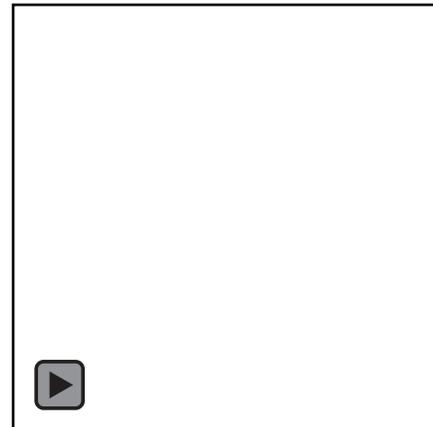


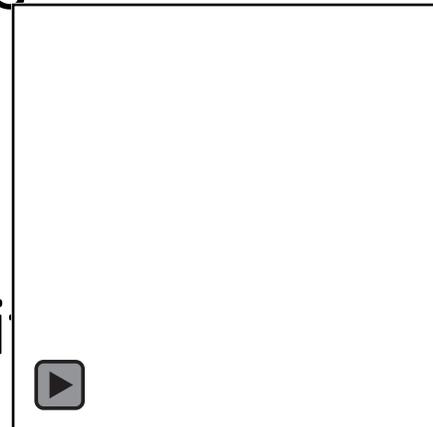
Advancing Regulatory Science for Chewable Tablets

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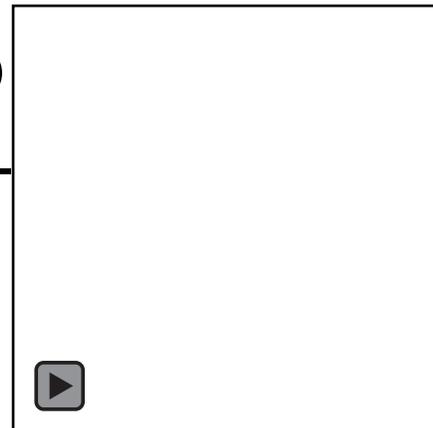
Comparison of Chewable Tablets – Animals vs. Humans

- Flavored Chewable tablets (including extruded tablets) are more common in the veterinary industry.
- Dosage is based on mg/kgbw and can be for multiple species. This can lead to a large range of chewable tablet sizes to bridge bioequivalence (BE) using dissolution, with some tablets weighing multiple grams.
- Species-specific physiological differences.
- Species-dependent toxicity of some excipients (e.g., xylitol)



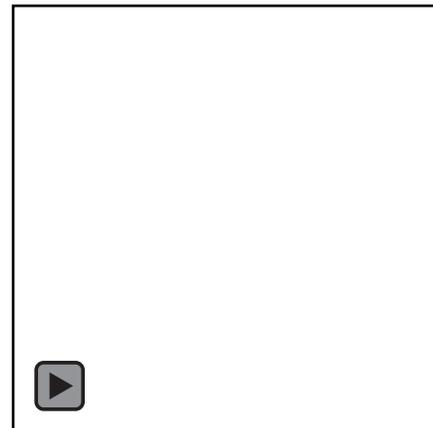
Comparison of Chewable Tablets – Animals vs. Humans

- Flavorings make up a higher proportion of the formulation – >15% in animal drugs vs. <3% in human drugs
- They are intended to enhance acceptability to the animal (i.e., ‘treats’), instead of “masking flavor”.
- Unlike humans who can be convinced to take medication, animals won't consume products they find unpalatable—matter how therapeutically beneficial.



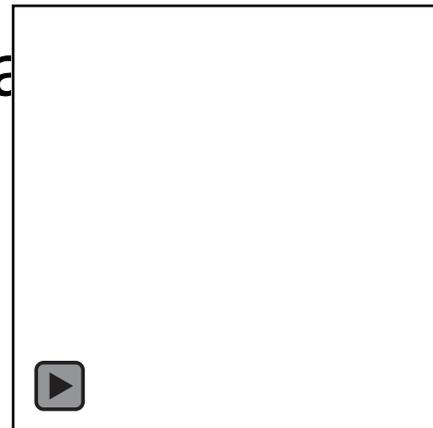
Challenges to address

- What is the impact on *in vivo* bioavailability and dissolution if chewing occurs?
- Due to the large weight range and dosing in mg/kgbw, even within the same species there is a difference in chewing patterns.



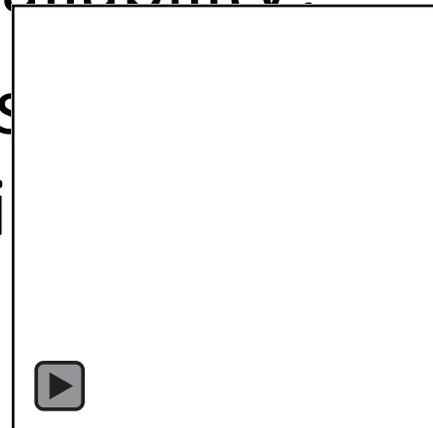
Challenges to address (cont.)

- What are the Critical Material Attributes for extruded chewable tablets?
- What post-approval changes would necessitate additional *in vivo* bioequivalence studies?
- Can any deviation from a common blend be considered for bridging between strengths using a validated, discriminating dissolution method?



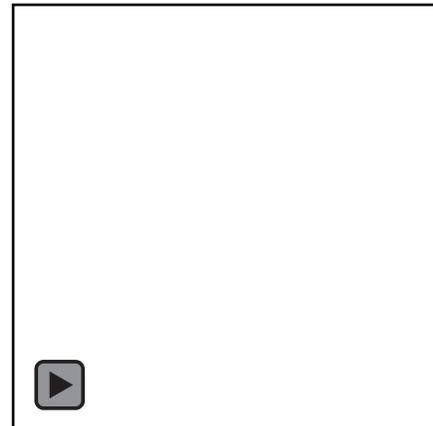
Current Challenges (cont.)

- Flavors can be complex mixtures that may interact with active pharmaceutical ingredients, affect stability, alter dissolution profiles, and potentially impact bioavailability.
- How does variation in flavor components (e.g. fat content, co-processed components vs simple mixture) impact bioavailability?
- With flavorings comprising $\geq 20\%$ of the formulation in some cases, what are the potential impacts on manufacturability, product quality and *in vivo* performance?



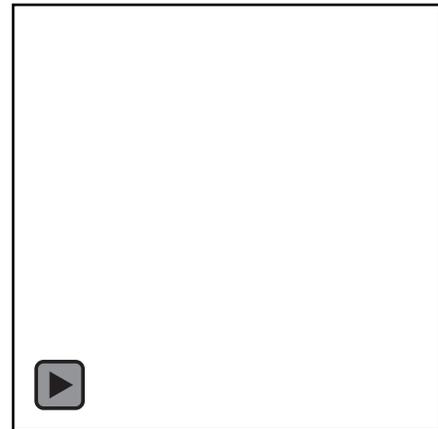
Benefits

- Better understanding of critical attributes, bioavailability, and manufacturability of extruded chewables.
- Potential reduction in the need for *in vivo* studies to support post-approval changes.
- Benefit to the pharmaceutical industry for potentially allowing small differences in formulations between strengths.
- Predictability of the review outcome.
- Enhanced confidence in generic animal drug approvals.





Questions?





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