MOTIVATION AND PRINCIPLES OF INDIVIDUAL AND POPULATION BIOEQUIVALENCE

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UNDERLYING QUESTION

What does a comparison of average values in a sample of healthy volunteers tell us about the clinical context of patients switching from one formulation to another?

Hwang et al. (1978 *J Pharm Sci*) -- call for consideration of subject-by-product interaction

Definition: Subject-by-formulation interaction is the extent to which individuals differ in their Test/Reference (mean) comparison

SOME HISTORY

- 75/75 rule – at least 75% of individual Test/Reference ratios within (0.75,1.25) (Haynes, 1981 *J Pharm Sci*) addressed within-subject comparison

- Anderson and Hauck (1990 *JPB*) -- introduced terms individual and population bioequivalence; originally motivated by 75/75 rule.

WHAT SHOULD WE EXPECT OF BIOEQUIVALENT FORMULATIONS?

- **SWITCHABILITY** -- if have a **patient who is successfully controlled** on pioneer product or generic they can be switched to another bioequivalent formulation and **retain essentially the same efficacy and safety profile**

- **PRESCRIBABILITY** -- if have a **drug naive patient, can give him/her either** of the bioequivalent formulations with the same expectation of efficacy and safety.

THEORETICAL FRAMEWORK FOR INDIVIDUAL BIOEQUIVALENCE

INDIVIDUAL THERAPEUTIC WINDOW -- the window in which an individual's bioavailability must be maintained in order to assure continued efficacy and safety **for that individual**.

Note: The window concept tells you not only what you need but also what you don't. That is, if the window is wide, two formulations don't need to be (nearly) identical to be equivalent.

CRITERIA

- Individual bioequivalence criterion -- one developed to assure switchability

- Population bioequivalence criterion -- one developed to assure prescribability