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Throckmorton, Douglas C

From: Hausner, Elizabeth A
Sent: Wednesday, March 05, 2003 9:09 AM
To: Defelice, Albert F; Throckmorton, Douglas C
Subject: FW: 0300923.pdf In case you have not seen this



0300923.pdf

Good morning,

The attached is a letter from the director of the NCCAM sent to Dr McClellan and forwarded by Lois Freed to the rest of the Botanicals Subcommittee.

Yesterday's discussion of ephedra was very interesting and for the purpose of helping CFSAN. Since food can't be held to the rigorous specs of a pharmaceutical, they need a different system for setting standards and holding the manufacturers to account. The discussion was to the end of ultimately devising meaningful assays with characterization not of ephedrine per se, but of the components of the six Ephedra species commonly used for making "herbal" ephedra under the current standards of preparation. The alkaloid profiles and copious other active ingredients vary among the six species. Three of the species used are not used in traditional Chinese medicine (TCM), and the current methods of preparation are nothing like the TCM. There was also a comment that most of the ephedra plants being processed are coming from the Afghanistan-Pakistan border. At this point, the products don't seem to have any connection whatsoever to TCM, so the arguments that these products have been safely used for 5000 years really are not applicable.

To keep this relatively succinct, here are the main points of discussion with as little commentary as is constitutionally possible:

A. Chemistry and Analytical

1. AOAC and FDA are validating analytical methods for the 6 major ephedra alkaloids in products and bodily fluids.

2. NIST is producing standard reference materials both for *E. sinica* and for botanical matrices.

3. NCNPR (National Center for Natural Products Research) at U. Miss has characterized the composition of several Ephedra spp. and has started comparisons with commercial product. Ikhlas showed the difference in spectra before and after acid or base extractions. Based on some chromatograms, it appears that extracted alkaloids are being added to "herbal" products. Wouldn't that make this a drug?

Clinical/Regulatory

1. Patricia Beaston-Wimmer from Metabolic and Endocrine said that she currently had 3 INDs were for ephedrine, 1 for herbal ephedra. One IND sought to put ephedra and caffeine into 8 year old children.

2. Peggy Miller from the Women's Health Initiative said that many women of childbearing years are taking ephedra products, finding out that they are pregnant and so asking about first trimester exposure. The question for FDA is about exposure to the combinations of ingredients. Hence the discussion about reprotox studies.

C. Plans

1. to standardize extraction/preparation of materials
2. there has to be a way to standardize the material that is used for the in vitro and in vivo tests.