AHPA President Gives Preliminary Analysis of FDA Ephedra Ruling

Editorial Staff | DIGITAL EXCLUSIVE

On Feb. 26, American Herbal Products Association President Michael McGuffin issued an e-mail to members of the AHPA's Chinese Herbal Products Committee and other interested parties on the FDA's ruling on ephedrine-containing dietary supplements. *Acupuncture Today* recently obtained a copy of Mr. McGuffin's e-mail, and has posted it here for review by the profession.

* * *

Impact of FDA's Ephedrine-Containing Dietary Supplement Tule on TCM
Preliminary Analysis

To: Members of AHPA's Chinese Herbal Products Committee and other interested persons

From: Michael McGuffin, AHPA President

I have heard from several of you to request information as to AHPA's understanding of the impact on TCM and Chinese patent formulas of FDA's final rule that will effectively ban all products marketed as dietary supplements that contain any amount of ephedrine alkaloids. The ban will have an impact on any and all botanical sources of ephedrine alkaloids (e.g., Asian species of Ephedra [but not North American species IF those species are free of even traces of ephedrine alkaloids]; Pinellia ternata; Sida cordifolia; etc.), and goes into effect on April 12, 2004.

I have heard several questions to date, some related to manufacturers, some to retailer (especially herb stores) and some to practitioners. This preliminary response primarily addresses questions related to manufacturers and marketers, with some attention to the other questions.

The responses given here are my current best thinking on these issues. They are not definitive and they are not a substitute for legal opinions. You are encouraged to seek legal counsel if you have any intention to continue to sell any product - food, dietary supplement, or medicine - after April 12, 2004 that contains any amount of ephedrine alkaloids.

Please feel free to distribute this as you see fit. Though I have tried to be inclusive in my e-mail list, I may have overlooked someone. Please reiterate, however, my immediately preceding statement that this document is not a substitute for legal counsel.

Questions received to date:

Q: Will the federal law preempt the laws in other states, especially in California, Illinois and New York, which established tolerances for the sale of products (and in California, specifically dietary supplements) containing ephedrine alkaloids to licensed practitioners? In other words, can a

manufacturer sell products containing ephedrine alkaloids to practitioners in these states, and if so, how must these products be manufactured and labeled?

A: The blunt answer is: the federal law absolutely DOES preempt the state laws. Stating the question-and-answer differently:

Q: Can ephedrine-containing dietary supplements be sold to practitioners in California (something that is allowed by California law but not allowed by federal law (as of April 12)?

A: No.

Here's what FDA said (on page 6849 of the *Federal Register* of February 11, under "Federalism"):

? "FDA has determined that the rule has a preemptive effect on State law."
? "State laws establishing labeling requirements or other requirements that contemplate the continued marketing of these products conflict with this final rule and, consequently, are preempted."

So FDA trumps the states and FDA states that all dietary supplement containing ephedrine alkaloids are adulterated and so shall not be sold to anyone, with no exceptions.

Now comes the hard part. FDA also said (in the Feb. 11 final rule):

? "This final rule does not affect the use of Ephedra preparations in traditional Asian medicine..."
? "This rule applies only to products regulated as dietary supplements."
? "...botanical sources of ephedrine alkaloids in traditional Asian herbal therapies are not covered by this rule."
? "Traditional Asian medicine practitioners do not typically use products marketed as dietary supplements."

What did FDA mean by these statements? The better question: what did they mean by the first three statements, because the last one (as you know from marketing many dietary supplements to traditional Asian medicine practitioners - aka: acupuncturists) is not correct.

Or again, more to the point:

Q: Do these statements imply that FDA meant for your company to be allowed to sell ephedrine-containing products that are not dietary supplements (or that are traditional Asian medicines)?

A: Well, FDA does not say that. They just say that this rule "does not affect" those and that those "are not covered" by the rule. FDA did not affirmatively state: "You are allowed to sell ephedrine-containing traditional Asian medicines."

Q: If this is not the rule under which ephedrine-containing traditional Asian medicines are regulated, what is the rule that applies to such products?

A: FDA would almost certainly determine that labeling an ephedrine-alkaloid containing product as a "medicine" is synonymous to labeling the product as a drug, that there is no other category for it, and FDA and state drug regulations would therefore apply to these, as they apply to all products that meet the drug definition (i.e., "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and articles (other than food) intended to affect the

structure or any function of the body of man or other animals.")

Q: If FDA does determine that a product sold as a "traditional Asian medicine" is a drug, is ephedra a "new drug" or an "old drug," and why does that matter?

A: "New drugs" are those that were "introduced" into the U.S. marketplace after the passage of the Federal Food, Drug, and Cosmetic Act in 1938. Ephedra could be classed as an "old drug" if it can be shown that it was already marketed in the U.S. at that time and earlier. If it is not an "old drug" a new drug application would need to be filed, but there would not be a reasonable possibility for approval. Alternately, a notice of "material time and extent" could be filed in an attempt to have ephedra classified as an OTC drug. I doubt that this is a reasonable possibility, however, given FDA's emphasis on the role of medical practitioners in discussing traditional use of ephedra.

Q: If we are successful in showing that ephedra is an "old drug" (or if we are successful with a new drug application or with an OTC application), what manufacturing practices would be required?

A: Current good manufacturing practice for finished pharmaceuticals (21 CFR 211).

Q: If we are successful in establishing ephedra (or an ephedrine-containing traditional Asian medicine) as an old drug, what other regulatory requirements would apply?

A: Numerous state and federal rules would apply, including the need to register with FDA as a manufacturer of finished pharmaceuticals and to list the ephedrine-containing products as a drug that you are manufacturing.

Q: Michael, how would you sell an ephedrine-containing traditional Asian medicine after April 12, 2004?

A: This question reaches the limits of my authority and experience. I have spoken to AHPA General Counsel Tony Young about this and requested that he attend the meeting of the Chinese Herbal Products Committee in Anaheim from 10:30 am to noon on Friday, March 5. Tony has agreed to be at this meeting and may recommend that the group engage legal counsel to address this issue by crafting an opinion letter that would set out how to lawfully label and market these products as old drugs, if there is available evidence (something that goes beyond "we all know it was") that ephedra was in use prior to 1938 in the traditional medicine community. He will also be prepared to revisit the questions and answers presented here.

Q: Are Chinese patent formulas dietary supplements or "traditional Asian medicines"? What are the implications of this to (1) manufacturers, and (2) practitioners?

A: The U.S laws that govern the sale of all of these products place primary emphasis on what you say about the products. The laws do not comment on which regulated class Chinese patent formulas fall into. Rather, a Chinese patent formula that is labeled as a "dietary supplement" is subject to regulation as a dietary supplement (so the manufacturing is governed today by the food cGMP; and the allowable ingredients are limited to those that are included in the DSHEA definition [which clearly includes essentially all herbal ingredients, so long as they are not "new"]; claims are limited to "statements of nutritional support" [including "structure-function claims"]; and no drug claims (disease claims) may be made, etc).

Similarly, a Chinese patent formula labeled as a "traditional Asian medicine" would be subject to regulation as such. Of course there is no such specific category, so we are left with an unanswered question: how would FDA regulate manufacturers of such products? I have provided some discussion of this above.

On the other hand, FDA has no interest in regulating practitioners as this is done on a state level. Licensed practitioners of traditional Asian medicine (I think we usually call those "acupuncturists") are allowed in most states to use "medicines." Thus we have a quandary in that it appears as if the practitioner is allowed to prescribe a product even though we are not clear what regulations are required to be met to legally manufactured and sell such a product.

Q: Will it be legal for a raw material supplier to sell ephedra herb for resale by retailers?

A: That question must be answered with a question - for resale for what purpose?

The new rule identifies "dietary supplements containing ephedrine alkaloids" as adulterated. The rule does not apply to ephedra herb (or pinellia rhizome; etc.) that is not labeled as a dietary supplement. But then what would its use be?

A company that chooses to sell raw materials containing ephedrine alkaloids cannot, as a practical matter in the environment of this final FDA regulation, take the position that they are selling an item of commerce only and are not responsible for its subsequent use. This is an important Federal rule and the consequences of trying to sneak around it could be serious.

Q: Will practitioners be allowed to dispense ephedra herb after April 12, 2004? If so, will that allowance extend to herbal practitioners who practice something other than "traditional Asian medicine"? What about licensed practitioners versus unlicensed practitioners?

A: As stated above, the rule does not apply to ephedra herb (or pinellia rhizome; etc.) when used in traditional Asian medicine. There is no reason to think that there would be any differentiation between use of ephedra herb by a licensed or unlicensed practitioner of any herbal discipline - FDA has not established a rule on the use of ephedra herb by practitioners, FDA has only said that the ephedra dietary supplement rule does not apply to this use.

Q: What did FDA mean when they said that the final rule "does not apply to conventional food products that contain ephedrine alkaloids"? Does that mean that it is okay to sell tea products that contain ephedrine alkaloids?

A: It is not okay to sell tea products that contain ephedrine alkaloids as is evident from the three sentences that follow the above cited statement by FDA:

Substances intentionally added to a conventional food are generally considered to be food additives...[e]phedrine alkaloids contained in conventional foods would generally be considered unsafe food additives ...[a] food that contains an unsafe food additive is adulterated..."

In other words, ephedrine alkaloids in a food product (such as a tea) would adulterate the food.

Q: Did FDA exempt the North American (ephedrine alkaloid-free) species of Ephedra?

A: FDA expressed its belief that "most" North American species of Ephedra do not contain ephedrine

alkaloids (AHPA believes that all such species are absent ephedrine alkaloids and has an article published in 2001 to substantiate this). The agency did state, however, that "any dietary supplement that contains any ephedrine alkaloids from any botanical source, including from a North American species of Ephedra, is subject to this rule."

Q: Can a formula that contains a small percentage of pinellia be legally sold?

A: The test is whether the dietary supplement contains any amount of ephedrine alkaloids. A marketer of a dietary supplement that contains pinellia would be wise to conduct analysis for ephedrine alkaloids with a very sensitive limit of detection.

Q: Are analytical methods for ephedrine alkaloids available? What is the cost of such analysis?

A: AHPA has identified two analytical labs that are prepared to conduct HPLC analysis for ephedrine alkaloids. The cost is between $210-260 per sample and multiple samples would need to be submitted simultaneously to achieve the lower cost. Please contact the AHPA office for more information.

Q: Will companies be allowed to sell essentially the same dietary supplement that they sell simply by relabeling it as a "conventional food" or "traditional Asian medicine"?

A: No.

Michael McGuffin, President
American Herbal Products Association
8484 Georgia Avenue, Suite 370
Silver Spring, MD 20910
Telephone: 301-588-1171 x 201
Fax: 301-588-1174