On Thursday, June 17th the FDA issued a draft guidance entitled “Quality Attribute Considerations for Chewable Tablets.” The document “describes the critical quality attributes that should be considered when developing chewable tablets and recommends that the selected acceptance criteria be appropriate and meaningful indicators of product performance throughout the shelf life of the product.”

What are “Chewable Tablets”?
According to the FDA, “chewable tablets are an immediate release (IR) oral dosage form intended to be chewed and then swallowed by the patient rather than swallowed whole.” The Agency notes that tablets should:

- Have a pleasant taste
- Be easily chewed and swallowed
- Be safe and easy to use in a diverse patient population

**Types of Chewable Tablets**

Many over-the-counter (OTC) and prescription drug products are available in the form of a chewable tablet. According to the draft guidance, “the United States Pharmacopeia (USP) recognizes and differentiates between two types of chewable tablets:

1. Those that may be chewed for ease of administration, and
2. Those that must be chewed or crushed before swallowing to avoid choking and/or to ensure the release of the active ingredient.”

The recommendations in this draft guidance apply to both types.

**Adverse Events**

There are a number of potential adverse events that patients could experience when taking chewable tablets. These can include “gastrointestinal (GI) obstruction resulting from patients swallowing whole or incompletely chewed tablets, as well as tooth damage and denture breakage resulting from excessive tablet hardness. A related potential adverse event that sponsors should also consider is esophageal irritation from chewable tablets.”

**Critical Quality Attributes of Chewable Tablets**

There are a variety of critical quality attributes that should be considered by manufacturers of chewable tablets. These include hardness, disintegration, and dissolution, in addition to any other factors that could influence the bioavailability and bioequivalence of the drug. FDA states that “careful attention should be given to tablet size, thickness, and friability, as well as taste, which may impact the ability or willingness of a patient to chew the chewable tablet (i.e., a patient may swallow whole, rather than chew, a bad tasting tablet).”

Manufacturers should not consider one characteristic more heavily than another, but rather “the goal should be to develop the proper combination of these attributes to ensure the performance of the chewable tablet for its intended use.”

**Hardness**

FDA notes that “the hardness of chewable tablets should be such that they withstand the rigors of manufacturing, packaging, shipping, and distribution, as well as be easily chewed by the intended patient population.”

There are many units in which tablet hardness may be measured and expressed; FDA
recommends that manufacturers “use the same unit of measure in reporting results and specifications.”

**Disintegration**

A product’s disintegration time is defined as “the time required for a tablet to break up into small particles.” In its draft guidance, FDA states that the disintegration time for chewable tablets should be short enough to prevent GI obstruction if a patient fails to chew the tablet completely.

Manufacturers should conduct in vitro disintegration testing using intact tablets and established disintegration equipment and methods.

**Dissolution**

“Drug absorption from chewable tablets depends on the release of the drug substance(s) from the intact or the chewed tablets; therefore, in vitro dissolution testing of chewable tablets should follow the principles of dissolution testing of conventional IR tablets.”

**Performance in Simulated Physiological Media**

FDA recommends that chewable tablets “be evaluated using dissolution media such as simulated fasted and fed state gastric and intestinal fluids with enzymes.” After exposure to small quantities of human or simulated saliva, the tablet’s hardness should be tested. The draft guidance suggests that the conduct of such studies could provide a better understanding of the tablet’s in vivo performance.

“In vitro testing in physiological media, consistent with the targeted patient population characteristics may support further characterization of the drug product and its critical quality attributes.”

**Biowaiver & Postapproval Considerations**

“The solubility and permeability characteristics of the drug substance may be used to determine where the drug fits within the Biopharmaceutics Classification System (BCS).” Additionally, the document notes that “changes in the chemistry, manufacturing and controls after approval of the chewable tablets should be made in conformance with the principles outlined in the Scale-up and Post-Approval Changes Immediate Release (SUPAC IR) guidance document.”

**FDA Recommendations**

The bulk of the draft guidance is focused on the Agency’s recommendations regarding considerations to take during the development of a chewable tablet. Interested in learning more? Details on FDA’s recommendations are available in our FDA News article entitled “FDA Issues Draft Guidance On Quality Attributes to Consider When Developing Chewable Tablets, Part Two: FDA’s Recommendations.”

Are you in the process of developing an OTC or prescription drug product? We can help you obtain FDA approval. To learn more about our services and how we can help you
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