CHPA CONSUMER HEALTHCARE PRODUCTS ASSOCIATION
founded 1881

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Food and Drug Administration
Division of Dockets Management (HFA-305),
Food and Drug Administration, 5630 Fishers Lane, rm. 1061
Rockville, MD 20852
Docket Number FDA-2016-D-1490

Dear Madam or Sir:

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 on FDA's request for comments concerning Quality Attribute Considerations for Chewable Tablets Guidance for Industry.

The availability of safe and effective, easy-to-use dosage forms is not only important in clinical practice but chewable tablets are available for many OTC products as well. We are supportive of these efforts to establish guidance for critical quality attributes for chewable tablets that could include hardness, disintegration, as well as other factors that may influence product safety.

Our member companies generally support the recommendations found in the guidance but have concerns about the scope of hardness measurements and maximum break strength value; the need for tablet dissolution studies; conformance to the Scale-up and Post-Approval Changes Immediate Release document (SUPAC-IR); and the Agency's expectations for "chewing evaluation" studies.

Hardness:

As a general test, hardness is appropriate for compacted, low moisture, chewable tablets but may be irrelevant (or even unmeasurable) for other types of chewable tablets. For example, ***soft*** chewable tablets are intended to have a higher moisture content, more pliability and may demonstrate different responses to physical stresses than ***hard*** chewable tablets. Measurements such as compressive extrusion, gumminess, puncturability (or firmness), and elasticity are much more relevant measurements for these types of dosage forms.

CHPA recommends that the agency expand the scope of "Hardness" to include other textural and mechanical measurements relative to the specific composition of the dosage form.

CHPA does not support proposing a maximum value of ≤12 kiloponds (kp) for tablet break strength hardness at this time. As the Agency notes, higher values are likely appropriate if after brief exposure to saliva, the tablets disintegrate or demonstrate significant loss of hardness. We are aware of companies which have approved ANDAs that include target hardness ranges above the proposed limit that have years of safety data which indicates that the AE concerns listed in the guidance may not be warranted for that specific product. While the agency provides a single example of simulated salivary fluid and a small range of experimental parameters, the producers of non-application products will not have the opportunity to work with FDA reviewers to discuss the ranges of approaches allowed within the guidance. CHPA recommends that FDA work with the OTC industry to develop a better understanding of the data that exists within the OTC industry concerning chewable tablets before proposing the recommended limits in this guidance. We would be happy to meet with the Agency to provide input and present information concerning industry practices and consumer survey data. Considering a product with an approved application, what data or steps would be necessary for the Agency to consider providing an exemption if the tablet break strength were outside of the proposed limits?

Disintegration/Dissolution

We agree that a variety of physical characteristics should be considered in the manufacturing process for a chewable tablet; however, dissolution is normally considered a bioavailability indicator and we believe disintegration is the more appropriate test in order to demonstrate the

physical breakdown of the tablet for this guidance. Tablet disintegration held to an IR standard is likewise appropriate for bioavailability, and may not however be appropriate as longer times may be tolerated before a safety risk is incurred. For example, over 10 USP Monographs for chewable tablets contain dissolution specifications of 45 minutes or longer (see USP Monographs: for Alumina, Magnesia, and Calcium Carbonate; Famotidine; Acetaminophen and Pseudoephedrine Hydrochloride Chewable Tablets (45 minutes) or 60 minutes for Carbamazepine Tablets).

Performance in Simulated Physiological Media

The Agency provided a single reference for a method to determine a chewing difficulty index along with a non-standard "recipe" for artificial saliva as a guide to the performance evaluation of chewable tablets. CHPA members can provide the Agency with a substantial body of references and data which can translate into a better understanding of the performance of chewable tablets. CHPA recommends that FDA meet with representatives of the OTC industry before finalizing the recommendations in this guidance. We believe this is especially important considering the manufacturers of products that are marketed without an NDA or ANDA do not have an opportunity to work directly with an Agency reviewer as can be done with an application submission.

Post-Approval Considerations

CHPA agrees that while the principles found in the guidance document "Scale-up and Post-Approval Changes Immediate Release" are generally applicable to all chewable tablets, guidance within the document referring to changes in formulation appear to be more specific to hard chewable tablets (as defined by USP <1151>) than to soft chewable tablets in general. Some excipient categories listed, such as lubricant and film coat, are irrelevant to many soft chewable tablet dosage forms that are extruded or deposited and additionally, other categories of excipients exist with soft chewable tablet dosage forms for which sound guidance is not found (gel forming excipients, texturizers such as fats and oils, and non-film forming coatings). There is concern that reference to the SUPAC-IR may cause confusion amongst product developers and manufacturers of non-compacted dosage forms to inappropriately categorize excipients found

within their dosage forms to a specific excipient category found within the SUPAC-IR. For example, a firm may inappropriately categorize gum acacia as a filler due to lack of a more appropriate excipient category. SUPAC-IR's purpose is to maintain in-vivo bioequivalence through various principles including in-vitro dissolution testing. Since the goal for chewable tablets is efficacy in the chewed form, the guidance should be amended to include safety implications from un-chewed dose forms. CHPA recommends that an addendum to the SUPAC-IR be drafted to help broaden the guidance to include safety considerations from off-label (un-chewed) use and non-compacted chewable dosage forms.

In summary, the critical quality attributes described in the guidance that should be considered when developing chewable tablets does not appropriately address non-application OTC products in general, OTC products with approved ANDA's with higher than proposed tablet hardness values, and specifically does not consider non-compacted chewable dosage forms. The OTC industry is willing to work with the Agency to help develop recommendations in the guidance and select criteria that are appropriate and meaningful indicators of chewable tablet product performance throughout the shelf life of these important dosage forms.

Best regards,

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