CHPA® CONSUMER HEALTHCARE PRODUCTS ASSOCIATION
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September 18, 2014

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

Re: OTC Product Monographs

Dear Dr. Potts:

On behalf of the Consumer Healthcare Products Association (CHPA), a 133 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 draft publication: Over-the-Counter (OTC) Medicines Marketed under the Food and Drug Administration's Over-the-Counter (FDA OTC) GRASE Regulations: Strategy for Developing Compendial Quality Standards prior to publication in Pharmacopeial Forum.

CHPA is generally supportive of the proposal to rely on a general chapter structure and publishing quality standards for new compendial drug product monographs. We would however request that the publication of Chapters <321> and <327> be delayed until a number of errors and technical details can be addressed. USP is aware of a number of issues with the proposed assay and impurities chapters (e.g. it is very ambitious and complicated, is basically not QC friendly, has interferences with known excipients including flavors, uses UHPLC and does not offer an HPLC alternative and may not work on different brands of UHPLCs without condition modification).

While many drug substances and drug products have USP monographs with assay specifications and identification methods, frequently the USP monographs lack specifications and methods for determining process impurities and degradation products.

Also USP drug product monographs for many of the active ingredient combinations currently marketed do not exist. Developing USP product monographs with generally applicable methods for assays for drug active ingredients and degradation products is quite challenging and was the driving force behind the CHPA's Monograph Modernization Committee and subsequently the OTC Project Team.

We recommend that the chapter <321> approach focus on a smaller set of actives that are coordinated with the efforts of CHPA's Monograph Modernization Committee OR a USP expert panel with support from the OTC Project Team. These include acetaminophen, diphenhydramine (HCl and citrate), pseudoephedrine (HCl and sulfate), chlorpheniramine maleate, phenylephrine HCl, and dextromethorphan (HBr), guaifenesin and doxylamine succinate.

The CHPA Monograph Modernization Committee is currently working to develop a set of recommended degradation products for the actives found in cough and cold products. CHPA currently has data from a number of companies and hopes to soon have up to a total of eight. From this effort the Monograph Modernization Committee hopes to define the major degradants of concern which could pave the way for methods to cover impurities for a proposed group.

By focusing on the above active ingredients the group assay and impurities general chapters would encompass the majority of cough/cold product combinations currently marketed. We think this smaller group would also create a more robust set of methods and increase the chances of success.

In summary, CHPA strongly supports improving USP test methods to establish specifications for drug substances and drug products. Modern assay and impurities methods can provide an additional measure of safety for OTC products. CHPA supports the draft proposal for a strategy using a general chapter approach for grouping products but suggests narrowing the current scope of the chapter <321> relative to the smaller set of

actives listed above and delay <327> until the data are available for the cough and cold products. See Attachment 1 for specific comments.

CHPA appreciates the opportunity to comment on the proposed general chapter approach to OTC monograph modernization. I am happy to speak with you about this issue at greater length and detail. Feel free to contact me directly at your convenience. I have attached more detailed comments addressing the stimuli article below.

Best Regards,

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

ATTACHMENT 1

Introduction:

Recommend reducing the content to focus on the basic interest in exploring alternatives to traditional USP product monographs for OTC's. The discussion as written could be misinterpreted with a negative view towards the FDA systems, a goal to move forward instead of evaluating the new approach, or that the USP OTC monographs are a priority over other USP/NF monographs.

Is the USP OTC product monograph the proper classification? If a current OTC product not regulated by NDA/ANDA adds a label claim that triggers an NDA, the same USP monograph would presumably apply. Perhaps USP needs to consider having monographs developed to cover OTC products not regulated by NDA/ANDA but not necessarily limited to them once they become official. For existing USP monographs would the new general chapter method get added to it? Existing USP monographs have validated content and chapter proposals are not validated for every application. Interfering with existing content during initial development may be too ambitious for this proposal.

We strongly suggest an example of the USP monograph proposal that would demonstrate the general chapter approach be published at the same time as the stimuli article.

USP Role in Law:

The USP role in the law is described in the general notices and there is apparently no proposal here that changes this position. The 2 pages of information is in some sections redundant, others not clear and not adding value, and detracts from the focus of the proposal - we suggest that this section be deleted.

Identification and Assay Procedures:

These tests are not validated to every application and apply advanced technology. In addition to lacking flexibility to handle interfering excipient peaks, there needs to be flexibility in the chapters to acknowledge their limitations and clearly allow other methods.

Line 254-266:

Bullet 1, Testing is a means of monitoring not control. Additionally, there is no change in the role of a USP monograph, everything from "bolstering..." on should be deleted.

Bullet 3, Modern technologies is not an advantage as it may interfere with current testing.

Bullet 5, Delete - Efficiencies in the USP lab will not be reflected within the industry and is not a justification for developing a public standard.

Table 1, Remove preservatives from the list.

Section 4.2 – "Bucket" testing should be based on logical collection of products and product ingredients and not an interpretation based on the analytical applications.

Line 290-295 – Adulteration of an API should be controlled with the API not the product.