol Dugas, EMD Millipore

Ronald Eichenberger, F. Hoffmann – La Roche

Christophe Fagot, Aptar Pharma

Marco Falzolgher, Edmond Pharma

Heidi Faris, Teva Animal Health

Mark Feaster, Novartis

Raul Fernandez, Praxis Pharmaceutical

Clay Flowers, Northern Lipids

Christine Fonger-Rist, Baxter HealthCare

Jens Gemmecker, Optima Group Pharma

Frederic Georges, Sanofi Pasteur

Jean Gildner, National Institutes of Health

Marcelo Godoy-Rigobello, Deutsche Post DHL

Daniel Gold, BioMarin

Hideo Goto, Kitasato Daiichi Sankyo Vaccine

Nicole Green, Central Biomedia

Kyle Green, Allergan

Andreas Hagelin, AstraZeneca

Sarabeth Hahn

Anne Hassler, F. Hoffmann - La Roche

Emilia Hatib, Allergan

Melanie Hempel, CSL Behring

Simon Hendry, ALK-Abello

Inka Henze, Schott

Adam Hirsh

Guido Huelsemann, Bayer HealthCare

Willem Huisman, Intervet International

Pierre Humbert, Sanofi Pasteur

Masaharu Inoue, Asahi Kasei Technosystem

Rebecca James, Abbott Laboratories

Raymond Jansen, Particle Measuring Systems

Sarah Janus, Ben Venue Laboratories

Richard Jarrett, Praxair España

Hania Johnson, DPT Lakewood

Arlee Kachensky, Kachena Pharma Consultants

Hiral Kadakia, Watson Pharmaceuticals

Amanda Keighley, Worcester Polytechnic Institute

Sherry Kim, Abbott Laboratories

Joan Klane, Sirtex Wilmington

Stefan Kunze, F. Hoffmann - La Roche

Maria La

Kristoffer Laursen, Novo Nordisk

Yannic Lepage, GSK Biologicals

Michael Levitt, Quintiles Consulting

Dee Dee Li, Johnson and Johnson

Gerald Llorach, Genentech

Kirsten Luz, Pfizer

Aljosa Maglica, LEK Pharmaceuticals

Jeremy Mainville, Amgen

Sree Rama Murthy Mallipeddi, Exela Pharma Sciences

Massimiliano Malone, TGRX

Damien Manning, Schering Plough

Katherine Mercier, Dendreon

Jeff Meringer, Johnson & Johnson

Sergio Molina, Grifols

Petra Mullerova, Institute for State Control of Veterinary Biologicals and Medicaments

Adolfo Munoz, Dendreon

Takahiro Nagasawa, Kitasato Daiichi Sankyo Vaccine

Kerstin Olevall, Novozymes

Greg Orders, Therapeutic Goods Administration

Manish Parekh, Humanzyme

Joo-sung Park, JW Pharmaceutical

Amy Patterson, Genentech

Douglas Pedersen, ViroPharma

Stephanie Pellet, A. Raymondlife

Matthias Plitzko, Meridion Technologies

Sunil Potdar, SGS

Jurij Pracek, LEK Pharmaceuticals

Georgina Pujals Naranjo, The Ministry of Health, Social Policy and Equality

Fan Qian, Haorui Pharma-Chem

Gayathri Ratnaswamy, Agensys

Michael Rosenblum, Cool Containers

Reza Salehzadeh-Asl, Health Canada

Idamarie Santiago, AstraZeneca

Steve Schultz, Abbott Laboratories

Eleonora Scoseria, Infodynamics

Jose Segui, Grifols

Keqiang Shen, Laureate Biopharmaceutical Services

Michael Sherwin, Shire Pharmaceuticals

Toshiaki Shimizu, Mitsubishi Tanabe Pharma

Ron Shook, Aqua-Chem

Joan Shurtz, Bayer HealthCare

Christopher Skog, Novozymes Biopharma

Bradley Songui, Boehringer Ingelheim

Hanne Sten, Novo Nordisk

Shingo Sugisawa, Kitasato Daiichi Sankyo Vaccine

Jennifer Sullivan

Yoshihisa Takeda, Kitasato Daiichi Sankyo Vaccine

Hwan Tan, ApotheekZorg

Sebastien Trichot, Sanofi Pasteur

Vasia Tsapra, Vianex

Christopher Tyree, Ompi of America

Yushi Uetera, University of Tokyo Hospital

Dieter Unseld, Alstran

Elise Vallet, Sanofi Aventis

Annette van Utteren, Synthon

Marco Vega Lugo, Lilly

Kimberly Wilson-Lamarre, Pfizer

Adam Yacoub, Valsource

The Parenteral Drug Association presents...

2012 PDA Europe Clinical Trial Materials

Innovations and Current Trends

The Conference

Key Notes:

- Current Regulatory Trends
- Clinical Manufacturing of IMPs
- Primary Packaging for Parenterals
- Devices in Clinical Trials
- Usability Studies

7-8 February 2012
Basel | Switzerland

Two Tracks: Biologicals and Small Molecules

- Early Stage Formulations and Supply Strategies
- The API and the Requirements for Formulation Development
- Formulation Challenges and Solutions

Plenary Presentations

Extractable and Leachable Testing for Clinical Trial Materials
New Developments of Excipients: Suppliers Report
QbD, Technical and Business Considerations

- QbD - a Reality Check
- Case Studies

Panel Discussion about Current Trends in Clinical Trial Manufacturing

The Site Visit at Roche

Clinical Trial Manufacturing
Plant B97 in Basel

Scientific Planning Committee

Chair: Hanns-Christian Mahler, *Roche*
Karoline Bechtold-Peters, *Roche*
Gerrit Hauck, *Sanofi*
Hans Lindner, *Bayer Healthcare*
Ingo Presser, *Boehringer Ingelheim*
Siegfried Schmitt, *Parexel*
Ailyn Kandora, *PDA Europe*
Georg Roessling, *PDA Europe*

https://europe.pda.org/ClinicalTrial2012

PDA Tools For Success

Brought to you by the PDA Career Center.
Go to www.pda.org/careers for the latest opportunities.

10 Mistakes Job Seekers Make ... And How to Avoid Them

Ford R. Myers, Career Potential

Many people make significant job search mistakes and never even know about it. These blunders are easy to make, and they can cost you the job offer or lose you thousands of dollars.

Below, I reveal 10 of the biggest mistakes, and explain how to avoid them.

Mistake 1
Relying on Online Job Postings

In general, job postings and "want ads" produce little value. However, it is also a mistake to ignore them altogether. Some of the best chances for jobs from ads are in specialty trade publications and websites of specific industries. I suggest you spend no more than five percent of your valuable time on public job postings.

Mistake 2
Mailing Unsolicited Resumes

Unsolicited resumes are considered garbage, scrap paper and wasted effort. Secretaries kill them, HR managers file them away, and hiring decision-makers pitch them. I advocate abandoning this job search tactic completely.

Mistake 3
Looking Only for Job Openings

Searching only for companies with "openings" is an obsolete job hunting method. The best jobs are rarely listed "vacancies" or "openings." Rather, many good positions are created for the candidate, often at the interview. The key is to shift your focus from "openings" to "opportunities" (which exist nearly everywhere). Remember: every company is hiring all the time, if you have what they need when they need it!

Mistake 4
Ineffective Networking

Networking should be the primary focus of every job search—occupying about 90% of your time. However, I find that most people go about it the wrong way—by talking too much and by asking for jobs. The best networkers are big listeners rather than big talkers. They have a clear agenda and are not shy about asking for feedback and guidance. Remember: networking is more about giving than it is about taking, so always come from an attitude of generosity.

Mistake 5
Leaving Yourself Open to Too Many Kinds of Jobs

Another key to a successful job search is to focus on finding the *right* job—not "just any job." Critical factors to consider include satisfaction, growth potential, location, cultural fit, great co-workers, a pleasing environment and competitive compensation. When the job market is really tough, it's imperative to be more focused than ever.

Mistake 6
Being Unplanned in Your Search

Most people spend more time planning a vacation than planning a job search. I suggest the following tips to conduct a proper job search: a well-thought out methodology, daily solitude and planning, space in the home dedicated to the search, a tracking tool to measure your progress and a system for accountability.

Mistake 7
Doing it Alone

You pay a mechanic to change your oil; an attorney to create an estate plan. Why would you not invest in professional help with your job search? Career Coaches provide objective guidance, help you articulate your value and provide a proven system for job search success. Many offer excellent advice on salary negotiations—often exceeding the job seeker's expectations. If you can't afford a Career Coach, take advantage of low-cost or free support from non-profit groups, universities, municipal programs, and so forth.

Mistake 8
Letting Others Control Your Job Search

I suggest working with a small selec-

tion of professional recruiters—they can serve an important role in your search. But you'll need to maintain control over the whole process. Of course, it is best to conduct your own research and target the right companies yourself. Remember: only you can "sell yourself" effectively and land a job.

Mistake 9
Not Preparing Well Enough for Job Interviews

When you boil it down, all job interviews are comprised of five basic elements: articulating your value, conveying your knowledge of the company, asking intelligent questions, negotiating compensation, and following-through. Each of these items has to be practiced in advance, so you can "ace" the job interview. "Winging it" just won't do! Also, be sure to do extensive research on the company and the interviewer ahead of time.

Mistake 10
Not Knowing Your Market Value

You must research and assess your value in the marketplace, so you'll be able to negotiate effectively. Never disclose your salary requirements—always get the employer to name the salary or range first. The time to talk money is when the employer has made it clear that you are their top candidate, and after they make an offer.

It is very easy for even the savviest of job seekers to make these mistakes. By learning how to navigate these potential pitfalls from the outset, your job search will be more productive and yield more positive results!

Combination Products Specialty Positions Evolving

Pharma/biopharma companies are establishing new positions related to the growing number of combination products on the market and in development. That these positions are being developed is an indication firms believe combination products require a specific focus and expertise.

Some of the new positions created in recent years include: Director, Combination Products Program Manager, Strategic Quality, Combination Products Regulatory Affairs Manager, Drug/Device Combination Products.

Doug Mead, Director, Global RA-CMC Medical Devices and Combination Products, Johnson & Johnson, spoke to the *PDA Letter* about the trend. He said that in the future, it will be more common for people to have specialties inside companies with titles that include: "combination products," "medical devices" or "delivery devices" in their title. Case in point is Principal Technical Manager, Combination Products – Design Assurance, External Quality **Paulo Villanueva,** who told the PDA Letter that he has held his new position for 18 months at Genentech.

While contract manufacturing organizations and device suppliers often provide technical services, it is not sufficient to rely solely upon external organizations when ensuring the quality of the finished products. In the ideal scenario, according to Paulo, drug companies will have a highly knowledgeable team that can partner with CMOs /suppliers to clearly define product requirements and to help drive continuous improvement into the manufacturing processes.

Indeed, Doug said teams are already forming to focus on delivery devices and that is not unusual for some drug companies to have as many as 25 engineers and scientists that look at the selection of devices and the testing that is needed to qualify them.

Currently, Paulo said, employers are seeking candidates with extensive experience in the development and manufacture of combination products or medical devices (particularly drug delivery systems). "Professionals that were responsible for bringing the initial generations of prefilled syringes, pen injectors and auto-injectors to market are in high demand."

Suzanne Kiani of MedImmune might not have the phrase "combination products" in her title, but she is responsible for combination products regulatory filings as the Associate Director, CMC Regulatory Affairs. Suzanne told the *PDA Letter* that combination products are typically very different than other pharmaceutical products, and, as such, having a specific designation in a title helps.

It is important, Paulo said, to have employees with direct experience and a specific focus in this area as it can often be a complex exercise to navigate the combo product regulatory landscape. Suzanne agreed. She advised someone wanting to become a combo products expert to work at a device company and drug company to see how both sides are run from people who make these products as their primary business.

snapshot

Interest Group *Corner*

N.A. and EU Filtration IG Leaders Speak About Upcoming Projects

Russell Madsen and **Michiel Rook**, the leaders of the North American and European branches of the PDA Filtration Interest Group (IG), respectively, answered some questions from the *PDA Letter* about what hot topics the IGs are facing and what projects they are currently working on.

Both groups are only separated by geography, not ideology. Each provide a forum for discussion related to filtration in pharmaceutical and biopharmaceutical applications. This includes the sterilizing filtration of liquids and gases, depth filtration of process streams and process systems, and viral removal and purification.

PDA Letter: What are some of the hot topics the IG is facing?

Madsen: Currently, the most important topic appears to be the European guidance requiring pre-filtration post-sterilization integrity testing of sterilizing filters. The U.S. FDA does not require such testing. From a risk perspective, post-sterilization integrity testing has the potential to compromise the sterility of the processing train (i.e., that section of the filtration system downstream of the sterilizing filter).

Post-sterilization integrity testing has been and will be the topic at Filtration IG meetings. The next meeting will be held in conjunction with the 2012 PDA Annual Meeting in Phoenix, Ariz.

Rook: We see the same hot topics in paragraph 113 from Annex 1 of the EU GMP directive. It focuses on integrity testing of a sterilized grade filter post-sterilization and pre-use. Many competent authorities in Europe require this test to be performed, although the risk of breaching sterility, hence having a nonsterile product, is relatively big. The scientific need for this test is questionable, and the impact of implementing this testing procedure in an existing process is significant. Whether you produce aseptically manufactured product in Europe or for the European market, the requirement remains the same. This is a hot topic for U.S. producers as well.

PDA Letter: How is your IG addressing post-sterilization integrity testing?

Madsen: Post-sterilization integrity testing has been and will be a topic at Filtration IG meetings. The next meeting will be held in conjunction with the *2012 PDA Annual Meeting* in Phoenix, Ariz.

Rook: At our IG meeting, we were able to discuss this matter with filter users and filter manufacturers present. Two industry case studies were discussed, and the group concluded that point 113 should be looked at on a case-by-case basis. It also was decided that proper risk assessment should be applied, and inspectors should evaluate the risk assessment to agree or not to implement point 113. Today, industry is faced with some inspectors who require the implementation "because it is written" in Annex 1.

As an outcome of the IG meeting, PDA was able to organize a separate meeting during the PDA/EMA Joint Conference last May with the inspectors from the following agencies:

- EMA
- MHRA
- AGES PharmMed
- Finnish Medicines Agency

In this meeting, there was a suggestion that a PDA draft Q&A on the topic could be considered for publication on EMA's website. PDA is in the process of coordinating this opportunity.

PDA Letter: What are some upcoming major projects that your IG is working on right now?

Madsen: There are preliminary plans to develop a white paper on the advantages and disadvantages of post-sterilization integrity testing. The issue will be elucidated in the paper via a formal risk analysis. Advisability and timing for the paper will be discussed at the IG meeting in Phoenix. Once completed, it is likely that the paper will be submitted to the *PDA Journal* for publication.

continued at bottom of page 22

Task Force *Corner*

Cleaning/Disinfection Task Force Completing Tech Report

Emily Hough, PDA

The Fundamentals of Cleaning and Disinfection Programs Task Force (TF) is in the process of conducting final editing for the technical report on control contamination, cleaning and disinfecting of controlled GMP environments.

The technical report will include a "how to" discussion on controlling contamination, cleaning and disinfecting GMP areas. This subject, according to TF Chair **Art Vellutato**, CEO, Veltek Associates, has not been extensively covered in worldwide industry guidelines, leaving industry professionals without specific instruction on how to accomplish such tasks effectively. The international regulatory focus is primarily on bioburden reduction, Vellutato said. He noted that those who manage cleanrooms have specific concerns for remaining residuals from a disinfecting agent that might go into a drug agent, corrosion of surfaces and potentially harmful vapors, to name a few. "We have concerns that nobody else has."

There is also no accord among regulatory bodies on what should or should not be done. Vellutato explained: "I don't think most GMP operations understand what is expected, as comments from regulatory agencies vary and contradict each other. All understand that you have to disinfect something in some manner, but they don't understand that you must also control contamination from entering the controlled environments and also routinely clean surfaces in addition to disinfection. Further disharmony exists with what are appropriate validation requirements. The lack of specific guidance leaves many firms consistently questioning their systems or in jeopardy to and agencies unknown expectations. "

According to Vellutato, except for USP <1072> "Disinfectants and Antiseptics", no other documents have been published on controlling contaminants and cleaning and disinfecting the GMP cleanroom. Unfortunately, the USP Chapter has generated more questions than answers.

The Fundamentals of Cleaning and Disinfection Programs Task Force is striving to author a reference document for the people working in cleanrooms and standardizing approaches to inspections of disinfection in GMP areas for regulators. The group referenced two popular PDA TRI courses—Aseptic Training and Contamination Control—to help shape this guidance.

Vellutato says that the strongest part of the document is its step-by-step discussion of how to develop a system in one's operation. Readers will be able to implement the system section by section and, in the end, find themselves with a compliant system that should meet all regulatory requirements.

Currently, the task force is completing the final draft.

Members of the TF

Arthur Vellutato, Jr., Veltek Associates (Chair)

Michael B. Dolan, Merck and Company

Barbara M. Andon, Merck and Company

Roger E. Deschenes, Amgen

Steve Trombetta, Novartis Vaccines and Diagnostics

Barry A. Friedman, PhD, Consultant

Pamela D. Deschenes, Veltek Associates

Brent Watkins, Veltek Associates

Carol Molinaro, Sanofi Pasteur

Jayne Dovin, Sanofi Pasteur

James N. Polarine, Jr., Steris Corporation

Mike Sarlis, Steris Corporation

Michael A. Szymanski, GlaxoSmithKline Biologicals

Cindy Adams, Northampton Community College

Alison Livsey, Contec

Peter Koger, Veltek Associates

Jill K. Giulianelli, Baxter Healthcare Corporation

Dona Reber, Pfizer

About the Expert

Art Vellutato, Jr., President and CEO, Veltek Associates, is a frequent industry speaker with over 50 industry publications and is one of the leading consultants in the pharmaceutical and biotechnology industry specializing in contamination control, cleaning, disinfection, gowning and environmental monitoring. He is also the President and Senior Consultant of Aseptic Processing, Inc., the consulting division of Veltek Associates, Inc. He lends over 26 years of valuable experience that include his tenure as the Director of Quality Assurance at VAI for nine years, the Director of Manufacturing for six years.

Interest Group Corner continued from page 20

Rook: Apart from putting Q&A's on EMA's website regarding point 113, it is likely that our IG will be discussing the production of water for injection using filtration techniques such as reverse osmosis. In the United States, this technique has been applied for many years, yet it has never been allowed in Europe. This year, some interesting discussions have started within the European inspection groups on this subject. We will follow them closely and report to the interest group members.

About the Experts

Russell Madsen, President, The Williamsburg Group, is involved in pharmaceutical consulting in the areas of CGMP compliance and auditing, quality systems, design review, aseptic processing and sterilization technology, sterile filtration, due diligence evaluation, process validation, regulatory liaison and general technical services. He currently is the Vice-Chairman of ASTM E55.03 General Pharmaceutical Standards; serves as a member of the USP Microbiology Expert Committee; is the Chairman of the USP Visual Inspection of Parenterals Expert Panel; is a member of the Editorial Advisory Board for *Pharmaceutical Technology*'s Editorial Advisory Board; and is a member of PDA's SAB.

Michiel Rook, owner and principal consultant, Global ConSeptS–Consultancy, is a competent bio-pharmaceutical consultant and an independent expert in aseptic filtration. His company specializes in the qualification of parenteral manufacturing processes and the initiation of Quality by Design projects. Michiel has over 20 years of experience with FDA and European regulated processes in the bio-pharmaceutical industry.

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The Importance of Neutralizing Disinfectants

Eric Petat, ACM Pharma Laboratory

How do you choose disinfectants?

Such a decision is truly critical within pharmaceutical cleanrooms as these disinfectants play an integral role in the maintenance of adequate aseptic conditions. But, how often is the question of neutralization of such disinfectants asked? Maybe not enough.

An environmental monitoring (EM) program is central in the pharmaceutical industry to guarantee the state of control of the manufacturing area. For that reason, an appropriate monitoring solution must rapidly detect changes or deviations from established alert/action limits that can compromise a facility's environment. The trend analysis highly depends on the performances of culture media used during sampling. This includes, of course, growth promotion but also neutralization of disinfectant residues. Pharmacopoeias provide some hints about what kind of neutralizers are suitable to properly counteract chemicals used in sanitizers. Usually culture media solutions available on the market propose these neutralizers in their formulation. But are they really efficient on all disinfectants? Is this efficacy universal?

The validation of disinfectants is a daunting task as is the validation of culture media dedicated to recover stressed microorganisms in cleanrooms. As a consequence, the disinfectant neutralization must not be forgotten during validation of both products. Using EM culture media with insufficient disinfectant neutralization validation carries a significant risk as microflora present in the clean environments may not be clearly observed.

My study investigated antimicrobial properties of some commonly used biocides**.** To determine the toxicity in an agar culture medium, the recovery rates of identical inocula of pharmaceutical wild isolates in the presence, or absence, of a pure and 1:10 dilution of the biocide were compared. A correlation between the concentration of residues on surfaces and the efficacy of the disinfectant was also demonstrated. Disinfectants that left a high concentration of very toxic residues were the most difficult to neutralize.

Following these results, three culture media with neutralizers were challenged with a disinfectant found to be really stringent during the previous analysis. The formulation of these culture media included various neutralizers such as:

- The four main neutralizers: lecithin, polysorbate 80, L-histidine and thiosulfate (Medium B)
- The Dey and Engley neutralizing formulation (Medium C)
- A medium with enhanced neutralizers dedicated to the neutralization of stringent disinfectants (Medium A)

Both culture media A and B showed excellent growth performance and 100% of the test microorganisms had a recovery rate higher than 50%. But, Medium C with D/E neutralizing formulation showed a poor growth performance. More than 58% of tested microorganisms did not reach the threshold of 50% recovery rate. Two microorganisms did not grow at all! A likely explanation is the toxicity of the neutralizers in the agar. That is not acceptable for a culture medium dedicated to EM where sensitivity to detect and enumerate stressed strains is critical. Despite the poor growth promotion performance of the D/E neutralizing agar, this media demonstrated good neutralization properties.

This was not the case for Medium B with pharmacopoeia neutralizers. These neutralizers were not able to reduce the toxicity of disinfectant residues. Only Medium A with enhanced neutralizers showed both excellent growth promotion and neutralization performance. One hundred percent of test strains had a recovery rate greater than 50% in the presence of the stringent disinfectant.

These results highlight the real difficulty to find the perfect culture media solution to guarantee the reliability of environmental monitoring because a complete neutralization is important for the accuracy of a trend analysis. cGMP processes advise sterile drug manufacturers to pay close attention to the quality of their manufacturing environment as this has strong public health implications. Growth performance of EM culture media as well as sufficient validation of disinfectant neutralization is integral to this requirement.

[Editor's Note: This article alludes to a study that has been submitted to the *PDA Journal of Pharmaceutical Science and Technology* for consideration.**]**

About the Author

Eric Petat is the CEO and scientific director of both entities ACM and ACM Pharma. In 1990, he founded ACM, a consulting company that provides advice and lab services for the food industry. In 1998, a new division was created: ACM Pharma, which was fully dedicated to pharmaceuticals and cosmetic microbiology. He has had more than 30 years of experience in the fields of immunology and microbiology and has previously worked for several French health authorities in Burundi as well as the Federal Islamic Republic of Comoros on Salmonella and Shigella infections.

To contact Eric about this article, email him at acm.epmf@wanadoo.fr.

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STUDENT CALL FOR POSTERS

The 2012 PDA Annual Meeting Program Planning Committee encourages students to submit an abstract for poster presentation at the *2012 PDA Annual Meeting*, which will be held on April 16-18, 2012 in Phoenix. Abstracts must be noncommercial, describe developments, strategies or work and significantly contribute to the body of knowledge relating to pharmaceutical manufacturing, process knowledge, quality management and technology. Abstracts related to sterile product manufacture, cellular and gene therapy, or production of biopharmaceuticals are preferred, but those addressing other technologies are welcome. All abstracts will be reviewed by the Program Planning Committee for consideration.

ABSTRACTS MUST BE RECEIVED BY FEBRUARY 6, 2012 FOR CONSIDERATION

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Suggested topics include, but are not limited to:

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PERSONALIZED MEDICINE/CELLULAR THERAPEUTICS

- Diagnostics
- Challenges in Quality for ACIs
- Challenges in Manufacturing
- Expiration of Products, Logistics and Shipping
- Stem Cells

CONTROL STRATEGIES FOR BIOPHARMACEUTICALS

- Testing Characterization, Stability
- Room Decontamination and H_2O_2
- Upstream/Downstream: Chromatography
- Cold Chain
- Sterilization
- Bioburden/Biofilm
- Mycoplasma/Virus
- Process Validation
- Cleaning Methods and Validation

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Please visit www.pdaannualmeeting.org to submit your abstract.

Please include the following information with your abstracts:

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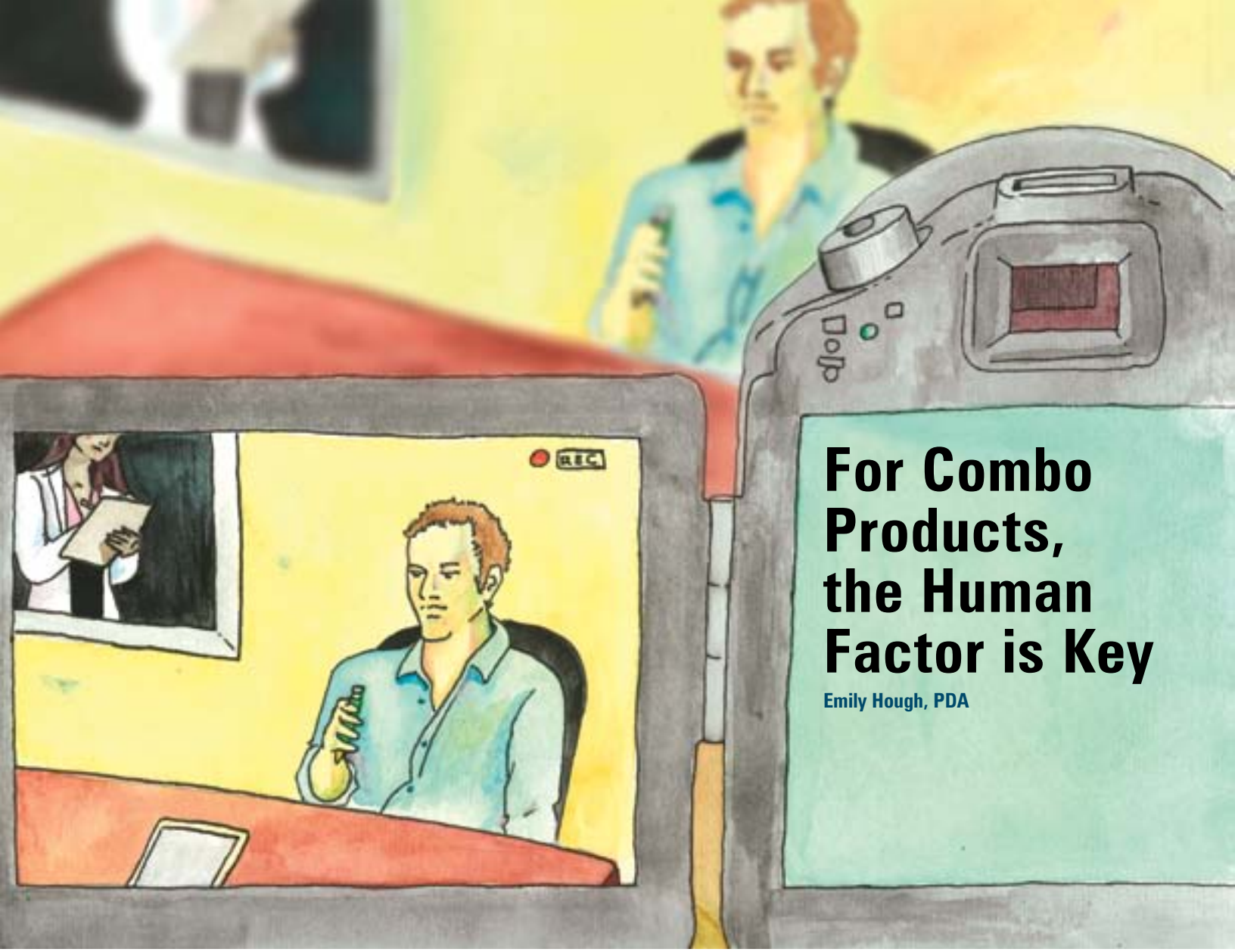
- Phone number
- 2-3 paragraph abstract, summarizing your topic and the appropriate forum (case study, discussion, traditional, panel, etc.)
- Take-home benefits
- Presentation objectives

For more information, please contact Jason Brown, Senior Programs Manager at brown@pda.org or 301-656-5900 ext. 131.



For Combo Products, the Human Factor is Key

Emily Hough, PDA

Human factors engineering has become an integral component of product development for medical devices, and consequently, combination products. By executing user tests in simulated environments, manufacturers try to determine how consumers will use and interact with the product. If problems arise during testing and manufacturers determine the problems represent moderate to high risk of error, mitigation strategies might be necessary.

Human factors/usability engineering is a component of product design validation with which not all traditional drug and biologics companies now entering the combination products world are familiar.

PDA's *2011 Combination Products Workshop* including a session on this emerging topic; presentations provided an overview of human factors/usability engineering and a case study on including usability testing data in post-approval submissions.

Michael Wiklund, Founder, Wiklund Research & Design, spoke from the perspective of a human factors analyst. He asserted that low-grade panic has inundated the medical device industry as FDA has begun citing firms for faulty or subpar human factor testing. He assured the audience that there is no need for panic and noted that FDA has provided direction for the industry in the form of a draft guidance. The document, in his judgment, was inspired both by the Agency receiving many IDE, 510(k) and PMA applications that did not adequately address human factors and by manufacturers expressing their interest for more detailed guidance on the subject.

The June 2011 draft guidance, titled *Applying Human Factors and Usability Engineering to Optimize Medical Device Design*, summarizes the Agency's expectations for human factors studies, or as known more commonly on the drug side, usability testing (see related article, page 34). FDA states clearly in the guidance that the human factor must be considered in making the final decision as to a product's safety and effectiveness: *For the device to be considered to be optimized with respect to safety and effectiveness of use, validation testing should be designed such that it is sufficiently sensitive to capture use-related problems that exist whether the users are aware of use er-*

rors or not. Further, the test results should show no patterns of use failure or difficulties that could be eliminated or reduced through further modification of the design of the user interface.

Picking Which Tasks to Perform

Wiklund noted that it is important to understand that that use errors commonly occur, but solutions are not always easy. "It may be a function of the participant failing to do something in some way, something you think they ought to do properly. But, more often, it is the device that has a flaw of some sort that induced the problem." Once an error has been captured, it is essential to avoid blaming the participant, but rather look at what led to the error; look at the product's design, tactile qualities and user interface that led to the use error.

Human factors testing should challenge the product's design. To do this, test subjects should be instructed to use the product in a controlled environment and observed to see what errors are made—if any. For example, companies of pen injectors must determine if users will prime the injectors for use. According to Wiklund, this is often overlooked or forgotten by users. User testing for this element involves asking participants to use a pen injector and watch what they do. If they forget to prime the device, it is necessary to figure out why this occurred and to come up with a solution. A potential resolution would be to reconstruct the device into one that does not need to be primed.

Prefilled syringes are a popular drug-device combination product

In any case, a cost analysis benefit needs to be performed after testing as part of post-testing analysis to determine ultimately if the construction of the device will cause unsafe or ineffective medical treatment.

Formative and Summative Testing

Use errors, within human factors testing, are typically captured during the formative usability testing. This test identifies an evolving device's interactive strengths and weaknesses with eight to twelve participants. With this test, users perform more hands-on tasks that are important to the usability of the product, and, when it is appropriate, test administrator assistance can be given with the tasks. As the tasks are completed, the human factors professional will have a discussion with the user about what they liked or didn't about the product. The human factors professional will also identify safety issues but also problems that can make the device difficult to use.

FDA recommends that the validation process and the results of the human factors tests are included in a premarket approval application

The summative usability test involves more people and determines if a finished device is vulnerable to potentially harmful use errors. If any assistance is given, the summative usability test automatically is considered a failure.

It is crucial that the formative test is performed first, and then the summative usability test. Wiklund told the audience, "We have never conducted a summative usability test as the first test and had the product continue on to be approved. If you go into summative usability testing without doing any formative usability testing, you will not pass."

According to FDA, human use testing might be necessary during clinical trials, depending on the nature of the device. FDA recommends that the validation process and the results of the human factors tests are included in a premarket approval application. The report should provide information pertaining to device use safety and should highlight the major human factors considerations, issues, resolutions, and conclusions.

This information is needed for changes to existing combo product as well. Even a "small" change is subject to scrutiny.

Talk to FDA

Steve Johnson, Principal Consultant, Global Regulatory Affairs, CMC, Eli Lilly, told audience members that it is prudent to submit human factors protocols to the FDA for review prior to execution for all products. "This review may take time, but it may save time to approval," he said. **[Editor's Note:** Related article for discussion of the growing role of combination products specialists in the pharmaceutical industry, page 19.**]**

Johnson presented a case in which Lilly experienced some minor difficulty clearing a post-marketing change with FDA because of human factors issues. In 2010, Johnson's firm modified its HumaPen® Luxura HD™ product, a reusable 30-dose insulin pen injector. The firm was altering the 30-dose device-drug combo to allow for a minimum dose of 0.5 unit (see Figure 1 on page 30). After updating its user manual instructions and submitting additional data to support the dose accuracy to the

Article at a Glance

- FDA has provided direction for the industry in the form of a draft guidance
- Human factors testing should be done in a simulated user environment and challenge the product's design
- Human factors testing is required regardless of the size of the change that is made to the product

Slide 8 from Steve Johnson's slide deck

FDA Follow up Questions

1. Regarding your response to deficiency 1b, you provided narrative discussion to address the request for use-related risk analysis. However, risk analysis documentation is necessary to complete our review. Please ensure that your use-related risk analysis is presented in a tabular format that includes specific use-related hazards associated with the modification (the minimum dosage that the pen can deliver), and mitigation strategies that you may have taken to reduce the risk associated with the device. In this analysis, please demonstrate that any potential new use-related risks associated with this modification have been addressed and they do not in turn affect the overall device's risk profile.

2. Regarding your response to deficiency 1c, you stated that the 2006 Design Validation study included fifty-one in-person interviews conducted among a total of 40 participants including children with diabetes and adults who inject insulin in four US cities. The results of this study demonstrated that ninety percent were able to use the pen successfully without referring to the user manual. However, for the modification proposed in the current submission, it is not clear how you have evaluated user performance focusing on the modified aspects of use, and determined that the modification have acceptable user performance, and does not create no new use-related problems. Please also clarify how you have determined that a new human factors validation is not necessary. Alternatively, please provide results of a validation study that is based on user performance focused on the use scenarios intended to be changed by your device modification. The study should be designed so that user/device interaction and possible use-errors are subject to capture by performance measures and include subjective assessment by users (typically not rating scales) regarding the specific aspects of use under consideration.

FDA, the firm thought it could move on to its next project.

After it had received the post-approval supplement from Lilly, however, FDA wanted some additional information to ensure that all anticipated risks of user error had been addressed adequately. Specifically, the Agency wanted to know about the:

- Intended user population, use environment, user interface, and anticipated user interaction with the proposed device
- Use-related risks in the context of overall risk management of the device and mitigation strategies to reduce the risk associated with the device
- Human factor/usability testing and results for the device

In response, Lilly first tried to clarify with FDA that the supplement was for an existing approved product, not a new device, and reiterated that the only change to the product was the addition of the 0.5 unit minimum dose. Then, the firm discussed its risk management plan, its failure mode and effects analysis (FMEA) program and its global device safety surveillance data. It also provided information from the original pen injector's design validation study confirming patients could successfully perform tasks expected with the device.

In response to the latter, FDA came back with more specific inquiries. For example, it asked the firm to demonstrate potential new use-related risks associated with the modification, as well as the results of a validation study focusing on changes in user performance based on the modification of the device.

Johnson said that Lilly had not considered the new 0.5 unit mark to be a modification to the user interface, so only the functional elements of the device had been evaluated. "We thought the user interface was the same. You pick up the pen, you turn the dial to your selected dose and then you inject the dose. We didn't see any change."

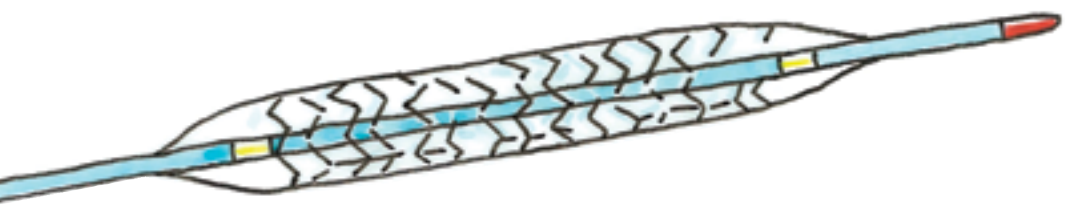
Johnson said that at this point, "we were getting a little bit more concerned about the direction of the questions, and we were beginning to wonder if we had the data to satisfy FDA's needs. Clearly our validation studies did not meet the current expectations of a new human factors study."

Next, Johnson said, Lilly turned to its marketing application to examine the original human factors/usability engineering studies completed as part of the design validation. That data showed that test subjects were evaluated in their ability to successfully select half-unit doses, like 2.5 and 11.5 unit doses. Lilly sent this information to FDA. Satisfied, FDA approved the supplement.

Johnson explained that the hang-up over the change could be distilled down to a few key points that the firm has learned from with future submissions:

- The FDA reviewer was looking for an iterative design approach that included design modifications based on learning from Human Factors studies.
- The reviewer was concerned that the user interface had changed and there was the potential for new/different user errors *even though the changes to the pen were minimal.* **[Editor's Note:** italics added for emphasis**]**
- Greater discussion of risk, risk analysis and risk mitigation is expected with the submission. Information from Human Factors studies, Application FMEAs and other information (Assurance Case Reports) should be used to show all appropriate risks are adequately addressed.

In conclusion, Johnson said: "It is clear that there are greater expectations for human factors information. In this case we were able to use existing data because the change was very minimal and the previous user studies addressed the potential changes in the user interface



Drug coated stents are another common drug-device combination product

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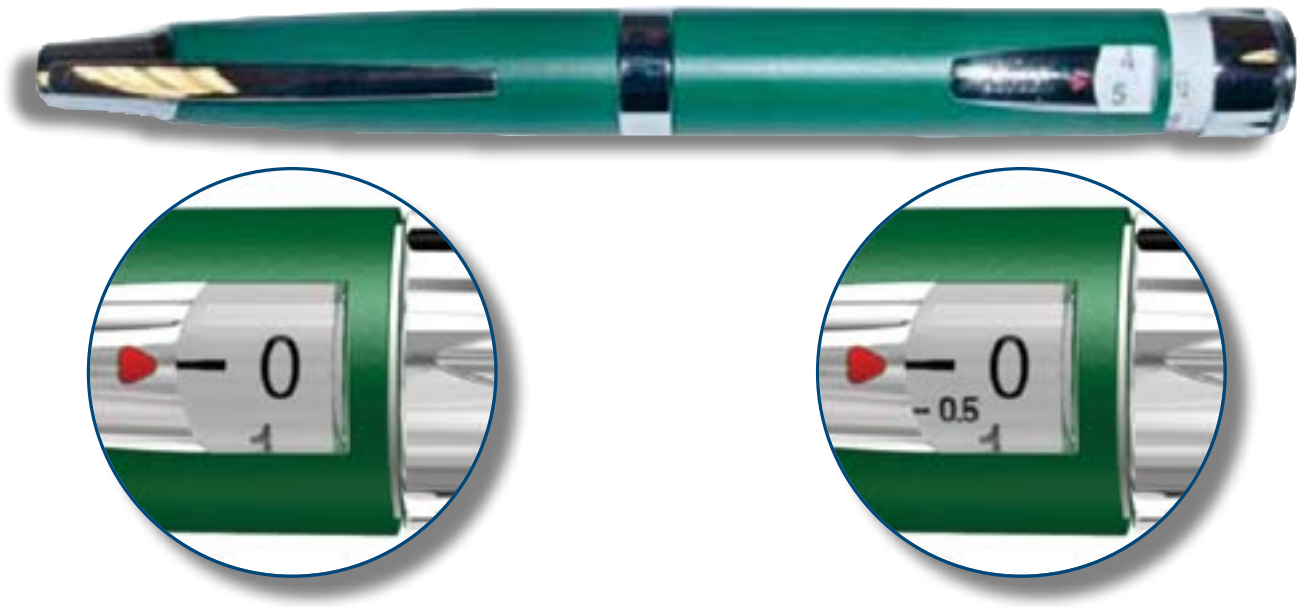
Figure 1



Original Design **Revised Design**

Steven Johnson displayed this image during his talk to illustrate the change Lilly made to its HumaPen ® Luxura HD™

continued at top of page 32

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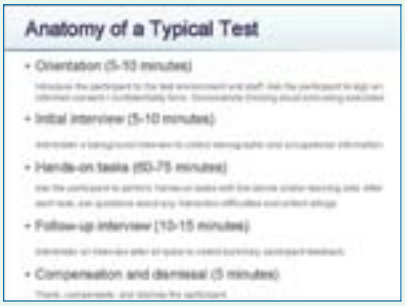
Human Factor Professionals and Participants

The job of the human factor professional is to present many different scenarios to users and document what happens to ensure that when the product hits the marketplace it is as safe and efficacious as it can be. The test administrator sits with a test participant in a controlled setting where the environment can be adjusted as needed to mimic real life situations and places. The testing ensures that the product is reasonably safe for release, at least from a user interaction standpoint.



Each test includes participants from representative user groups. According to **Michael Wiklund,** Founder, Wiklund Research & Design, the rule of thumb that is typical with combination products is to have five distinct user groups. The characteristics of these groups may vary by factors such as background knowledge and skills, and anticipated device interactions. Participants will also be sought out within a specific user group who vary according to secondary characteristics such as age, gender, and years of relevant experience with the product. Wiklund said that it was important to include participants who reflect a cross-section of the patient population in each group.

According to Wiklund, in test cases with multiple user groups, the FDA wants at least 15 representatives of each distinct user group. If the product will be used by a single homogeneous group, i.e., critical care nurses who all have advanced life saving training, you are better off including at least 25 representatives of that group in a test aimed at validating the device's user interface.

Wiklund said, "Human factor testing is not a threat. It is an opportunity. Usability testing is one of the most important things that we can do to make sure that your products perform well."

and the potential failure modes were reduced by the change."

More Attention on the Human Factor

As more drug and biopharmaceutical companies enter the combination products arena, they will have to become more aware of the human factor. Just as product design validation is a large aspect of medical device development, it will be for the ever-expanding array of drug-device combination products.

Human factors/usability engineering and testing gives all parties--manufacturers, regulators, and most importantly, patients confidence that new drug-device combos can be used safely.

Definitions

Combination Product— According to the *Current Good Manufacturing Practice for Combination Products* guidance, a combination product is a product composed of any combination of a drug and a device; a biological product and a device; a drug and a biological product; or a drug, device, and a biological product.

Human Factors/Usability Engineering— According to the U.S. FDA, human factors/usability engineering focuses on the interactions between people and devices. Human factors/usability engineering is used to design the machine-human (device-user) interface. The user interface includes all components with which users interact while preparing the device for use (e.g., unpacking, set up, calibration), using the device, or performing maintenance (e.g., cleaning, replacing a battery, making repairs). For medical devices, the most important goal of the human factors/usability engineering process is to minimize use-related hazards and risks and then confirm that these efforts were successful and users can use the device safely and effectively.

About the Experts

Michael Wiklund is the president of Wiklund Research & Design, a human factors consulting firm that specializes in making medical devices safe, effective, usable and appealing. He received his M.S. Degree in Engineering Design (Human Factors) from Tufts University, where he annually teaches a graduate course on applied user interface design. He has written many books on human factors, including, Usability *Testing of Medical Devices; Handbook on Human Factors in Medical Devices; Usability in Practice; and Designing Usability into Medical Products.* Funded by the U.S. FDA, he developed the original text for AAMI HE74:2001, *Human Factors Process for Medical Device Design.* He was also a lead author of several sections of AAMI HE75:2009, *Human Factors Engineering – Design of Medical Devices.*

Steven T. Johnson is a Principal Consultant in Global Regulatory Affairs at Eli Lilly. He joined Lilly in 1988. He has held a variety of positions in API manufacturing operations, process engineering, construction design and management, environmental quality, quality assurance, global auditing and regulatory management at Lilly. In his current position in regulatory affairs, he supports worldwide registration of drug/device and biologic/device combination products as well as medical devices. Steve is active in industry groups including PDA's Combination Products Task force and Regulations Subcommittee.

The pen injector is another type of drug-device combo product on the market

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FDA's Devices Center Preparing Human Factors Guidance

Bio/Pharma companies seek clarity on applicability to combo products

Walter Morris, PDA

The U.S. FDA Center for Devices and Radiological Health (CDRH) is currently taking steps to finalize a draft guidance on human factors testing, issued in on June 22, 2011.

The draft, titled *Draft Guidance for Industry and Food and Drug Administration Staff: Applying Human Factors and Usability Engineering to Optimize Medical Device Design,* is the second guidance issued by the devices center on this topic. In June 2000, CDRH published *Guidance for Industry and FDA Premarket and Design Control Reviewers: Medical Devices Use-Safety: Incorporating Human Factors Engineering into Risk Management.*

Whereas the latter document focused primarily on linking human factors into risk management programs, the new draft guidance explores various aspects of human factors testing and usability engineering. FDA deems the document timely as it views use errors as a significant problem for medical devices. Patients and other device users (practitioners, etc.) are either misunderstanding or misinterpreting how to use certain devices, so the guidance is written to help firms focus on the human factors/usability engineering to better mitigate these problems.

For example, the draft document includes a chapter called "Device Users, User Environments and User Interfaces." FDA explains: *When users interact with a device, they perceive any information provided by the device, then interpret and process the information to make decisions. After that, the user may interact with the device to change some aspect of it.* The device, in turn, processes the user input and produces feedback or an output to the user. The user interface is where the transaction between the user and the device occurs (think your keyboard, mouse and monitor for you computer—the user interface).

FDA advises firms establishing human factors/usability engineering analyses to consider the following factors for each component of the transaction:

A few pharmaceutical companies involved with drug-device combination products requested that FDA clearly state the guidance's applicability to such products

Device users:

- Identification of the end-users of the device (e.g., patient, family member, physician, nurse, professional caregiver)
- The level of training users will have and/or receive
- User characteristics (e.g., functional capabilities, attitudes and behaviors) that could impact the safe and effective use of the device
- Ways in which users might use the device that could cause harm

Device use environment:

- Hospital, surgical suite, home, emergency use, public use, etc.
- Special environments (e.g., emergency transport, mass casualty event, sterile isolation, hospital intensive care unit)
- Interoperability with other devices

Device user interface:

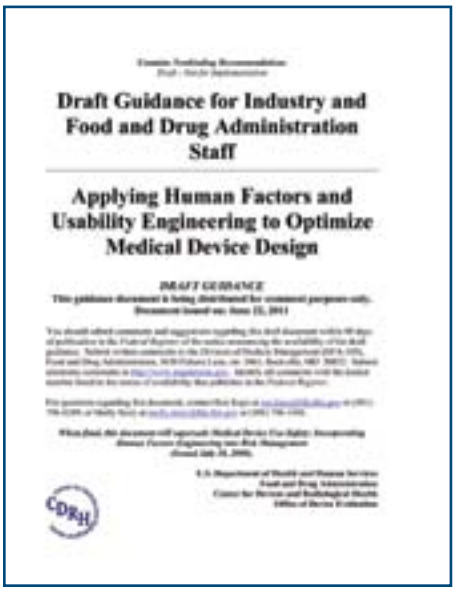
- E.g., functions, capabilities, features, maintenance requirements
- Indicated uses

The chapter goes on to discuss in detail these components. The draft guidance also addresses: identification of known problems; formative evaluations; mitigation and control of use-related hazards; design verification testing; human factors validation testing; clinical validation testing; and documentation. In three appendices, FDA gives an example of a human factors/usability engineering report; elaborates on choosing sample sizes for human factors validation testing; and provides references.

Industry comment on the 2011 draft was generally very favorable, but a few pharmaceutical companies involved with drug-device combination products requested that FDA clearly state the guidance's applicability to such products.

For example, AstraZeneca stated in its comments submitted Sept. 12, 2011 that the guidance "should clearly" state whether it applies or not to combination products that include medical devices as constituent components. Furthermore, FDA should *provide recommendations on how the human factors/usability engineering of the medical device constituent should be evaluated, i.e., independently or in consideration to the overall combination product, and indicate which analytical methods and evaluations are most relevant or not applicable in these cases, if any.* Merk KGaA affiliate EMD Serono stated similar comments on Sept. 19. It said that the scope of the draft *does not reference combination products.* The firm believes that it is reasonable to expect firms to interpret the guidance to apply to all devices, including those used as components in a combo product, but advised that *greater clarity is needed to avoid possible confusion.*

GlaxoSmithKline echoed these sentiments, but also expressed concern about how this document would be applied inside FDA for combo products. GSK wrote: *it would be helpful if the guidance acknowledged and outlined inter-center coordination.*



Draft Guidance for Industry and Food and Drug Administration Staff

Applying Human Factors and Usability Engineering to Optimize Medical Device Design

DRAFT GUIDANCE

A PDF of the draft guidance can be found at tinyurl.com/62ktkms

IPAC-RS—an industry group that represents primarily drug/biologics manufacturers of inhalation products—also highlighted the need for clarity with respect to combo products.

While Genentech did not suggest that there would be confusion as to the applicability of the guidance to combo products as it is currently written, the firm instead stated in its comments that: *Overall, this is a very comprehensive guidance document. However it is missing additional consideration or unique considerations that should be made when developing a combination product.*

It is clear from the overall response from medical device firms and associations that represent them (e.g., AdvaMed and AAMI) that this guidance is a welcomed and deemed helpful.

RMM Sessions Catch Blogger's Attention

Michael J. Miller, PhD, Microbiology Consultants, LLC

Long-time PDA volunteer Michael Miller maintains a blog for the firm's website: ***rapidmicromethods.com****. Miller routinely blogs about various topics of interest from the RMM community. This year, he covered five sessions from the* PDA 6th Annual Pharmaceutical Microbiology Conference*, and has graciously allowed us to share some of his posts in the* PDA Letter. *Go to his website to read his other blog posts from the meeting.*

Dr. Fung Discusses a 30 Year Review of Rapid Methods in the Food Industry

The opening keynote address was being presented by a world-renowned microbiologist and subject matter expert in rapid methods for the food industry, **Daniel Y.C. Fung,** PhD. Fung is an industry professor of Food and Science at Kansas State University. His presentation focused on "Global Developments of Rapid Methods and Automation in Microbiology: A Thirty Year Review and Predictions into the Future."

Rapid methods and automation in microbiology is a dynamic area of technological advancement sustaining a stream of emerging technologies. Rapid microbial methods continue to offer unique opportunities for improving product quality assurance and economy of quality control and manufacturing operations. Almost ten years ago, improvements in microbial isolation, rapid detection, characterization, and enumeration lead to his prediction "…companies that aren't converting to rapid methods won't be in business in 10 years…."

Fung reviewed the use of rapid methods within the food and medical sectors since the 1960's. Methods have included modifications of traditional, growth-based procedures using conventional medium, including a double tube agar method Fung developed himself. In this procedure C. perfringens were able to be viewed within a few hours. And over the years, more automated systems were being introduced. For example, impedance microbiology procedures have been around for more than 30 years, as well as methods for the detection of ATP.

Immunological dip-sticks then came on the market, which provided results on the presence of food-borne pathogens in as early as 10 minutes. Today, we can utilize a wide variety of molecular and nucleic amplification systems, including automated, real-time PCR, as well as novel biosensors, microarrays and nanosensors.

Within the food processing sector, it was projected that more than 740 million micro tests were performed in 2008 by more than 40,000 food processing plants, and it is estimated that the worldwide market for micro testing is more than $2 billion. And the market for food microbiology testing continues to grow, year over year. For example, the rate of growth of micro testing from 2008 to 2010 was more than 6%. But Fung also stated that the use of rapid methods can also provide considerable cost savings, depending on the method being utilized.

The take home message from Fung's keynote is that the number of microbiology assays associated with the monitoring of food will continue to increase, especially in light of recent contamination events, and that rapid technologies will play a very important role in protecting the world's food supplies.

When asked what the pharmaceutical industry can learn from the food industry (in terms of the adoption of rapid methods), Fung stated that the expectations for microbiological safety is much higher in the pharmaceutical industry than in the food industry, and that we can benefit greatly from the implementation of rapid methods. Interestingly, the food industry looks up to the pharma industry for guidance on excellence in microbiology testing. Their perception is that we pharma microbiologists strive for perfection, and that we are always looking at ways to implement new technologies. Unfortunately (from my point of view), our industry has been extremely slow to adopt rapid methods for a number of reasons, and that the food industry is actually well ahead of where we are today.

Rapid Methods Session 1 at the PDA Global Microbiology Conference

This was the first of two rapid method sessions at the PDA Micro Conference. The first speaker was **Michele J. Storrs-Mabilat**, PhD, Global Scientific Partnerships Manager, Industrial Microbiology Division, bioMerieux. She presented information on a novel rapid and automated prototype system for the microbiological monitoring of sterile pharmaceutical environments. The Midass system was introduced, and Midass is an acronym for microbial detection in air system for space. This technology was originally developed for use by astronauts on route to and from Mars, where the air in the space capsule will recirculate for a period of up to three years, and there will be a need to assess the microbiological state of the capsule environment during the journey.

For the pharma industry, the Midass system is a complete system for monitoring surfaces, personnel and air. The system utilizes a peppermill-type collection device for air sampling, cellular lysis and nucleic acid purification. A separate NASBA card, which contains primers and probes/beacons, is used to amplify the purified rRNA targets. NASBA is used instead of conventional DNA/PCR amplification because RNA is a better predictor of cellular viability, is not susceptible to contamination by extraneous DNA, and the amplification reaction is carried out at a single temperature instead of multiple temperatures as is required by PCR. Amplification takes

place in 60-90 minutes, and the system will detect both bacteria and fungi. The time to result is three hours, but there is an opportunity to reduce this time in the future. A table-top instrument is used to process the peppermill and the amplification card.

Total viable counts are obtained not in the form of colony forming units (cfu), but in gene copies or genomic equivalents (Geqs). Sensitivity is estimated at 1 cfu (or 1 Geq) per cubic meter of air or per 25 cm^2 for fungi, and 20 cfu (20 Geqs) per 25 cm^2 for bacteria (work is still underway to determine the sensitivity for bacteria in air). Initial testing shows encouraging equivalence between a cfu and a Geq. Finally, the system is considered to be non-destructive, where the purified nucleic acid material may be stored for further analysis, such as microbial identification.

The second speaker was **Gene Zhang**, PhD, Principal Scientist, Bayer Healthcare Pharmaceutical, who presented a case study on validating a microbial ID system to meet the new regulatory requirements for Part 11.

There are a number of microbial identification rapid methods systems available and many are operating via computerized systems. The pharma industry is now expected to ensure that the data management capabilities and electronic records for these types of systems meet Part 11 compliance. In fact, U.S. FDA warning letters have included reference to computer systems that have not been validated against the expectations to Part 11 requirements. Zhang reviewed how a firm can meet these requirements and used a rapid nucleic acid amplification identification system based on 16S rRNA sequencing as an example.

About the Author

Michael J. Miller, PhD, is President of Microbiology Consultants, LLC and is an internationally recognized microbiology consultant. He is a subject matter expert in pharmaceutical microbiology and cutting-edge rapid microbiological methods and new technologies and the editor of the popular, three-volume PDA/DHI book, *Encyclopedia of Rapid Microbiological Methods,* available at www.pda.org/bookstore. He has held numerous technical, consulting, management and senior leadership roles within Research and Development, Manufacturing, Quality Assurance and Business Development at renowned companies such as Johnson & Johnson, Eli Lilly and Company and Bausch & Lomb.

Regulatory Briefs

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

Europe

EMA Requests Comments on Similar Biological Medicinal Product Guideline

The EMA has released a concept paper explaining the need for revision to the similar biological medicinal products guideline. EMA has asked industry to review the Similar Biological Medicinal Product guideline to propose changes where necessary.

Comments should be submitted by February 29.

EC Releases Concept Paper on Importation of Active Substances

Introducing EU-wide rules for the importation of active substances, the European Commission has released a concept paper for public consultation.

The paper address three consultation topics:

1. Equivalence assessment of the rule for GMP
2. Equivalence assessment of the regularity of inspections to verify compliance with GMP and the effectiveness of enforcement of GMP
3. Regularity and rapidity of information provided by the third country relating to the non-compliant producers of active substances

Comments should be submitted by March 23.

EC's Introduces Safety Features on Medicinal Products for Human Use

The European Commission has posted a concept paper for public consultation on unique identifiers for medicinal products on its website. *Delegated Act on the Detailed Rules for a Unique Identifier for Medicinal Products for Human Use and Its Verification*, also known as Directive 2011/62/EU, introduces obligatory safety features on medicinal products for human use such as a unique identifier to help provide verification of a product's authenticity. The safety features will also help verify via the labeling on the outer packaging of the medicinal product, if the outer packaging has been tampered with.

Comment by April 27.

EMA to Revise Annex 16 of the GMP Guide

The European Medicines Agency announced that it will revise Annex 16 of the GMP guide, *Certification by a Qualified Person and Batch Release.*

The revision will bring the chapter up-to-date with:

1. New legislation
2. Positive and negative trends seen in the medicines business environment
3. Developments in science and technology.

A revision will also harmonize the GMP guidance and interpretation between the Member States.

The consultation deadline is January 31.

Asia-Pacific

TGA Seeks Comments on OTC Regulatory Guideline Revisions

The Australian Therapeutic Goods Administration (TGA) is seeking comments on its proposed revisions to the 2003 *Australian regulatory guidelines for over-the-counter medicines* (ARGOM).

Five revised appendices that provide sponsors with greater clarity on the data requirements for submitting effective OTC medicine applications to the TGA have been released.

At a later date, the TGA will seek comments on the remaining ARGOM chapters which are associated with the process and format of OTC medicine applications, as well as post-market activities

Comments on the document should be submitted by February 11.

Key Regulatory Dates

Comments Due:

January 31 — EMA to Revise Annex 16 of the GMP Guide

February 11 — TGA Seeks Comments on OTC Regulatory Guideline Revisions

February 29 — EMA Requests Comments on Similar Biological Medicinal Product Guideline

March 23 — EC Releases Concept Paper on Importation of Active Substances

April 27 — European Commission's Concept Paper Introduces Obligatory Safety Features on Medicinal Products for Human Use

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Learn at the Biennial Training Conference

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Co-chairs Joyce Winters, J Winters Consulting and Tim Gillum, PhD, Baxter Healthcare

On behalf of the Program Planning Committee and PDA, we would like to invite you and your staff to attend the *2012 PDA Biennial Training Conference & TRI Training Courses* from October 8-11th in Bethesda, Md. You'll want to be a part of this exciting opportunity to enhance your skills, gain new tools and network with others working to optimize learning within a regulated environment.

Recognizing the far-reaching impact of the evolving regulatory landscape, budgetary constraints and increasing emphasis on organizational learning, the Program Planning Committee has selected *From Training to Learning - Improving Performance in a Regulated Environment* as the 2012 conference theme. We will offer concurrent sessions featuring topics that are designed for all levels of learning professionals.

The presentations that will be given will fit in the following three tracks:

- From Training Programs to Learning Programs
- Training System Effectiveness
- From Theory to Practice

Additionally, plenary speakers, round table discussions and networking activities will provide opportunities suited to all learning styles. This forum not only enables you to learn from the experiences and successes of fellow learning professionals, but also the ability to share your own practices and accomplishments.

With dynamic programs presented by outstanding training professionals and networking opportunities galore, you will have all the ingredients and tools to expand your knowledge. Complementing the conference, PDA's Training and Research Institute will be hosting four training courses following the *2012 PDA Biennial Training Conference.*

We look forward to seeing you in Bethesda, Md. in October.

PDA/FDA Virus and TSE Safety Conference

Proactive Approaches to Mitigate Virus & TSE Risk

May 15-17, 2012 | Hyatt Regency Bethesda | Bethesda, Maryland

CALL FOR POSTERS / CASE STUDIES

The 2012 PDA/FDA Virus and TSE Safety Program Planning Committee invite you to submit a scientific abstract for posters at the PDA/FDA Virus and TSE Safety Conference. The theme of this conference is: ***Proactive Approaches to Mitigate Virus and TSE Risk***. The conference will bring together all levels of industry and regulatory professionals to network and benefit from a program that demystifies the underlying science of Virus and Transmissible Spongiform Encephalopathy Safety and seek to solve the problems that our industry faces on a daily basis.

Suggested topics include, but are not limited to:

- **Current Virus Clearance Technologies, Mechanism of Action; Critical Process Parameters**
- **New Virus Clearance Methods; Novel Unit Operations**
- **Quality by Design and DoE Concepts for Virus Clearance Studies**
- **Application of the Risk Assessment Tools for the Development of an Appropriate Study Design**
- **Model Viruses Used for Virus Clearance Studies; Characterization of Virus Spikes Used for Clearance Studies**
- **Risk Mitigation Strategies for Raw Materials; Treatments to Assure Viral Safety; Inactivation of FBS or Trypsin or Other Animal Derived Raw Materials.**
- **New Viruses of Concern – How Can We be Proactive?**
- **Investigational TSE Studies, Detection Methods and Characterization of Spike preparations; comparative TSE studies (methods used for detection of TSE agents; different spike preparations).**
- **Cell Culture Techniques for Detection of TSE Agents**

Abstracts must be received by March 9, 2012 for consideration.
Please visit **www.pda.org/virustse2012** to submit your abstract.

Case studies are particularly desired. Commercial abstracts featuring promotion of products and services will not be considered. Submitters will be advised in writing of the status of their abstract after March 23, 2012. All poster presenters are required to register for the conference at the prevailing registration fee; in addition, poster presenters are responsible for their own travel and lodging.

QUESTIONS?

Contact PDA:
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ALL ABSTRACTS WILL BE REVIEWED

All submitted abstracts will be reviewed by the Program Planning Committee for inclusion as a poster presentation.

ATTENTION EXHIBITORS

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www.pda.org/virustse2012

PDA Europe Thanks Universe of Pre-Filled Syringes

Two Ways to Minimize the Delamination Risk of Glass Containers

Volker Rupertus, PhD, SCHOTT Pharmaceutical Packaging and Uwe Rothhaar, PhD, SCHOTT Pharma Services

Introduction

The recent spike in market recalls for injectable drug products due to visible flaky particles associated with "glass delamination" demonstrates the need to solve these problems. It is important for both drug product and container manufacturers to understand the underlying mechanisms, to test for the potential risk, and to control drug container interactions to provide patients with safe medicine.

The recalls span multiple types of drugs, buffers, containers, and age of product on the market, demonstrating that this is a multi-factorial root cause problem. The good news is that there are multiple commercial packaging solutions from various manufacturers available to solve this problem, along with the drug formulation changes that (theoretically) can be made. But due to the lack in response time of the "delamination" appearance, it is urgent to have tools on hand which give a quick confirmation about potential risks of the chosen drug-container combination.

Formation mechanism and influencing factors

Glass delamination is the result of chemical attack on the interior container surface involving well known glass corrosion mechanisms **(1),** namely dissolution by hydrolysis and ion exchange (leaching) that depend on the pH **(2).** The visually inspectable outcome in the drug product is the appearance of "glass flakes" that happens in the majority of cases months after filling. More than 40 years ago SCHOTT published first data about "glass flakes" found in ampoules **(3).**

The chemical properties of the drug/formulation components and their ability to promote glass corrosion are the dominant factors for the generation of these flakes. Corrosion of glass by pharmaceutically relevant chemistries (i.e., citrate, phosphate acetate buffers) and pH (acidic, neutral, basic) have been known for decades **(4).** Beside some obvious parameters like glass composition, storage temperature, time and environment a variety of other factors from container manufacturing, subsequent optional chemical treatment and processing at the pharmaceutical filling line can influence the delamination process as summarized in a newsletter of SCHOTT Pharmaceutical Tubing **(5).**

If delamination is observed in tubular converted glass containers like vials and ampoules it starts at the areas where heat is applied during the forming steps; near the bottom and the neck. After filling the drug product chemical interaction processes occur and initiate corrosion mechanisms at the glass surface leading to a layer with an altered glass composition as an early stage of delamination. A typical related surface situation can be seen in a SEM cross-section micrograph **(Figure 1)** sourced from a SCHOTT internal study about the hydrolytic attack of vials: this layer ranges over a depth of about 100 nanometers featuring a rough and porous surface morphology.

Figure 1: SEM cross-section micrograph of transition zone (wall near bottom) prior to glass flakes being observed.

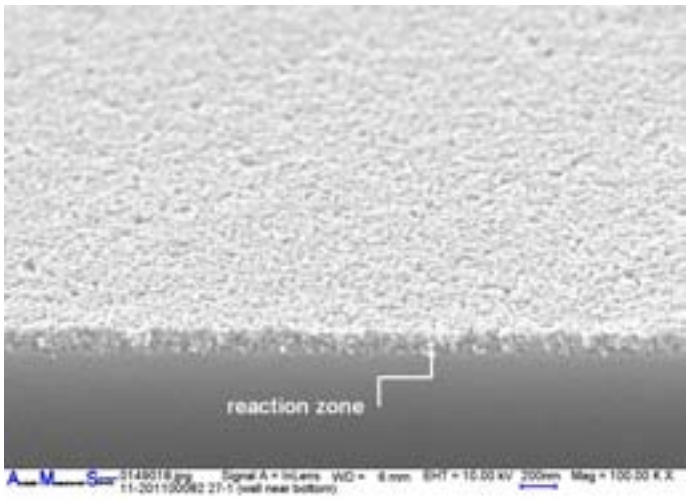
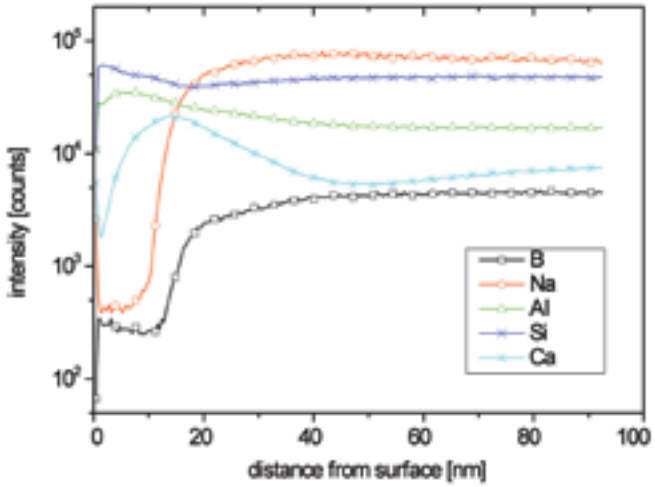


Figure 2: SIMS depth profiles of interior vial surface of transition zone revealing sodium and boron depletion.



Compared to the bulk glass composition a depletion of sodium and boron is observed within this layer as revealed by SIMS sputter depth-profile analysis **(see Figure 2).** With proceeding reaction this layer will grow, detach, and is a potential source for the built-up of a silica-like flake. Please note, that this may be the most common but not the only possible delamination mechanism. In some cases the flakes contain compounds made of buffer and glass elements like aluminum-phosphate, indicating that certain phosphate buffers react with the glass via a different reaction pathway.

The fact that a large number of substances are used in drug formulations and packaged in type I containers without incident is a testament to the high chemical durability of type I glass. The glass composition contribution to delamination is subtle, based upon the interplay between the amounts of alkali, alkaline earths, silicon, aluminum, boron, the container formation temperature leading to changed interior surface chemistries compared to the bulk composition, and the rate of attack by a given drug formulation. Independent of container manufacturing process, drug product formulations exist that will attack both moulded and tubular containers.

Test methods

Because delamination requires drug product exposure to occur, no conclusive incoming inspection method currently exists to determine upon receipt of a container from the glass manufacturer if a vial will or will not delaminate.

Regarding the variety of chemicals used for drugs and formulations and the variety of filling, sterilization, and autoclaving procedures it seems reasonable that no one general test will be able to assess the specific delamination risk.

Knowing the big variety of influencing manufacturing parameters the state-of–the-art technology of type I glass containers does not force an implementation of validated processes guaranteeing "mimimal delamination risk" for all container types. Therefore the first way to minimize delamination should be the implementation of a standard test method like ISO 4802/ Ph.Eur. 7.0 for the chemical durability of container glass which defines maximal tolerances for a kind of delamination affinity. Such a qualitative testing method, used in the routine control for the daily production, would help to sensitize the machine operators to an invisible container property. The testing method has to be adapted to a few container sizes, because the delamination tendency of larger vials is higher due to the larger amount of bulk glass reshaped during the forming processes. Within SCHOTT a testing procedure has been developed to give a "go" / "no go" hint to the specific production process.

The second way to minimize delamination is strongly addressed to the drug product manufacturers to implement accelerated aging tests for container screening methods during stability testing. If the current container/drug product generates glass flakes, from the container perspective one can quickly test other type I glass(es) or containers by the same manufacturer, switch to a different manufacturer, use a coated container

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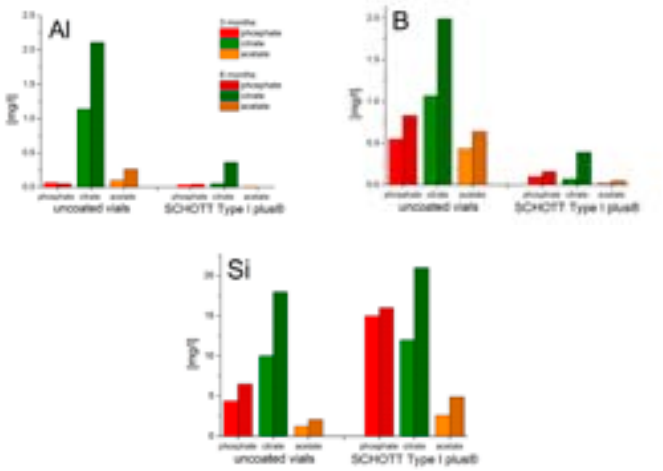
like SCHOTT Type I plus®, or switch to a plastic container like SCHOTT TopPac®. These accelerated stress tests of individual container-drug interactions are also offered by specialized analytical service providers like SCHOTT pharma services, to combine the glass know-how with analytical expertise. Standardized analytical screening methods looking at the container surface morphology (SEM) and composition of the surface near layer (SIMS), quantifying the concentration of glass elements in solution (ICP-MS), and determining the chemical composition (SEM-EDS) of glass flakes are readily available to implement the appropriate testing during stability studies to select a stable drug solution/container presentation **(6).**

Overall it is important to note that the vast majority of injectable drug products on the market today are safely packaged in Type I glass.

Testing Results

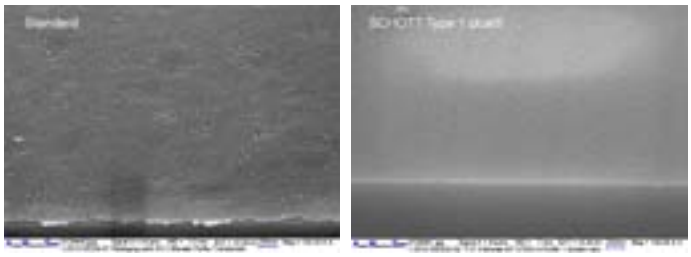
A recent internal study **(7)** has focused on the attack of various buffer formulations on standard 2 ml vials and SCHOTT Type I plus® vials (SiO_2 coated) under accelerated conditions, both made of SCHOTT FIOLAX® Type I tubing glass. As representative commonly used formulations 10 mM solutions of phosphate (pH 7.0), citrate (pH 6.0), and acetate (pH 5.2) buffers with 150 mM NaCl and 0.005% Tween 20 were studied. After 3 and 6 months of storage at 40ºC/75%RH, we found a formulation dependent attack, as demonstrated by the concentration of dissolved glass elements silicon, aluminum, and boron as depicted in **Figure 3.**

Figure 3: Solution ICP-MS data for Al, B, Si at 3 and 6 months storage at 40ºC/75% RH.



The highest concentrations are generated by the citrate buffer which shows a linear increase from 3 to 6 month's value. In contrast, the dissolution caused by the phosphate and the acetate buffer is found to be less pronounced, the increase from 3 to 6 month's value is not linear. For the case of the SiO_2-coated SCHOTT Type I plus® vials only significant silicon concentrations were observed, which demonstrates the protective effect of the several hundred nanometer thick quartz-like coating **(8).** Due to the different morphology of glass and the SiO_2-coating the very early stage of the dissolution behavior leads in the case of phosphate buffers to a higher amount of Silicon in the solution for the coated vial in **Figure 3** (the perfect barrier diffusion behaviour of the SiO_2-coating protects all other glass components from the dissolution attack). As soon as steady state conditions are reached, the ratio for Silicon dissolution becomes significant smaller for the coated vials compared to uncoated ones. Additionally, SEM cross-section analyses of the interior surface were conducted after 3 month's storage **(Figure 4).**

Figure 4: SEM cross-section micrograph of transition zone (wall near bottom) after 3 months for phosphate buffer standard Fiolax Type I (left) and SCHOTT Type I plus® (right)



The morphology appears more or less unchanged for the citrate and acetate buffers. In contrast a thin altered layer was observed at the wall area near the bottom of standard vials filled with phosphate buffer, whereas the corresponding SCHOTT Type I plus® vial does not show comparable features. Such a layer denotes an early stage of delamination.

The results demonstrate various levels of attack of the Fiolax Type I container but no significant attack on the SCHOTT Type I plus® container. For container/drug formulation studies, it is crucial to ensure that the rate/type of attack (diffusion/kinetic) is not affected/changed by choice of too aggressive accelerated conditions (i.e. temperature). From the perspective of a manufacturer of glass containers such studies are helpful to understand the corrosion mechanism, but not suitable to control or steer the production.

Conclusion

In summary, glass delamination is a known problem for a limited number of drug formulations/containers, with multiple solutions. To minimize the risk of delamination we strongly recommend a two way strategy:

1) Implementation of container screening studies evaluating the glass surface morphology, glass surface composition, and solution composition of leached glass elements should be included as part of normal stability studies to determine if glass delamination occurs and what the root cause is (drug formulation/container process or drug formulation/container composition).

2) To optimize the process window of the container production the implementation of an offline "fast" testing method for the use in daily operation can also help to run the production lines in a "low delamination risk" mode.

References

1. Paul A. Chemistry of Glasses, Chapman & Hall 1990, 180-204
2. Ennis RD, Pritchard R, et al., Glass vials for small volume parenterals: influence of drug and manufacturing process on glass delamination. Pharm. Dev. and Tech. 2001; 6(3):393-405.
3. Rehm, K. The Effect of the Manufacturing Conditions of Ampoules on the Chemical Resistance of Their Inner Surface, Schott Pamphlet #293e, 1965.
4. Bacon, F.R., Raggon, F.C. Promotion of Attack on Glass and Silica by Citrate and Other Anions in Neutral Solution, J. Am. Cer. Soc., 1959, 42(4): 199-205.
5. M. Roessler,SCHOTT Pharmaceutical Tubing, Newsletter No. 14: Particles in Glass Containers: Flakes: http://www.schott.com/tubing
6. Friedbacher G., Bubert H.(eds.) Surface and Thin Film Analysis, Wiley-VCH 2011, Weinheim ISBN-13: 978-3-527-32047-9
7. Haines D., Klause M. (SCHOTT) Rx 360 Glass Delamination Scientific Symposium, 25 May 2011.
8. Walther, M., Rupertus, V., Seeman, C., Brecht J., Hormes R., Swift R.W. Pharmaceutical Vials with Extremely High Chemical Inertness, J. Pharm. Sci. Tech. 2002, 124-129.

John Brecker, Fleet Laboratories

John Brecker has spent thirty years as a Quality Control Microbiologist for pharmaceutical, biopharmaceutical and personal care product manufacturers. Currently, his responsibilities as a Pharmaceutical Microbiologist at Fleet Laboratories include identifying fungi using visual examination and rapid methods. It is no surprise that John teaches a mycology course for TRI since his expertise includes microbial identifications, microbiological testing and validations, environmental monitoring, research and development.

Course that you teach for PDA: "Environmental Mycology Identification Workshop"

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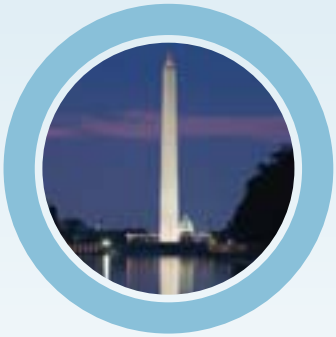

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Editor's Message

Inspired by the Human Factor

In most situations, the human factor is very important. At a time of year when performance reviews have been completed, we are very aware of how our interactions impact the workplace. Sometimes you can see the impact of the human factor outside a building when the lawn is worn out from people cutting across areas originally not designed for foot traffic. Or, cars in traffic cutting through parking lots and other areas not meant for traffic. In each case, lack of attention to the human factor can be an issue. We often find that tensions in the office or poor performances can be corrected by paying attention to how teams of people actually interact. Keeping people off the grass might involve figuring out why they walk over it in the first place—like, perhaps, the absence of a direct walkway to the doorways or the parking lots. And we could wax poetic about all the reasons why people do crazy things in traffic, particularly when you live in the Washington metro area!

For years in the pharmaceutical industry, the human factor didn't play much consideration in product development. If a company could explain its dosing instructions clearly and provide proper product warnings, it was assumed most practitioners, patients and other users could figure out how to administer/take the product. With drug-device combination products becoming more common, particularly for parenteral preparations, this is no longer the case. How can a company be sure patients can set the proper dosage on a pen injector? Will patients prime a prefilled syringe? Companies making these products must find answers to these questions, and the regulatory agencies have in place expectations for human factors/usability engineering which must be met in order to market drug-device combo products.

Emily Hough listened to talks on this topic at the PDA Combination Products Workshop in late 2011 and was impressed with the topic. As such, she provides a complete report of the session in this issue. Her work prompted me to take a look at a recent U.S. FDA draft guidance on human factors/usability engineering and analyze the public comments to see how pharmaceutical/biopharmaceutical companies feel about it with respect to their combo products. It was a very enlightening task putting these articles together. The topic even inspired our designer, **Katja Yount,** to create original artwork by pulling out her watercolors to paint sketches for the Letter. She then scanned them and placed the designs in the issue. With the issue now completed, I'm going to have to sit down and analyze my data to find out what factors inspired such hard work and creativity from my team!

I know what factor inspires **Michael Miller:** Rapid Microbiological Methods. It is our pleasure to once again publish a few of his blog posts on the topic from the *2011 PDA Pharmaceutical Microbiology Conference.* Be sure to check out photos from the event in the Faces and Places.

PDA Letter

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The Task Force charged with updating the document ensured that the new version reflects the continuing changes that have occurred in aseptic processing technology within the global industry over the last decade and a half. They have attempted to address the subject as fully as possible, recognizing the notable contributions by other organizations, regulators, compendia and individuals who have worked in this area. In addition the report provides guidance where risk-based approaches may be applied.

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