

MEMORANDUM

TO: Ed Novotny
FROM: Damany Ransom
DATE: May 17, 2007
RE: The FDA's final rule banning dietary supplements containing ephedrine alkaloids

I. QUESTION PRESENTED

Whether the Food and Drug Administration's final rule prohibits the sale of ephedra products that do not contain ephedrine alkaloids?

II. ANALYSIS

Under the Food, Drug and Cosmetics Act (FDCA), the Food and Drug Administration (FDA) is provided broad authority to regulate food, drug and dietary supplement products to ensure public health and safety. In 1994, Congress amended the FDCA to include the Dietary Supplement Health and Education Act (DSHEA), which authorizes the FDA to prevent "adulterated" dietary supplements from entering the market. Pursuant to DSHEA, a dietary supplement is "adulterated" if it "presents a significant or unreasonable risk of illness or injury under (i) conditions of use recommended or suggested in labeling, or (ii) if no conditions of use are suggested or recommended in the labeling, under ordinary conditions of use." 21 U.S.C. § 342(f)(1)(A).

On February 6, 2004, the FDA announced that it was publishing a final rule declaring all dietary supplements containing ephedrine alkaloids adulterated. The final rule was published on February 11, 2004, and became effective sixty days later, on April 12, 2004.

In the final rule, the FDA concluded that dietary supplements containing ephedrine alkaloids are adulterated because they present an unreasonable risk of illness or injury under the

conditions of use recommended or suggested in labeling or, if no conditions of use are suggested or recommended in labeling, under ordinary conditions of use. To reach this conclusion, the FDA considered numerous studies and data related to the safety of dietary supplements containing ephedrine alkaloids. The data came from three principal sources: (i) the pharmacology of ephedrine alkaloids; (ii) scientific literature on the effects of ephedrine alkaloids; and (iii) adverse events that occurred in individuals who consumed dietary supplements containing ephedrine alkaloids.

After examining the data, the FDA determined that dietary supplements containing ephedrine alkaloids pose a risk of serious adverse events, including heart attack, stroke, and death. It further concluded that those risks were unreasonable in light of the modest, short-term benefits that result from using such products. The FDA also noted that it had not been presented with sufficient evidence to establish a safe dose of ephedrine or ephedrine alkaloids. Because no such dose could be identified, the FDA determined that even minimal amounts of ephedrine alkaloids present unreasonable risks and should not be allowed on the market.

The six principal ephedrine alkaloids that are pharmacologically active in botanicals include ephedrine, pseudoephedrine, norephedrine, methylephedrine, norpseudoephedrine and methylpseudoephedrine. Each of these alkaloids is included in the ban. Accordingly, a range of dietary supplements derived from botanicals are banned, including ma huang, *Sida cordifolia* L. (also known as country mallow and bala), *Pinellia ternate* (also known as ban xia), and most members of the genus *Ephedra* that contain ephedrine alkaloids (*Ephedra sinica* Stapf, *Ephedra equisetina* Bunge, *Ephedra intermedia* var. *tibetica* Stapf and *Ephedra distachya* L.).

The FDA made clear, however, that several products are not included in the ban. For instance, the prohibition does not apply to conventional food products that contain ephedrine

alkaloids. The final rule also does not apply to over-the-counter drugs or prescription drugs containing ephedrine alkaloids. Further, the rule does not affect preparations under traditional Chinese medicine, because such preparations are intended for episodic (*e.g.*, respiratory infections) rather than chronic use.

Moreover, the final rule does not indicate that ephedrine alkaloid-free dietary supplements are included in the ban. Nor does the FDA indicate that there is any evidence that ephedrine alkaloid-free products present significant or unreasonable risks. Thus, ephedrine alkaloid-free dietary supplements do not appear to be affected by the final rule. Indeed, the FDA noted that most North American species of *Ephedra* (*e.g.*, Mormon tea) do not contain ephedrine alkaloids and, therefore, excluded them from the ban.¹

III. CONCLUSION

The Final Rule applies to all dietary supplements that contain ephedrine alkaloids. Ephedrine alkaloid-free dietary supplements do not appear to be included. Therefore, assuming it is possible to make a dietary supplement from ephedra which contains no ephedrine alkaloids, it appears that such a product would not be subject to the Final Rule.

¹ The FDA stated, however, that any dietary supplement that contains ephedrine alkaloids from any botanical source, including from a North American species of *Ephedra*, is subject to the rule. This obviously implies that the FDA makes the distinction between *Ephedra*, the plant, and ephedrine alkaloids.