CHPA CONSUMER HEALTHCARE PRODUCTS ASSOCIATION
founded 1881

April 03, 2015

Alan Potts
Principal Scientific Liaison
US Pharmacopeia ("USP")
12601 Twinbrook Parkway
Rockville, MD 20852-1790

Re: **Proposals for Developing Compendial Quality Standards for OTC Drugs. *Pharmacopeial Forum*, Vol. 41(1) [Jan-Feb 2015]**

USP Correspondence Number—C150881, C150882, and related Stimuli article (Medicines Marketed under the Food and Drug Administration Over-The-Counter Drug Monograph System Regulations: Strategy for Developing Compendial Quality Standards)

Dear Dr. Potts:

On behalf of the Consumer Healthcare Products Association (CHPA), a 134 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 **proposals for developing compendial quality standards for OTC drugs. *Pharmacopeial Forum*, Vol. 41(1) [Jan-Feb 2015].**

CHPA supports improving the compendial test methods and establishing product standards for outdated or "missing" monographs which can provide an additional measure of safety for OTC products. As you know one of the challenges in developing public standards for these products is the total number of OTC drug products. We think there may be as many as 100,000 items and the list is comprised of products which are frequently reformulated. If the USP's goal is to develop a monograph for each marketed product then obviously a "one product one monograph" approach will be an enormous task. CHPA supports developing a comprehensive strategy to develop appropriate public quality standards using product monographs for some attributes ("thin monographs") and capturing the assay and identity, and specified impurities procedures in two general chapters, but is concerned that the current content of the proposed general chapters

‹321› and ‹322› is too ambitious. CHPA believes that USP (working closely with FDA) must address several items to minimize the impact to the OTC drug industry and prevent possible shortages of OTC products.

We believe that an evolutionary or step wise approach to developing the general chapters in concert with a USP small molecule expert panel should be considered. CHPA members and USP can develop standards for single active ingredients in multiple formulations before moving to products containing multiple active ingredients, using the chapter approach to capture the procedures as appropriate. As you have indicated in proposed general chapter ‹321›, if different preparation procedures are needed for the different formulations it could be captured in the product monograph.

Although the general chapter approach has the advantage of serving as a place to store robust procedures that can be validated for multiple formulations and as a result do not have to be duplicated in different places in USP-NF, CHPA believes the chapters will need to be constantly revised as new formulations of products are determined not to be amenable to the chromatographic procedure described. Based upon the rapid innovation and diverse formulations in OTC products how can a regulatory authority conclude that a stakeholder's product complies with the methodology provided in the current official general chapter? While we recognize that our companies may work with the USP to modify the general chapter (or monograph) to allow for compliance, it is not reasonable for a company to delay marketing a product while working through the USP revision process on repetitive general chapter updates.

We appreciate that our members may use alternate analytical methods for demonstrating compliance. However, if a regulatory body conducts product surveillance or investigational testing employing the current compendial method, this results in a product at risk of not meeting the established criteria. CHPA believes that a clarification of the FDA's enforcement approach is required in order for stakeholders to comply with the proposed general chapter approach.

Furthermore CHPA believes that USP must also consider the impact of the proposed general chapters on other regulatory authorities and organizations outside of the United States which tend to be more rigid in their interpretation and enforcement of USP-NF.

To a large extent and for a number of reasons the USP compendial methods are typically not used on a routine basis for product manufacturing and release testing. We recommend that the USP continue to work with stakeholders to understand the practical usage and implementation of USP-NF test methods

in the routine manufacturing environment. While the FDA and USP clearly state that alternate methods can be employed, the USP test is the official test in the case of disputes. We encourage USP to work with FDA enforcement and compliance officials to develop appropriate compendial standard methods which leverage the accumulated experiences of manufacturers and their products.

CHPA members have reservations about requiring UPLC for the compendial method as described in ‹321› and ‹327›. Some of our members have communicated to USP confidential product-specific problems with the method in ‹321› when applied to their products. We are also aware of differences in chromatographic behaviors of identical samples on different brands of UPLC instruments and many companies simply do not have these devices in the QC laboratories. UPLC is of course being widely used but currently primarily in an R&D role and not commonly found in the QC environment. The impact to the industry is not small. To demonstrate the equivalency of a current QC HPLC method to the proposed UPLC method may cost as much as $50,000 for a contract laboratory to perform which is a disproportionate amount for some of our smaller companies to bear. The concern of compendial methods relying on UPLC is not restricted to smaller companies. In fact some of the largest CHPA members have already purchased UPLC but they have not been fitted with PDA-UV detectors therefore the proposed ID test would not be able to be performed. There is also concern about the readiness of existing chromatographic data systems and whether their design allows for the collection and saving of the UV-spectra associated with the proposed ID test. A second ID test (presumably intended for enforcement activities) should be proposed in collaboration with the appropriate FDA division.

CHPA is well aware that the addition of new OTC product monographs into USP-NF will potentially cause confusion with product naming. In the absence of an official monograph members have been very careful to meet the FDA labeling requirements as described in the appropriate FDA monograph. We understand that the name established in the compendia should be included on the labeling of the product but the FDA has historically practiced enforcement discretion in this area for OTC products. We cannot emphasize enough how critical it is that the USP work closely with stakeholders (perhaps through CHPA) and include the FDA to ensure that the compliance risk is minimized and that the definitions and usage of the established names is clearly understood as product monographs are developed.

In summary, CHPA supports improving the compendial test methods and establishing product standards for outdated or "missing" monographs which can provide an additional measure of safety for OTC products. The challenges in developing public standards for as many as 100,000 items are substantial and developing a comprehensive strategy to develop appropriate public quality standards

using product monographs for some of the attributes and capturing assay, identification and specified impurities into general chapters is appropriate.

We believe that an evolutionary approach to developing the general chapters in concert with a USP small molecule expert panel should be considered. CHPA members and USP can develop standards for single active ingredients in multiple formulations before moving to products containing multiple active ingredients. A clarification of the FDA's enforcement approach is required in order for our members to comply with the proposed general chapter approach.

CHPA members have reservations about requiring UPLC for the compendial methods for technical and the practical reason that many companies will be burdened by adding these devices to the QC laboratories or contracting with an outside lab to demonstrate an established method is equivalent to a UPLC method.

We understand that the official name established in the compendia should be included on the labeling of the product but the FDA has historically practiced enforcement discretion in this area for OTC products and it is critical that the USP work closely with stakeholders to ensure that the compliance risk is minimized.

CHPA appreciates the opportunity to comment on the proposed revisions. 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: Jon Clark