



Ms. Angela G. Long  
Executive Secretariat  
The United States Pharmacopeial Convention, Inc.  
12601 Twinbrook Parkway  
Rockville, MD 20852

REF: 11-13-011-PS

Dear Ms. Long,

In August 2009, FDA issued a guidance for industry on *Pharmaceutical Components at Risk for Melamine Contamination*. In the guidance was a list of drug product components at risk for melamine contamination, including Gelatin, NF. Gelatin was included in the list because it might be tested for total nitrogen to estimate its protein content, and then sold on that basis. The presence of melamine, a nitrogen rich compound, in gelatin might then falsely increase the reported protein content, as was experienced in the melamine adulteration of infant formula in China in 2008 and pet food ingredients imported from China into the U.S. in 2007.

The Gelatin Manufacturer's Institute of America (GMIA) requested that FDA remove gelatin from the list of components at risk, and submitted the following laboratory study report and supplemental comments to the guidance's public docket in support (docket documents can be accessed at: <http://www.regulations.gov/> - !documentDetail;D=FDA-2009-D-0354-0011):

- Melamine Spiking Study Technical Report - *The Impact of Melamine Spiking on the Gel Strength and Viscosity of Gelatin*
- GMIA's Supplemental Comments on *FDA Guidance for Industry, Pharmaceutical Components at Risk for Melamine Contamination, August 2009*

FDA has evaluated the melamine spiking study and other information submitted by GMIA and has conducted additional analytical studies to investigate further. The FDA studies include evaluations of several analytical methods to detect the presence of melamine spiked into samples of NF-grade gelatin. Two methods, powder x-ray diffraction (PXRD) and near-IR spectroscopy (NIRS), were found capable of producing accurate, quantitative measurement of melamine in gelatin in a reasonable timeframe, at levels greater than 1% w/w. More commonly-available methods found suitable of qualitative assessment of melamine in gelatin included Fourier transform infra-red (FT-IR) and Fourier transform Raman (FT-Raman) spectroscopy. This study data will be provided to you upon request.

We recommend that, as part of the general monograph modernization effort, USP consider adding a new analytical test or tests, as above, to the Gelatin, NF monograph. As noted in USP General Chapter <197>, IR and UV tests have general applicability to identification testing, and can be useful in detection of contaminants such as melamine. Additionally, we think that revision of the current *Identification* (Test B) might be useful so that it could qualitatively detect

the presence of certain adulterants, such as melamine, that can alter the physico-chemical characteristics of gelatin.

We suggest that representatives of our Melamine/Gelatin Working Group meet with USP Monograph Modernization staff to discuss in greater detail. Please let us know what might be a convenient date and time for you. Our FDA liaisons to the USP Excipients Expert Committee can also assist in this effort and provide additional technical information as it is needed.

Best regards,



Larry A. Ouderkirk  
Co-Chair, Monograph Modernization Task Group  
Office of Compliance  
Center for Drug Evaluation & Research



Paul Seo, Ph.D.  
Co-Chair, Monograph Modernization Task Group  
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