NEW ENGLAND PDA NEWSLETTER

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Connecting People, Science and Regulation

Upcoming Event

New England Chapter

March 2010

Dinner Meeting-Facility Tour:

Masy Systems

Topic:

Cold Chain Qualification

Cold Chain Monitoring.

Date:

March 10, 2010

Time:

530 – 900PM

(Tour times to be announced)

Plant Tour:

Facilty Tour of Masy Systems, including their new BioPharma Storage Facility

Dinner Meeting venue:

Alpine Grove

19 South Depot Rd,

Route 111A, Hollis, NH

New FDA Guidance on Risk of Melamine Contamination

By Roland Bizanek, PhD, MPD

Biogen-Idec, Inc., Cambridge

Roland.bizanek@biogenidec.com

Introduction

In March 2007, the FDA learned that certain pet foods were contaminated with Melamine causing sickness and death in cats and dogs and resulting in a large scale recall of pet foods in the US. The joint investigation by the FDA and the USDA determined the root cause to be Melamine contamination of vegetable protein imported from China and subsequently used animal feed. (http://www.fda.gov/AnimalVeterinary/SafetyHealth/RecallsWithdrawals/ucm129575.htm)

In 2008, several reports reached the US of infant hospitalizations and fatalities in China caused by contamination of infant formula with Melamine. The investigation determined the root cause as Melamine contamination of milk used in the production of infant formula distributed in China. Subsequently, on September 12, 2008, the FDA issued a Health Information Advisory to assure the American consumers that there was not threat of Melamine contamination of US manufactured infant formula.
(http://www.fda.gov/NewsEvents/PublicHealthFocus/ucm179005.htm)

The common element of these contamination issues was economically motivated adulteration with Melamine to bolster the apparent protein content of the contaminated material. The analytical methodology used to determine the protein content relied on non-specific total nitrogen content in the sample, which is not able to distinguish between nitrogen from protein vs. Melamine. While these situations were limited to the food industry and no adulteration has been reported on pharmaceuticals by Melamine to date, the FDA issued proactively a new guidance in August 2009 titled: “Guidance for Industry – Pharmaceutical Components at Risk for Melamine Contamination”.
(http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM175984.pdf)

This article will discuss the requirements, expectations and recommendations by FDA as expressed by this new guidance document.

Melamine

Melamine also known as Triaminotriazine, Cyanuramide, Cyanuric acid amide is an industrial chemical used in resin manufacturing (Figure 1). Its high nitrogen content combined with its relatively low price, made it ideal as a counterfeit material to bolster the apparent protein content in material, which is tested for protein content by determination of total nitrogen content. While to date no Melamine contamination in pharmaceutical components has been reported, many components used in drugs are tested for total nitrogen content and therefore, make them susceptible to adulteration by Melamine.

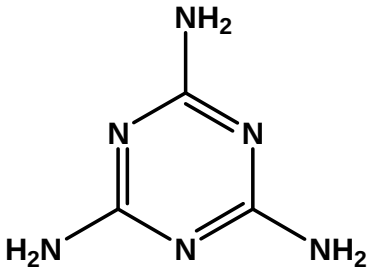

Figure 1 – Chemical Structure of Melamine

Regulatory Considerations

The presence of Melamine in any drug (unless specifically approved as an impurity) will be considered an adulteration under sections (501(a)(2)(B) and 501(d)) of the FD&C Act. (FD&C Act: Food, Drug & Cosmetic Act, 21 U.S.C. 351 (a)(2)(B) and 351(d))

Additionally, under cGMP regulations all components need to be tested prior to their release for manufacture/preparation of drug product (21 CFR 211.84). This testing should consider confidence levels and precision needed, and past supplier performance (21 CFR 211.84(b) and (d)).

At Risk-Components

The FDA lists in their new guidance document at risk-components based on their assessment of the USP/NF and the FDA's own Inactive Ingredient Database (IID). (http://www.accessdata.fda.gov/scripts/cder/iig/index.cfm) The list was determined by listing all USP/NF monographs, which specify a test for total nitrogen content (USP <761>). Other non-compendial components were included, if they were derived from animal based materials and that could be tested with non-specific methods to identify their identity and structure. Additionally, any compound containing more than 2.5 % nitrogen is considered at risk for economically motivated adulteration.

Solution and Path Forward

Each manufacturer of finished pharmaceutical product should start with performing a risk assessment of their supply chains and manufacturing processes. If initially no at risk-components (as defined above) are used in the manufacturing processes, the findings should be documented and initially no additional work needs to be performed. If at risk-components are being utilized, the manufacturer should be consider to implement testing the at risk-component for Melamine. The FDA has provided specific test methods in their guidance document with a limit of detection down to at least 2.5 ppm. (http://www.fda.gov/AnimalVeterinary/ScienceResearch/ToolsResources/ucm135002.htm) Alternatively, the manufacturer could request the supplier of the at risk-component to certify that the material has been tested for Melamine. The manufacturer should verify these results periodically to ensure that validity of the test results.

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While testing adds a degree of assurance, the manufacturer should monitor their supply chain to understand the identity and role of their component suppliers. It is critical to identify the actual manufacture of the component and any repackager and distributor handling this material in the supply chain. Additionally, the manufacturer should implement an audit program of their component suppliers to ensure compliance with cGMP expectations and to monitor their supply chain starting at the actual manufacturer of the component.

If the license holder (NDA, ANDA, or IND) is not the actual manufacturer of the finished pharmaceutical product, the license holder should obtain certification that their products, which utilize at risk-components, are tested for Melamine. The certification should be verified periodically by appropriate means, e.g., verification testing, audits.

Compounders using at risk-components should consider either appropriate testing of the components or ensuring that the testing has been performed by reliable suppliers.

Conclusion

In essence, the manufacturer/distributor of pharmaceutical products must not only understand their respective manufacturing processes for drug substance and drug products, but they also need to understand their supply chain in detail including the producers and processes of each components used in the manufacture of their pharmaceutical product. This knowledge is the foundation for securing the complex supply chains in a global world against any economically motivated adulteration of pharmaceutical components.

NEPDA PRESIDENT'S MESSAGE

By Jerry Boudreault
President
Drug Development Resources, Inc.

Greetings NEPDA Members,

I would like to take the opportunity to wish all of our members and sponsors a happy, healthy, and prosperous New Year. The last year was a great learning experience for me and I have enjoyed meeting many of the members at NEPA 2009 meetings. Thanks to all who supported the Chapter last year as you make it the success that it is. It is hard to believe that the first year of my two year term is over!

We set some fairly aggressive goals last year, and for the most part achieved them with the notable exception of increasing the number of PDA members in our area. We actually lost 70 members last year instead of adding 70 members as we had hoped. I personally called most of those with lapsed memberships and the reasons given were predominately economic in nature with companies watching expenses and limiting or the number of professional associations an employee could belong to or eliminating support altogether. Our goal was a casualty of the economic downturn! If you are reading this and your membership is lapsed I would like to know why. Please send an email and let me know. I can assure you that the Chapter Board of Directors is very interested in doing anything possible to help you get back and increase the value of your membership. To that end we will continue to provide members with outstanding development opportunities not available to non members.

This is a Chapter election year. If you are interested in assuming a leadership role in our Chapter, the way to start is as a member of our Event Planning Committee. We meet every other month, five times per year, for two hours. Meeting times and locations are posted on the chapter website. It is a relaxed and friendly atmosphere. Come on down!
I look forward to serving over the next year and I hope to meet you soon at an NEPDA event.

Sincerely,

Jerry Boudreault
boudreault@ddres.com

USP ACTIVITIES IMPACTING STERILIZATION & STERILITY ASSURANCE

by James Agalloco
Agalloco & Associates

Did you miss the January 2010 NEPDA Presentation by Jim Agalloco on the proposed USP chapters on Sterilization and Sterility? Check out the presentation on our chapter website by going to the following link:

http://www.pda.org/MainMenuCategory/Chapters/New-England/Presentations.aspx

Message from Global PDA President Regarding 2010 PDA Annual Meeting

Manufacturing Excellence

March 15-19, 2010 | Gaylord Palms Resort and Convention Center | Orlando, Florida

For 64 years, the Parenteral Drug Association (PDA), an industry non-profit, has been joining industry regulators, educators and policy-makers at the *PDA Annual Meeting* to discuss the latest scientific and technological innovations. We invite you to join our 500 industry leaders in this year's dialogue.

The theme and focus of the 2010 meeting is ***Manufacturing Excellence*** **and productivity in the regulated healthcare product industry**. This paramount issue not only affects your company's bottom line, but the optimization of benefits and values. As an industry we must realize the need for better productivity; identify the obstacles, and use our scientific and technical knowledge as a means to achieve *Manufacturing Excellence*.

The complete 3-day program includes more than 70 presentations given by some of the most knowledgeable professionals in our industry. To help you navigate the comprehensive program agenda, we have segmented the concurrent sessions into subject matters, including:

- Development Science
- Manufacturing Process Science
- Manufacturing Science
- Media Fills
- Microbiology
- Process Analytical Technology
- Process Development
- Process Validation
- Quality by Design
- Quality Science
- Rapid Micro Methods
- Risk Management

In addition to the extensive program agenda, PDA provides attendees with several formal and informal networking opportunities. These strategically placed gatherings allow you to interact with your speakers and peers in an idea exchanging environment to help you generate solutions for your specific challenges.

I encourage you to review the 2010 agenda to learn more about these program offerings and so much more. Be a part of the influential dialogue and join us in Orlando, Florida for the 64th PDA Annual Meeting.

Sincerely,

Richard M. Johnson
President, The Parenteral Drug Association (PDA)

P.S. Request a brochure today! Simply fill out the form online and you'll receive a hard copy of the *2010 PDA Annual Meeting* brochure by mail. Flip through the brochure to find a special message from the Program Chair, descriptions of sessions and presentations, details on the PDA TRI courses and post conference workshop, exhibition, networking events and more!

Trying to get Noticed??

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. A **business-card size advertising opportunities in our newsletter; at a cost of $100 per newsletter.**

The 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, and regulatory.**
- **We promote the newsletter at New England PDA's bi-monthly dinner meetings, often with company tours, which regularly attract 50-100 attendees.**
- **We post the newsletter on our chapter's website at Global PDA (www.pda.org), an organization that has over 10,000 members.**

Deadline	Publication Date
April 15, 2010	May 2010
July 15, 2010	August 2010
Oct 15, 2010	Dec 2010

If you are interested in advertising in the newsletter or need more information, contact Melissa Smith at melissa@mjqualitysolutions.com