ORALLY INHALED AND NASAL DRUG PRODUCTS SUBCOMMITTEE OF THE ADVISORY COMMITTEE FOR PHARMACEUTICAL SCIENCE

April 26, 2000
CDER Advisory Committee Conference Room 1066
5630 Fishers Lane
Rockville, MD

DRAFT QUESTIONS

(31 March 2000)

CMC - CONTENT UNIFORMITY

A. Should there be a single content uniformity standard for all orally inhaled and nasal drug products (OINDPs)?

B. Should the FDA continue development of the proposed statistical approach to evaluating content uniformity?

IN VITRO BA AND BE TESTING

A. Profile Analysis

1. Should all stages, including the inlet (throat) of the cascade impactor (CI) be considered in a comparison of test and reference products?

2. Should a statistical approach rather than a qualitative comparison be used for profile comparisons? If yes, does the chi-square comparative profile approach seem appropriate?

B. In Vitro Tests for DPIs: Comparability

1. Prior to doing in vivo studies to establish equivalence of a test DPI product, a firm would need to design its product to have the best likelihood of being found equivalent in these in vivo studies.

a. What design features of the device and formulation and what parameters should be considered in determining pharmaceutical equivalence?

b. What comparative in vitro tests should be conducted to help support bioequivalence?

IN VIVO BA AND BE TESTING

A. Clinical Studies for Local Delivery of Nasal Aerosols and Sprays

1. Three study designs have been proposed in the draft guidance for drugs intended to have local action: traditional treatment study; day(s) in the park study, and environmental exposure unit study. These study designs are based on seasonal allergic rhinitis (SAR).

   Is it feasible to demonstrate a dose-response for locally acting nasal drugs? If not, what other approaches can be relied upon to establish equivalent local delivery?

2. Can bioequivalence established based on SAR assure bioequivalence for other indications such as recurrence of nasal polyps, or other non-SAR conditions?

B. Clinical Studies for Local Delivery of Orally Inhaled Corticosteroids (ICS)

1. A number of approaches have been proposed to assess bioequivalence of ICS (e.g., clinical trials, bronchoprovocation tests, steroid reduction model, trials with surrogate measures such as exhaled nitric oxide (eNO), etc).

   Are any of these study designs proven to offer better discrimination in terms of dose-response sensitivity?

2. What other in vivo approaches (e.g., surrogate markers) might be sufficiently sensitive and validated to establish in vivo BA and BE for inhaled corticosteroids?

C. PK or PD Studies for Systemic Exposure of Locally Acting Drugs

Are there situations where in vitro data plus systemic PK and systemic PD data can be relied on to assure local drug delivery for either nasal or inhaled drugs?