Use of Bronchoprovocation to Determine Bioequivalence of Beta Agonists

Leslie Hendeles, Pharm.D.
University of Florida

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Summary

- FEV$_1$ lacks power for bioequivalence
- Methacholine challenge more powerful bioassay
- Many pitfalls
GRAPHIC DETERMINATION OF PC$_{20}$

\[
\% \Delta = \frac{\text{diluent} - \text{Meth}}{\text{diluent}} \times 100
\]

PERCENT CHANGE FEV$_1$

METHACHOLINE DOSE (mg/ml)

PC$_{20} = 3.5$
Figure 1. Mean percent change in FEV₁ over time for albuterol (○), isoetharine (□), metaproterenol (●), and placebo (■).
Relative Potency of Albuterol and Metaproterenol

Ahrens, Ann Allergy 9/91
Spiros – Bronchoprovocation Study

![Graph showing the relationship between dose of Albuterol and PC_{20}FEV1.]

- **Δ Albuterol Spiros**
- **Ventolin**

Ahrens et al. AJRCCM 1999;160:1240
Bioequivalence of Albuterol-HFA
Bronchodilator Response to Formoterol

Prabhakaran et al. Pharmacother 2011;31:449-57
Dose-Response of Formoterol

Relative Potency (90% CI)

Nov/Aer  1.13  (0.94, 1.38)
Statistical Power of Methacholine Bioassay

\[
s/b \text{ ratio} = \frac{\text{within subject variability}}{\text{slope of D-R curve}}
\]

The smaller the s/b ratio, the greater the power. Strive for least variability and steepest slope.
Variability in MC Results

- Delivery Method
- Dilutions
- Measurement of FEV$_1$
- Patient
Tidal Breathing vs. Dosimeter

Cockcroft et al. JACI 2006; 117:1244-8
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Leslie Hendeles, Pharm.D.
University of Florida
Health Science Center (Box 100486)
Gainesville, FL  32610-0486
Phone:  (352) 273-6027
Fax:  (352) 273-6120
E-mail:  hendeles@cop.ufl.edu