NEW ENGLAND PDA NEWSLETTER

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Connecting People, Science and Regulation

In This Issue:

May 16th NEPDA Meeting

Tour of Baker Company, Sanford, ME 04073
www.bakerco.com
Meeting at Village By The Sea, Wells, ME 04090
www.vbts.com

Event Topics/Titles:

- TR13 Fundamentals of Environmental Monitoring
- Emerging Decontamination Technologies for Cleanrooms:
Vaporized Hydrogen Peroxide (VHP) and Chlorine Dioxide Gas Decontamination Field Studies

Speakers:

Jeanne Moldenhauer, Excellent Pharma Consulting, Inc.
Peter Harris, B & V Testing, Inc

Go to the NEPDA website http://pdachapters.org/newengland for upcoming meetings, chapter policies, contact information, past presentations, archived newsletters and more.

Are you interested in submitting an article for a future NEPDA Newsletter? Then download and submit the "NEPDA Newsletter Article Submission Policy" at the Chapter Resources link at our website: http://pdachapters.org/newengland and submit it to melissa@mjqualitysolutions.com

Raw Materials Control: A Sink or Swim Odyssey

Enith Morillo, M.S., Supervisor Quality Control
enithcm@gmail.comm Tedor Pharma Inc.

Although pharma and biopharmaceuticals giants have at their disposal unlimited resources to develop and implement successful and efficacious sampling and testing programs for their raw materials, it is mid to small size companies that often lack resources to support more robust programs that can provide added assurance of raw material compliance.

Recently, I attended a training on "Best Practices in Biopharmaceutical (and Pharmaceuticals) Raw Materials Testing and Vendor Qualification" facilitated by the University of Wisconsin - Madison, Department of Engineering Professional Development. The training, conducted by experts in the field Paula J. Shadle, Ph.D and Daniel Lobato, both PDA members, took place in Las Vegas and was filled with valuable pointers on establishing effective and compliant procedures for the control of quality raw materials.

During the training, I learnt that working with raw materials is an evolutionary process for many. Experts of various technical backgrounds and training are often selected to take on supervisory roles in the control of raw materials, assuming the responsibility to oversee their sampling, testing and/or release. With a myriad of sources for active pharmaceutical ingredients (APIs) and excipients manufactured under various interpretations of quality from Raleigh, North Carolina to Gagillapur Village, India, raw materials control can be a risky business, if not a gamble.

Then, if as a microbiologist manager, veteran formulator, or qualified HPLC analyst, you find yourself suddenly in the raw materials ocean, take a hold of your USP/NF guide and, at the least, stay afloat.

Sampling: What are the odds?

Of course you always wanted to take challenging statistics courses but didn't get a chance to, between organic chemistry and microbiology. Yet here you are now: "the" raw materials person, "the" authority in their sampling, testing and release. You are responsible for deciding how many drums of an incoming batch need to get sampled, how much material is needed for analysis and retain, and if thief samples are required, all the while ensuring the company's sampling plan meets FDA regulations.

For starters, what makes a sample representative? Industry standard has been driven by a study published in the 1920s, where the miraculous $\sqrt{N}+1$ rule was first proposed for Agriculture. Why it was adopted as a sampling plan by the United Nations, the World Health Organization, the FDA, and pharmaceuticals worldwide is still being debated. What is important, is that this magical formula does meet and exceed the statistically sound American National Standard Institute (ANSI) Z1.4 standard. For larger shipments though, it might be cost efficient and practical to consider using the ANSI standard, especially for materials liable to microbiological contamination.

An effective sampling plan provides a statistically based representative sample size and can be devised to switch between stringent and moderate procedures, depending on the material's specifications, its vendor qualification status, and any history of rejected lots. Raw materials can be categorized based on these factors to activate the pertinent sampling plan to be implemented. A good rule of thumb to follow: when in doubt, sample more not less.

Specifications: Is harmony attainable?

With the drive for harmonization and the desire to market products globally, raw materials manufacturers are continuously adding to their specifications and testing to meet standards set by the United States Pharmacopoeia and National Formulary (USP/NF), and its European (Ph. Eur.), Japanese (JP), British (BP), and other international siblings.

So we might have started by setting raw material specifications based on the USP/NF and the manufacturer's certificate of analysis, to soon realize the material is being marketed globally to several industries. This realization carries the weight of an anchor, and is what guides us to thoroughly research our raw material and end product to determine the critical testing parameters necessary to ensure quality.

A raw material such as Talc, which is used in the manufacture of paper, detergents, paints, cosmetics, pharmaceuticals, and even animal feed, might have specifications set by the manufacturer relevant to all these industries. Yet, testing to meet compendia requirements and specs related to our industry and end product is probably sufficient to establish its quality.

Sending out an SOS: OOS

Just when you were learning to navigate raw materials sampling and specifications, an Out of Specification (OOS) rocks your boat. An OOS occurs when a raw material test results do not meet its specifications. FDA guidance for OOS stipulates that an investigation must be conducted to determine the root cause of the OOS, followed up by establishing a plan of action to avoid its reoccurrence. Statistics indicate most OOS results are caused by laboratory error and are not related to the manufacturing process. However, an effective OOS investigation should cover all probable causes, and in a timely, scientifically sound, well-documented manner determine if the test results are valid.

Needless to say, quality is the top priority and ultimate goal. Any OOS investigation should remain untainted by the need to invalidate test results and “release” a material. Unjustified retests should not be conducted to generate results that meet the specs. There won't always be a root cause identified, but an extensive investigation will leave you with enough data to develop a corrective and preventive action plan (a.k.a CAPA).

Retains: What's left?

FDA regulations suggest representative samples of raw materials be retained for a specified period of time under appropriate storage conditions. The amount of material retained should be enough to allow for the material to be tested in full at least twice. You won't know the importance of being generous when storing retain samples until you come across an OOS.

Salvation:

The demand for high quality, low cost drugs can be financially challenging for small to mid size pharmaceuticals. However, purchasing quality raw materials along with implementing efficacious sampling and testing procedures, undoubtedly results in top quality drugs that are profitable and beneficial to their consumers.

So whether you are using the survival travel stroke or expertly concentrating on your backstroke in the raw materials ocean, make sure you put quality and compliance above all, and continuously actualize your knowledge of industry trends to stay ahead of the race.

PRESIDENT'S MESSAGE: PDA Annual Meeting 2008 Overview:

May 2008, By ***Louis Zaczkiewicz, NEPDA President***

The global PDA organization has many conferences and programs throughout the year, four of which are labeled as their "signature" events: the Annual Meeting, the PDA/FDA Joint Regulatory Conference, the PDA/EMIA Joint Conference and the Asia-Pacific Conference. I attended the PDA Annual Meeting in April, held at the Broadmoor Resort in Colorado Springs, Colorado. I attended the meeting for many reasons:

- to represent the New England Chapter at the Chapter Council committee meeting
- to run the Chapter Council committee meeting in my capacity as its co-chair
- to address the new PDA members at the New Member Breakfast in my capacity as a member of the PDA Membership Committee
- to receive PDA Chair and President's appreciation award as President of the New England Chapter
- to network with old friends and to make some new ones
- to continue my education through attending the session presentations
- to attend a one-day training course on pre-filled syringe regulations put on by PDA's Training and Research Institute (TRI)

The conference began Sunday Night with the PDA Awards Banquet, held at the Cheyenne Lodge overlooking the city of Colorado Springs. Notable amongst the award recipients, Susan Schniepp (a NEPDA member and past chapter meeting presenter) received the 2007 Distinguished Service Award in recognition of the time and effort spent to further the reach and mission of the PDA by Board of Directors Chair John Shabushnig and PDA President Bob Myers.

The theme of this year's meeting was to bring the patient's perspective into the picture to help us understand why we all work as hard as we do and to see the fruits of that labor. The four keynote speakers drove that message home to the attendees. On Monday, Shelley Morrison, star of the TV show Will and Grace, walked us through her 10-year journey battling Breast cancer. She thanked us and our industry for being there to provide the diagnostic tests and the drugs to battle the cancer. Next, Linda Armstrong Kelly, cyclist Lance Armstrong's mother, rode us through the course that Lance and she went through in his battle against Stage 3 testicular cancer. On Wednesday, the closing speaker Johnnie Godwin described the advances he personally received due to the new medications against Age-Related Macular Degeneration (AMD). Although the drugs did not come out in time to help his parents and grand parents, his disease is fully controlled by the medicine and his sight has been restored. Finally in a message that much work still needs to be done, the PDA presented Dr. Randy Pausch's fight against the currently incurable disease Pancreatic Cancer by showing part of Randy's "Last Lecture" (available for viewing on the web – search for Randy Pausch).

The meeting sessions were all well run. Twenty seven educational sessions were held in virtually all aspects of parenteral drug development, manufacturing, testing, distribution and compliance. Additionally, thirteen interest groups held meetings to discuss their progress and to solicit new members. Finally the Board of Directors and Scientific Advisory Boards held their business meetings.

From Wednesday afternoon through Friday, there was a Global PDA workshop on "Quality Requirements for Phase 0/1 Pharmaceutical Development Study" along with eleven educational programs put on by the TRI. This year they involved classes in environmental monitoring, regulations, risk management, cleaning validation and Mycoplasma to name a few. I was able to attend the course on the quality and regulatory aspects of prefilled syringes and combination products taught by Dr. Michael Gross. Combination products are those that combine components regulated by more than one FDA office of compliance. For example with a syringe prefilled with a drug, the syringe is regulated by CDRH and the drug component is regulated by CDER (if the drug is a biologic then CBER would be involved instead). The approval process goes through the FDA's office for Combination Products, which assigns the agency that will handle the application based on its primary mode of action. Thus you only have to work with one compliance office instead of two (or three). Although the process can be cumbersome, in general this system has allowed many products to seamlessly pass the compliance journey onto approval.

As you can see this is a major event that touches all aspects of our work. It points out the fruit and failures and provides a venue for us to keep advancing the products and services that each of us provides. I encourage you to consider attending

PDA global meetings as they will help you, your work and your company. The next PDA Annual Meeting will be held on April 20-24, 2009, in Las Vegas, Nevada and will focus on the microchip (computerization and automation). They are now accepting abstracts. I wish to thank Global PDA and the NEPDA for paying for the conference, and for my employer, Hyaluron Contract Manufacturing (HCM), for picking up the rest of the expenses including the time to attend.

New England Parenteral Drug Association Chapter Announces Awards at 2008 Massachusetts State Science Fair

By Mark Staples, Cusp PharmaTech Consulting and Eleanor A. Tishler, Director of Corporate Development, Massachusetts State Science & Engineering Fair, Inc

NEPDA has re-initiated a program to sponsor awards for the Massachusetts State Science & Engineering Fair (MSSEF). Details of MSSEF can be viewed at http://www.scifair.com/.

NEPDA's involvement for the May 2-3 2008 Fair included provision of funds for awards and overhead to the Fair administration. The Chapter contributed one $1000 prize (awarded in the First Place tier of prizes) and three $500 prizes (awarded in the Third Place tier of prizes). An additional $250 was provided to the Fair to defray overhead expenses. This level of support places NEPDA at the Silver Donor level. The NEPDA Board intends to support the Fair at this level in the future, as part of the Chapter's commitment of outreach to the community to encourage interest in the pharmaceutical profession.

This year 400 students/300 projects were registered for the 59th Massachusetts State Science & Engineering Fair (MSSEF). Entries represented a wide range of fields (Behavioral Science, Biochemistry, Biology, Chemistry, Computers, Earth and Space Science, Engineering, Environmental Science, Mathematics, and Physics and Electronics). The Fair also featured programs for students, parents, science educators and guests. The Fair now includes a Science Fair Expo, with exhibitors drawn from well-known Massachusetts companies, colleges and professional organizations.

Mark Staples represented NEPDA at MSSEF. He reviewed the exhibits and provided a ranking of entries that were relevant to the pharmaceutical industry. This ranking was used by the official Fair judges to allocate awards. In some cases projects not involved with the pharmaceutical industry receive NEPDA awards because of the overall distribution of award-winning entries across different fields. For potential future improvements, NEPDA's representative should serve as an official judge. The Fair has grown and needs a significant number of judges, so NEPDA members are encouraged to volunteer for the 2009 Fair.

Mark Staples presented the NEPDA awards at the MSSEF Award Recognition Ceremony on Saturday, May 3rd in MIT's Kresge Auditorium. Mish Michaels, WBZ-TV meteorologist, served as Ceremony Emcee.

Your 2008 NEPDA-sponsored winners are:

$1000-First Place Tier

Kendyl Murtaugh and Marimo Shioda	Hudson High School	Water Filters and Potentially Harmful Estrogen-Mimicking Compound

$500-Third Place Tier

Anugraha Raman	Dover-Sherborn Regional High School	Computational Location of Epitopes in Shared-Cancer-Tumor Proteins
Yiling Chen	Boston Latin School	XRCC4 Deficiency Leads to Double-Stranded DNA Breaks at IgL Loci
Bennet Ferris, Zane Martin, and Emily Ury	Monument Mountain High School	How Soil Could Save the World

MSSEF provides, in addition to a congratulatory letter from the Executive Director, two awards -- placement pins & award certificates, to each winner in First to Third Place. Honorable Mention winners receive a certificate and a ribbon. NEPDA provided, in addition, a congratulatory letter that included the following components:

- A cash award of $1000.00 or $500.00 (check mailed by MSSEF)
- An invitation for the recipient and 2 guests to attend a NEPDA dinner meeting, to show their winning exhibit, and to summarize their project as part of the program (the first date available for the presentation will be the September 17 dinner meeting)
- A NEPDA souvenir golf shirt (the most exclusive prize of all-not available in stores!)

The New England Chapter of the PDA is pleased to announce the ***availability of advertising opportunities in our newsletter.*** Since its inception in 1988, our chapter has seen a significant growth in membership and participation. Our newsletter has the following reach:

- **Our direct e-mail distribution reaches over 1,800 contacts throughout New England.**
- **Our membership includes people from manufacturing, research, QA, QC, engineering, contract manufacturers, consultants, regulatory, etc.**
- **The newsletter is promoted at New England PDA's bi-monthly dinner meetings, often with company tours, which regularly attract 50-150 attendees.**
- **The newsletter is posted to our chapter's website at Global PDA (www.pda.org), an organization that has over 10,000 members.**

We offer vendors, consultants, operating companies and other organizations the opportunity to promote themselves and also support the NE PDA Chapter by purchasing advertising in our newsletter:

1. ***Download and fill out the "NEPDA Newsletter Advertising Policy" form located at the Chapter Resources link of the NEPDA website: http://pdachapters.org/newengland***
2. ***Email artwork along with a scanned copy of your completed form prior to the deadline to melissa@mjqualitysolutions.com***
3. ***Submit the completed form with check payable to***

New England PDA c/o Treasurer
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Deadline	Publication Date
July 15, 2008	August 2008
October 15, 2008	November 2008
January 15, 2009	February 2009

Questions:

About the newsletters and articles? E-mail Melissa at melissa@mjqualitysolutions.com
About advertising opportunities or artwork? E-mail Rusty at morrison@pdachapters.org