ONE HUNDRED EIGHTH CONGRESS

Congress of the United States

House of Representatives

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February 6, 2004

The Honorable Tommy G. Thompson
Secretary of Health and Human Services
U.S. Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Dear Mr. Secretary:

I was pleased at your announcement that the Food and Drug Administration finally intends to exercise its authority to remove ephedra-containing dietary supplements from the market. However, I continue to be concerned that potentially dangerous stimulant products are being marketed as substitutes for ephedra. On October 24, 2003, I wrote a letter to FDA Commissioner McClellan regarding the safety of dietary supplements containing stimulants such as synephrine. In that letter I asked if FDA was aware of evidence to demonstrate that these products are any safer than ephedra. I have not yet received a response to that letter.

While many manufacturers are advertising these substitutes as "safe" alternatives to ephedra, experts have told me that some of these substances are in fact closely related to ephedra and appear to have the potential to cause adverse effects on the cardiovascular system that are comparable to those of ephedra. For example, as FDA has acknowledged, synephrine, the primary active substance in Citrus aurantium (bitter orange), is, like ephedra, a sympathomimetic agent.[1] According to FDA, "Pharmacologically, synephrine is primarily … an adrenergic agonist that is used clinically to treat hypotension [i.e., raise the blood pressure]."[2] According to Dr. Ray Woosley, an expert in cardio-vascular drug adverse events, sympathomimetic agents have effects on the heart similar to adrenaline, and can raise both blood pressure and heart rate.[3] As Commissioner McClellan stated in the press conference announcing the decision to ban

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[1] Letter from Melinda K. Plaisier to Rep. Henry Waxman (July 11, 2001). In fact, Citrus aurantium contains several sympathomimetic agents, including synpehrine, N-methyltyramine, hordenine, tyramine, and octopamine.

[2] *Id.*

[3] Staff telephone interview of Dr. Ray Woosley, Vice President for Health Sciences, University of Arizona (Jan. 9, 2003).

ephedra, increases in blood pressure and other stresses on the circulatory system have been conclusively linked to serious heart problems, strokes, and death.

As I understand the rule issued today, FDA relied on the known pharmacology of ephedrine as a sympathomimetic agent, together with specific evidence that it increased blood pressure and heart rate, to conclude that ephedra posed an unreasonable or significant risk of illness or injury.

The experts that I have consulted say that because of the similarities between synephrine and ephedrine in pharmacology and their capacity to raise blood pressure and heart rate, dietary supplements containing synephrine may pose an unreasonable or significant risk of illness or injury. I am therefore seeking information on what steps you plan to take to protect American consumers from the potential dangers of this substitute for ephedra.

Please provide me with answers to the following questions:

1. Does the FDA believe that there is adequate information to establish that synephrine increases blood pressure and heart rate?

2. If not, what kind of additional data are required to establish synephrine's effects on blood pressure and heart rate?

3. What additional studies, beyond any needed to establish synephrine's effects on blood pressure and heart rate, would be needed to determine whether dietary supplements containing synephrine pose an unreasonable or significant risk of illness or injury?

4. If additional studies are necessary, either to establish synephrine's effects on blood pressure and heart rate or for other purposes, will you ask the National Center for Complementary and Alternative Medicine to carry out such studies? If not, why not?

5. In addition to evidence of synephrine's pharmacology and ability to raise blood pressure and heart rate, must FDA also have reports of adverse events related to synephrine use in order to take action against the ingredient? If so what kind of adverse events would be necessary?

6. Is FDA aware of evidence that proves that dietary supplements containing synephrine are effective for promoting long-term weight loss?

7. Has FDA examined dietary supplements containing Citrus aurantium to determine whether the ingredients in the products are natural or synthetic? If these products contain synthetic synephrine, can they be lawfully marketed as dietary supplements?

Thank you for your cooperation with this request. Please provide your response by February 27, 2004. If you have any questions, you may contact Sarah Despres on my staff at (202) 225-5420.

Sincerely,

Henry A. Waxman
Ranking Minority Member