Letter to the Editors

Efficacy of phenylephrine

Paul J. Desjardins & Roger G. Berlin
Wyeth Consumer Healthcare, Five Giralda Farms, Madison,
NJ 07940, USA

In his recent article, Dr Eccles' commented on the lack of studies in the public domain supporting the efficacy of oral phenylephrine (PE) as a nasal decongestant [1]. In 1976 the US Food & Drug Administration (FDA) reviewed 12 unpublished studies provided by pharmaceutical companies for the Monograph [2]. Although tedious to obtain, the information can be retrieved from the FDA's archives by utilizing the Freedom of Information Act (FOIA) by various means. First, one can request the information directly from the FDA. Secondly, one can view this information in the FDA reading rooms. Finally, third parties, for a cost, will obtain this information for clients.

We were able to obtain all of the studies cited in the 1976 Monograph via the FOIA. At that time, the FDA reviewed 12 unpublished studies and two published studies. We undertook our own review of these studies. We rejected two of the studies because one was a methodological paper that tested an oral combination product whose specific ingredients were unknown and the other was an abstract without any clinical data.

Five studies were reported to be negative with respect to PE efficacy. However closer examination showed that only one of these was a well-conducted study which failed to confirm efficacy of PE. In the other four, the 'active' controls also failed to show benefit bringing into question the sensitivity of the rhinometric assay performed in these studies.

On the other hand, seven double-blind, randomized trials were positive, i.e. PE demonstrated a significant reduction in nasal airway resistance (NAR) compared with placebo at doses ranging from 5 to 25 mg. In each study a clinically significant reduction in NAR (20% or greater peak effect) was achieved at the 5 and 10 mg doses.

Recently Hendeles & Hatton [3] questioned the oral efficacy of PE as a nasal decongestant. This article cited

three studies which examined PE efficacy. One was conducted by McLaurin [4]. As noted by Dr Eccles neither PE nor pseudoephedrine were different from placebo in this study. In addition, there is a positive study conducted by Cohen published in 1972 [5]. The effects of PE on NAR and subjective improvement of nasal symptoms were evaluated in 48 subjects with nasal congestion due to colds in a double-blind, randomized, placebo controlled, crossover study. All doses of PE tested (10–25 mg) showed a significant reduction in NAR and subjective scores of nasal congestion. Finally, Hendeles cited a study by Bickerman which failed to show efficacy of PE whereas it demonstrated efficacy for pseudoephedrine [6].

In a letter to Congressman Waxman, who had requested that the FDA look into PE efficacy, the US FDA stands by their 1976 decision to approve PE at a dose of 10 mg. In their correspondence to Mr Waxman they noted 'The conclusion about the effect of an active ingredient in light of both positive and negative trials is made based on the totality of findings and the quality of the data. The number of each type of study outcome is not generally a major factor in this determination' [7].

We recently submitted to the FDA our company's analysis of the studies reviewed by the FDA in 1976, studies cited by Dr Hendeles in his letter to the editor, and three additional studies that had been sponsored by our company in the 1960s and 1980s. Of the latter, two showed statistically significant benefits of 10 mg PE and the third was supportive. This summary should be accessible soon through the FOIA or on the FDA website at <http://www.fda.gov/ohrms/dockets/dailys/06/nov06/112006/112006.htm>.

In conclusion, we concur with the FDA opinion that the totality of the scientific evidence supports the nasal decongestant efficacy of PE based upon 12 studies of PE efficacy in the public domain in 1976. Seven of those studies supported the efficacy of oral PE, one was negative and four lacked sensitivity because the positive control failed. We also draw your attention to two additional published studies by Cohen (supportive of PE efficacy) and Bickerman (not supportive of PE) and

three previously unpublished studies that had been sponsored by our company which also supported the efficacy of PE 10 mg.

References

- 1 Eccles R. Substitution of phenylephrine for pseudoephedrine as a nasal decongestant. An illogical way to control methamphetamine abuse. *Br J Pharmacol* 2006; 63: 10–14.
- 2 FDA. Establishment of a monograph for OTC cold. Cough, Allergy, Bronchodilator and Antiasthmatic Products. Federal Register 1976; 38399–400.
- 3 Hendeles L, Hatton RC. Oral phenylephrine: an ineffective replacement for pseudoephedrine? *J Allergy Clin Immunol* 2006; 118: 279–80.
- 4 McLaurin JW, Shipman WF, Rosedal R Jr. Oral decongestants: a double blind comparison study of the effectiveness of four sympathomimetic drugs: objective and subjective. *Laryngoscope* 1961; 71: 54–67.
- 5 Cohen BM. Clinical and physiologic 'significance' in drug-induced changes in nasal flow/resistance. *Eur J Clin Pharmacol* 1972; 5: 81–6.
- 6 Bickerman HA. Physiologic and pharmacologic studies on nasal airway resistance (R_{N_0}). Presented at a Conference Sponsored by the Scientific Development Committee of the Proprietary Association, Washington DC, December 8, 1971.
- 7 Boyer DW. <http://www.democrats.reform.house.gov/Documents/20060922172818-85162.pdf>. Accessed January 2, 2006.

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Correspondence

Paul J. Desjardins, DMD, PhD, Wyeth Consumer Healthcare, Five Giralda Farms, Madison, NJ 07940, USA. Tel: +00 97 3660 6693; Fax: +00 97 3660 5254; E-mail: desjarp2@wyeth.com