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March 29, 2013

Matthew Van Hook, J.D.
Vice President and Assistant General Counsel
US Pharmacopeia ("USP")
12601 Twinbrook Parkway
Rockville, MD 20852-1790

Re: General Notices Section 5.60.30 Elemental Impurities in USP and NF Articles
Pharmacopeial Forum, Vol. 39(1) [Jan.-Feb. 2013]

Dear Mr. Van Hook:

On behalf of the Consumer Healthcare Products Association (CHPA), a 131 year-old trade association representing the nation's leading over-the-counter (OTC) medicine and nutritional supplement manufacturers, I'd like to thank you for the opportunity to comment on U.S. Pharmacopeia's proposed new provision in **General Notices 5.60.30: Elemental Impurities in USP and NF Articles, Published for Comment in *Pharmaceutical Forum* 39(1) Jan-Feb 2013.**

CHPA supports improving the compendial test methods and establishing product standards for levels of elemental impurities which can provide an additional measure of safety for OTC products. CHPA supports the improvement of elemental impurity analysis but is concerned with the proposed May 2014 implementation date for the current content of chapters <232> and <233>. CHPA believes that USP and FDA must address several items to minimize the impact to the business and prevent possible shortages of OTC products. Furthermore CHPA believes that the implementation of these chapters must be aligned with the implementation of the ICH Q3D guideline when it is completed.

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We strongly recommend that USP reconsider the May 2104 implementation date until there is clear guidance available from FDA concerning interpretation of analytical results and subsequent application to risk assessment. We propose an implementation date 2 years after the FDA guidance has been established and any additional changes that must be made to the USP chapters to harmonize with ICH Q3D have been made official. This interval would allow the industry time to understand the guidance and how it effects the requirements in <232>, and determine if additional formulation or testing of products is necessary to assure compliance.

While methodological burdens of variable matrices, sample digestion options and validation difficulties currently face CHPA members, PDE limits for different routes of administration and compliance options are also unknowns. The FDA guidance should allow scientific analysis of bioavailability studies to be incorporated into a risk assessment. The companies we represent produce products in multiple dosage forms (creams and ointments) with undefined daily dosages ("use as required"). Our member companies need a clear path towards submitting revised modern product monographs when their products cannot meet the specifications in <232> but are deemed safe after an appropriate risk assessment has been executed. Some products could require 2 years for reformulation and reregistration where required.

Additionally CHPA finds that there is widespread confusion concerning the responsibility of the industry to test ingredients as well as products. Chapter <232> does little to clarify (for example: "The limits presented in this chapter do not apply to excipients and drug substances….However, elemental impurity levels present in drug substances and excipients must be known and reported"). CHPA believes <232> or FDA guidance on evaluation of elemental impurities should clarify what is expected for compliance. CHPA believes levels in finished product, rather than specifying what is tested is most important.

Many of our companies are setting specifications for worldwide distribution and while we understand that USP will harmonize with ICH Q3D when ICH has finalized the guidance, having a path forward and a defined process with parallel timelines for the <232> chapter to reflect the ICH Q3D document is critical to ensure an uninterrupted product supply. OTC and dietary supplement manufacturers request regulatory certainty to ensure consistent product development

timelines and maintain quality and safety standards. These products provide meaningful health benefits to consumers at affordable prices. Manufacturers of OTCs need the confidence that they will not be subjected to a patchwork of USP requirements that could conflict with ICH Q3D. Subjecting these products to additional regulation could result in products disappearing from the marketplace, even temporarily, and restrictions on ingredient use that are inconsistent with their long history of safe use.

In summary, CHPA supports improving USP test methods and establishing specifications for elemental impurities which can provide an additional measure of safety for OTC products. CHPA supports the improvement of elemental impurity analysis but is concerned with the proposed May 2014 implementation date for the current content of chapters <232> and <233>. CHPA believes that the industry will require 2 years for compliance after publication of FDA guidance on Elemental Impurities in Drug Products. Furthermore a clear path towards revising or proposing a USP monograph for products that cannot meet <232> specifications but are deemed safe is needed as well as a process that will clearly align with the implementation of the ICH Q3D guideline when it is completed.

CHPA appreciates the opportunity to comment on the proposed revision. I am happy to speak to you about this issue at greater length and detail. Feel free to contact me directly at your convenience.

Best Regards,

John S. Punzi, Ph.D.
Director Quality Assurance and Technical Affairs

Cc: Todd Cecil, Ph.D., (USP)