U.S. FOOD & DRUG ADMINISTRATION

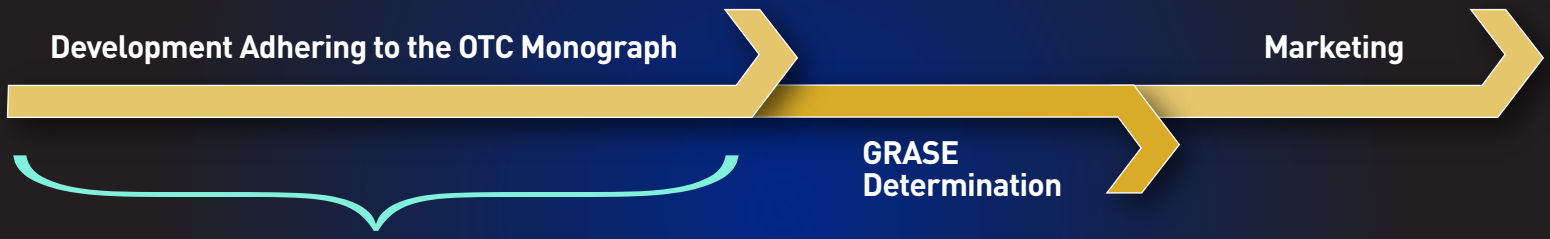
Background About the Guidance

MUsT has been used in the development of topical products in the prescription drug space for over 20 years. The unique application of the MUsT concept for OTC monographs is that a specific active ingredient and not a final drug product/formulation is under consideration. This guidance provides important recommendations to sponsors on critical study elements, data analysis, and considerations for special topic areas (e.g., pediatrics, geriatrics) for MUsT. The FDA will use information from a MUsT to identify the potential for systemic exposure and determine the need for additional safety data to support a finding that an OTC product with that active ingredient is generally recognized as safe and effective (GRASE) for its intended use. As follow up to publication of the sunscreen proposed rule in February 2019, this guidance provides industry with clear direction on how to approach MUsT studies.

Why is this guidance important?

As an example, despite what we know about prevention, skin cancer caused by sun exposure remains one of the most common cancers diagnosed in the United States. We know that the use of sunscreens, when used with other sun protective measures, is one of our most effective weapons against skin cancer. Because sunscreens are designed to work on the surface of the skin, some have proposed that sunscreens would not be absorbed in appreciable quantities, making MUsTs unnecessary. However, an original research article in the Journal of the American Medical Association found that application of 6 sunscreen active ingredients from 4 commercially available sunscreens resulted in plasma concentrations exceeding the FDA-established threshold for potentially waiving some nonclinical toxicology studies for sunscreens.

Drug Development Timeline – When to Apply the Guidance Recommendations?



During OTC Monograph Development:

The conduct of a MUsT should be consistent with maximal use of the product as specified by existing or anticipated labeling. Thus MUsTs for an OTC monograph product should be conducted as early as possible once both dosing frequency, amount to be applied, target populations, and other relevant factors are identified. Such testing should be conducted using multiple formulations, including formulations that are designed to maximize the potential for absorption. The collected samples from the MUsT should then be analyzed, and the systemic exposures to the active ingredients of interest should be evaluated using standard PK measures. The FDA expects to use the resulting in vivo PK data, in conjunction with data from animal toxicity studies, to estimate a safety margin for systemic exposure to the active ingredient in the relevant category of OTC monograph drug products.

To learn more about Maximal Usage Trials for Topical Active Ingredients Being Considered for Inclusion in an Over-The-Counter Monograph, read the guidance: https://www.fda.gov/media/125080/download