October 23, 2006

The Honorable Andrew C. von Eschenbach, M.D.
Acting Commissioner
U.S. Food and Drug Administration
U.S. Department of Health and Human Services
5600 Fishers Lane, Room 15-47
Rockville, MD 20857

Dear Dr. von Eschenbach:

I am writing to follow up on my letters to you regarding the recent surge in the use of phenylephrine in oral nasal decongestants as a replacement to pseudoephrine. The growth in the use of phenylephrine is a response to provisions in the 2006 reauthorization of the Patriot Act, which set a September 30, 2006, deadline for moving all pseudoephedrine products behind the counter.[1]

In both my August 23, 2006, and my September 22, 2006, letters, I urged you to convene a meeting of the Nonprescription Drugs Advisory Committee to conduct a thorough scientific review of phenylephrine's effectiveness at the monograph dose of 10 mg. I specifically urged that the advisory committee consider the recent analysis by Dr. Leslie Hendeles and Dr. Randy Hatton, who contend that there is little evidence establishing the effectiveness of phenylephrine when used as an oral nasal decongestant.[2] You responded on September 13, 2006, that you were unwilling to convene such a meeting because you were not aware of any data refuting the data considered by the advisory panel that originally evaluated phenylephrine in the 1970s.

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[1] USA PATRIOT Improvement and Reauthorization Act of 2005, Pub. L. No. 109-177, enacted March 9, 2006. The Combat Methamphetamine Epidemic Act of 2005 (H.R. 3889) was passed as Title VII of the Patriot Act.

[2] *See* Leslie Hendeles, PharmD, and Randy Hatton, PharmD, *Letter To the Editor — Oral Phenylephrine: An Ineffective Replacement for Pseudoephedrine?*, J. Allergy and Clin Immunology, Vol. 118, No. 1 (July 2006).

Your contention does not appear to be accurate. There have been additional relevant studies and reports conducted that the panel apparently did not review.[3] Further, as I pointed out in my September 22, 2006, letter, in 2006, Schering-Plough conducted and completed a clinical trial comparing phenylephrine both to pseudoephedrine and to placebo.[4] Although this trial has not been released publicly, Dr. Hendeles has reported that it calls into question the effectiveness of phenylephrine.[5]

Since my September 22, letter, I have learned that Schering has made a public announcement that it will not reformulate Claritin-D to switch to phenylephrine. Instead, it will continue to use pseudoephedrine. The enclosed advertisement of Claritin-D, which was recently published in the Washington Post, reads:

> Claritin-D makes bold move. Chooses to keep its long-lasting, powerful formula for allergy relief. Moves behind the pharmacy counter. (still no prescription needed) ... Unlike some allergy medicines that changes their formulas, we kept our original, proven formula and instead moved behind the pharmacy counter.[6]

The decision by Schering not to switch to phenylephrine would not have been taken lightly. As a result of the decision, Claritin-D will no longer be available on store shelves. Instead, the drug must be kept behind the counter and will be available only to customers who

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[3] *See, e.g.,* Cohen BM. Clinical and physiologic "significance" of drug-induced changes in nasal flow/resistance. *Eur J Clin Pharmacol.* 1972;5:81-86.; Hengstmann JH, Goronzy J. Pharmacokinetics of ^{3}H-phenylephrine in man. *Eur J Clin Pharmacol.* 1982;21:335-41; Martinsson A, Bevegård S, Hjemdahl P. Analysis of phenylephrine in plasma: initial data about the concentration-effect relationship. *Eur J Clin Pharmacol.* 1986;30:427-31; Chua SS. Benrimoj SI. Non-prescription sympathomimetic agents and hypertension. *Med Toxicol.* 1988;3:387-417.

[4] U.S. National Institutes of Health, ClinicalTrials.gov, *The Effects of Phenylephrine Compared With Those of Placebo and Pseudoephedrine on Nasal Congestion in Subjects With Seasonal Allergic Rhinitis (SAR) (Study P04579)* (online at www.clinicaltrials.gov/ct/show/NCT00276016;jsessionid=1B43B1BF395CA89630495B0A166321ED?order=1) (accessed on Oct. 17, 2006).

[5] *See* Letter from Rep. Henry A. Waxman to Acting FDA Commissioner Andrew C. von Eschenbach, M.D. (Sept. 22, 2006) (online at www.democrats.reform.house.gov/Documents/20060922171958-12220.pdf). Dr. Hendeles reported that the principal investigator of the Schering trial indicated to Dr. Hendeles that he agreed with the conclusions set forth in Dr. Hendeles' and Dr. Hatton's letter to the editor regarding the lack of evidence establishing phenylephrine's effectiveness (*supra*, note 2).

[6] Advertisement by Schering-Plough Corporation, Washington Post (Sept. 26, 2006).

present valid identification to the pharmacist or store employee, putting Claritin-D at a significant competitive disadvantage.

Schering's actions are unusual for a pharmaceutical company, and they suggest that the Schering study may have raised significant questions about the effectiveness of phenylephrine. They thus appear to provide an additional reason why it would be wise to promptly convene a meeting of the Nonprescription Drugs Advisory Committee to investigate whether phenylephrine should maintain its status as a monograph-approved active ingredient in oral nasal decongestants at the current dose of 10 mg.

To assist Congress in understanding these issues, I request answers to the following questions:

1. Have you requested the results of Schering-Plough's study entitled "The Effects of Phenylephrine Compared With Those of Placebo and Pseudoephedrine on Nasal Congestion in Subjects With Seasonal Allergic Rhinitis (SAR) (Study P04579)"?[7] If so, has the company provided the results to you?

2. If you have not yet requested the results of this study, do you intend to make such a request? If you do not intend to request the results, why not?

3. If you have obtained the results of the trial, what conclusions do you draw from them regarding the effectiveness of phenylephrine as an oral nasal decongestant? Do you intend to make these results publicly available? If not, why not?

Millions of Americans buy over-the-counter medications to relieve nasal congestion. They rely on FDA to make decisions about the safety and efficacy of these drugs based on a thorough review of all the relevant data. Your reluctance to re-examine phenylephrine in light of the new data calls into question whether FDA is meeting this standard and acting responsibly in this matter.

Sincerely,

Henry A. Waxman
Ranking Minority Member

[7] *Supra*, note 3.