CHPA® CONSUMER HEALTHCARE PRODUCTS ASSOCIATION
founded 1881

September 09, 2016

Robert Femia, Ph.D.
Leonel Santos, Ph.D.
U.S. Pharmacopeial Convention ("USP")
12601 Twinbrook Parkway
Rockville, MD 20852-1790

Re: Multiple Active Ingredient Product Monographs (Correspondence Numbers: 160310, 160309, and 160308).

Dear Drs. Femia and Santos:

On behalf of the Consumer Healthcare Products Association (CHPA), a 135 year-old trade association representing the nation's leading over-the-counter (OTC) medicine and dietary supplement manufacturers, I'd like to thank you for the opportunity to comment generally on proposed monographs for pharmaceuticals not regulated by a NDA or ANDA and specifically on three product monograph proposals containing multiple active ingredients proposed in Pharmacopeial Forum 2016: 42(4). Our members are requesting a delay in the deadline for submitting comments of 90 days since additional time is needed to obtain the materials required to properly evaluate the suitability of the methods and consider any compliance impact on their products containing these compounds. In addition, the three proposed monographs appear to be in conflict with the approaches that the USP has discussed previously within the USP/FDA/CHPA OTC project team. Due to the complexity and variety of assay and impurity methods across the industry that are used for multi active drug products, we propose that USP and its stakeholders identify and attempt to resolve any potential compliance issues early in the monograph development process, well before publication of a final draft monograph.

Acetaminophen, Guaifenesin, Dextromethorphan Hydrobromide, and Phenylephrine Hydrochloride Tablets; Acetaminophen, Guaifenesin, and Phenylephrine Hydrochloride Tablets and; Acetaminophen, Phenylephrine Hydrochloride, Chlorpheniramine Maleate, and Dextromethorphan Hydrobromide Oral Suspension are new product monographs proposed in PF 42(4). These combined proposals represent five active ingredients and contain 11 different impurities, including precise limits for unspecified and total impurities.

To properly evaluate the appropriateness and compliance impact on our products, several different chromatographic methods need to be evaluated along with the proposed dissolution test for each applicable product.

Reference standards for the tests are not readily available for all of the impurities. For example, obtaining Dextromethrohan-10-ol, has been problematic. To our knowledge the only known source is from Canada where dextromethorphan and related substances are officially classified as controlled substances. In order to obtain the reference standard, a "no objection letter" is needed from the Drug Enforcement Administration (DEA) which must then be sent to the vendor in Canada. The vendor, in turn, must file the letter with Canadian authorities before the substance can be ordered. Further delays can be experienced since the substance must clear through customs. CHPA members have stated that additional time is needed to obtain all the materials necessary to evaluate these proposals and request a delay for submitting comments of an additional 90 days.

CHPA acknowledges that the USP has standard procedures for evaluation of sponsor submitted data and needs to publish them in the PF as proposals for comment by stakeholders. To help accommodate effective monograph development, CHPA recommends a novel pathway to allow our members to help the USP in the monograph development process. For complex multi active OTC products, CHPA is proposing that prior to publication in the PF that the USP publish notification that the USP has initiated a work plan on a specific multi active OTC product and that companies may submit their methods for similar products prior to a proposed date. As you know this type of industry cooperative has been very successful through CHPA in development of 4-AP standards for acetaminophen drug substance and acetaminophen containing drug products.

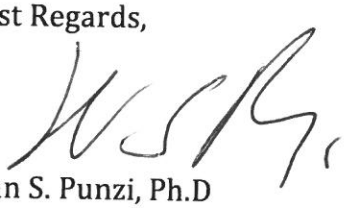
We can envision a number of ways to initiate this activity but public notification on USP's web site of the initiation of a monograph proposal could occur; prior to the USP initiating their own work on a multi active OTC product monograph; prior to expert committee review of a multi active OTC product monograph proposal provided by an industry stakeholder or; prior to publication of a sponsor's submission.

As you know CHPA supports improving the compendial test methods and establishing product standards which can provide an additional measure of safety for OTC products. CHPA generally supports the improvements included in recent monograph revisions but is concerned that the USP OTC Expert Committee (CM6) has not gained alignment on an approach to USP monograph modernization including setting limits for single unspecified impurities, total impurities and how to consider formulation variations in OTC products which as you know are frequently changed. Once alignment has been reached, and an

appropriate approach determined, CHPA suggests this approach be clearly communicated to industry.

I am happy to speak with you about this issue at greater length and detail. Feel free to contact me directly at your convenience.

Best Regards,



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