



founded 1881

February 2, 2011

Re: CHPA's Commitment to the USP Monograph Modernization Process

Dear members of the FDA/ USP/ CHPA Planning Committee on USP Monograph Modernization,

The Consumer Healthcare Product Association (CHPA) and its members, the manufacturers and developers of over-the-counter (OTC) medicines, recognize the need for modernization of U.S. Pharmacopeia (USP) monographs. CHPA believes it is imperative that the U.S. Food and Drug Administration (FDA), the USP, and the pharmaceutical industry partner in this effort to improve the quality of the USP monographs.

CHPA believes that modernization should be part of an overall process of compendial harmonization. It is hoped that USP shares the view that harmonization is the objective for all modernization activities. Therefore the changes advocated by the stakeholders should not be in conflict with other global compendial formats.

USP has identified 332 small molecule prescription and OTC ingredient and dosage form monographs that must be modernized.¹ FDA has focused on OTC drug dosage form monographs that do not appear to address degradants. CHPA seeks a course of action that is timely yet allows for a phased-in approach. To address the priorities of all three stakeholder organizations, CHPA member companies have aligned to propose the following path forward:

1. FDA identifies and prioritizes OTC drug products that require additional control of degradants.
2. Based on #1, USP identifies and prioritizes applicable OTC monographs.
3. A team with representatives from the three stakeholder organizations (FDA, USP and CHPA) will be assembled to propose draft modernized monographs that will proceed through the established Pharmacopeial Forum (PF) process. CHPA will identify industry experts for each identified monograph to participate in the modernization project.

Consumer Healthcare
Products Association
900 19th Street, NW, Suite 700
Washington, DC 20006
† 202.429.9260 ✉ 202.223.6835
www.chpa-info.org

Proposed FDA Role

FDA is the driving force in this effort. CHPA believes that FDA's role is clearly to identify and prioritize OTC drug products in need of modernization based on consumer exposure data (market volumes) for the ingredient/ drug product in question and on toxicity of specified degradants. FDA should also offer the degradant limit for each ingredient/ drug product on their prioritization list, with due consideration and transparent communication of appropriate scientific/toxicological data. CHPA recommends that FDA's involvement extend throughout the modernization process to provide continued guidance.

Proposed USP Role

USP has a robust process in place for collecting and vetting updated scientific information. We propose that USP should translate FDA's priority list of products/degradants into a prioritized list of monographs that require updating either individually or as monograph families. USP should then use existing or unique approaches to form teams (expert panels) comprised of subject matter experts (SMEs) from the three stakeholder organizations to develop modernization strategies and implement those strategies. USP should assure that these monograph modernization improvements go through public review as this process provides the most widely accepted and most robust final product.

Proposed CHPA Role

Consumers expect and deserve the highest quality medicines. To ensure safe and effective medicines, CHPA companies take aggressive, proactive actions toward improving quality. CHPA is committed to working with USP and FDA to achieve a more up-to-date public standard.

CHPA will identify and provide industry experts to participate on each USP team (expert panel) who will provide expertise and laboratory support (scope to be decided on case-by-case basis) as part of that team.

Currently, we have established a working group of member companies dedicated to addressing the need for modernization of USP monographs with a focus on specific degradants linked to OTC drug products. The working group will propose and submit revisions to USP of existing monographs and/or new General Chapter(s) specific to one or more monograph families with attention to specific degradants.

The first monograph revision should be based on the "prioritization list" in FDA's letter to USP. The FDA has classified certain acetaminophen and diphenhydramine monographs as a priority due to their degradant profiles. At this point, the list has not yet been shared with CHPA or CHPA member companies. We realize that our commitments will fully materialize once a thorough evaluation of the "prioritization list" is completed.

The CHPA working group will propose degradant standards in a prioritized approach. Our commitment includes a first phase proposal of modernized monographs that specify 4-aminophenol limits or a general chapter on 4-aminophenol, a common impurity formed in the degradation of acetaminophen.

This could be used as a model for subsequent modernization activity. CHPA will also establish a working group focused on product degradants of diphenhydramine. Evaluation of additional degradants, other than those identified by FDA as a primary concern, will be made by the CHPA working groups depending on the monograph and drug product in question.

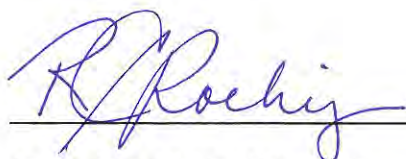
In parallel to CHPA activity, CHPA member companies are also encouraged to work directly with USP on monographs in need of modernization.

CHPA notes that the ICH Q3B (R2) guideline is intended to provide guidance on impurities in “new drug products produced from chemically synthesized new drug substances not previously registered in a region or member state...” CHPA is interested to clarify and discuss the appropriateness/applicability of ICHQ3B to OTC monograph drug products. To that end, CHPA has brought together company experts and toxicologists to develop a series of white papers, not specific to any one ingredient, to add clarification for OTC product manufacturers around the guidance offered in ICH Q3B (R2).

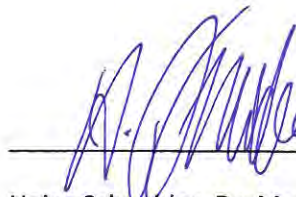
In Conclusion

Participation from all stakeholders is vital for successful identification, prioritization, modernization and implementation of USP monographs for OTC products. This extensive initiative requires all 3 stakeholders (FDA, USP and CHPA) involvement throughout the process and should be carried out in phases to ensure full understanding and acceptance of the monograph modifications as well as successful industry compliance.

1. Small Molecules and Excipients Monographs Needing Modernization. December 22, 2010. U.S. Pharmacopeia <http://www.usp.org/USPNF/submitMonograph/improveMon.html>, January 20, 1010.



Rachael Carlisle Roehrig, Ph.D.
Director, Technical & Scientific Affairs, CHPA



Heinz Schneider, Dr. Med
Vice President, Science & Medical Affairs