

# Author Response to the Letter Entitled “A Good and Reliable Bronchodilator Dose-Response Relationship”

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We appreciate the comments of Dr. Abdelrahim, and we agree that establishing bioequivalence is complex. However, the intent of our study was clinical response in moderate to severe subjects with stable asthma and chronic obstructive pulmonary disease with a demonstrated bronchodilator response to the most commonly used salbutamol/albuterol in the pulmonary function test laboratory to determine, with escalating doses, the amount of albuterol via transnasal pulmonary delivery required to elicit a similar degree of bronchodilator response. The cited FDA recommendation to determine therapeutic equivalence between pMDI and liquid formulations has been widely studied with a broad range of generics available for both [1–3]. The point of our study was to find the nominal

dose required for each patient to reach their response plateau. While imaging and pharmacokinetic and pharmacodynamic testing can attest to drug distribution, they do not, in and of themselves, establish levels required to reach maximum bronchodilation. Increasing lung and blood levels do not reflect the point at which plateau is reached. More importantly, patients' bronchodilation effects do not always correlate with their systemic potency, as many factors can affect the lung deposition and bioavailability [4].

As a practical matter, clinicians caring for hypoxic bronchospastic patients receiving nasal oxygen are less concerned with generic equivalence than evidence and guidance for establishing baseline doses for initiating bronchodilator aerosol therapy.

## References

- 1 Newhouse MT, Dolovich MB, Kazim F. Dose-effect relationship of the  $\beta$ -agonists fenoterol and salbutamol in patients with asthma. *Chest*. 1994 Jun;105(6):1738–42.
- 2 Dhand R, Duarte AG, Jubran A, Jenne JW, Fink JB, Fahey PJ, et al. Dose-response to bronchodilator delivered by metered-dose inhaler in ventilator-supported patients. *Am J Respir Crit Care Med*. 1996 Aug;154(2 Pt 1):388–93.
- 3 Fishwick D, Bradshaw L, Macdonald C, Beasley R, Gash D, Bengtsson T, et al. Cumulative and single-dose design to assess the bronchodilator effects of beta2-agonists in individuals with asthma. *Am J Respir Crit Care Med*. 2001 Feb;163(2):474–7.
- 4 Lipworth BJ. New perspectives on inhaled drug delivery and systemic bioactivity. *Thorax*. 1995 Feb;50(2):105–10.