



**Boston University School of Medicine**  
 Stone Epidemiology Unit

February 7, 2000

Jane Henney, M.D.  
 Commissioner, Food and Drug Administration  
 5600 Fishers Lane  
 Rockville, MD 20857

Re: Final FDA Regulations on Claims Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body

Dear Commissioner Henney,

I am writing in the hope that you will immediately reconsider the final rule regarding uses of dietary supplements during pregnancy, published on January 6, 2000. That rule classifies "ordinary morning sickness" and "leg edema associated with pregnancy" as common conditions that are not "diseases." Under the Dietary Supplement Health Education Act (DSHEA), that classification allows dietary supplement manufacturers to promote products as treatments of those conditions without first proving that the products are safe and effective.

I take strong exception to classifying these conditions as non-diseases, since they can lead to complications (such as dehydration) that can adversely affect the pregnant woman and her fetus. More urgently, however, to allow such claims to be made in the absence of evidence of fetal safety is to ignore the very history that made the FDA the world's most highly regarded regulatory agency.

Until forty years ago, the scientific community and public alike viewed the placenta as an effective barrier to exogenous drugs and chemicals. However, the thalidomide catastrophe, in which over 10,000 babies worldwide suffered terrible birth defects following their mothers' use of the drug, dramatically and instantly changed that view. The similarities to the current concern are both ironic and frightening: First, as would be permitted for supplements, thalidomide was promoted specifically for the treatment of nausea and vomiting and pregnancy. Second, just as dietary supplements are currently viewed as "safe", so too was thalidomide promoted as a "safe" alternative to then-current treatments (barbiturates).

The U.S. escaped the brunt of the thalidomide disaster because the FDA (via Dr. Kelsey) demanded more safety data before it would approve the drug for marketing. However, it was specifically the thalidomide disaster--and the public's demand to be protected from unsafe drugs--that led to a strengthening of FDA's regulatory authority and responsibilities.

The notion that vitamins and products derived from plants are safe may be debated with respect to the risks to the pregnant woman herself, but assumptions of safety are simply without foundation when it comes to the fetus. Indeed, we worry greatly about the fetal risks of high-

Log 2000 02 0000 43

1379 Beacon Street

Brookline, Massachusetts 02446-4955

(617) 734-6006

Fax: (617) 738-5119

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dose vitamin A, and the vitamin A congener isotretinoin (Accutane) is a classic and potent human teratogen. Further, we and others have now demonstrated that pseudoephedrine is likely responsible for an increased risk of the rare but potentially devastating birth defect gastroschisis (*Werler MM, Mitchell AA, Shapiro S. First trimester maternal medication use in relation to gastroschisis. Teratology 1992;45:361-367; Torfs CP, Katz EA, Bateson TF, Lam PK, Curry CJR. Maternal medications and environmental exposures as risk factors for gastroschisis. Teratology 1996; 54:84-92*). It should not go unnoticed that pseudoephedrine, derived from ephedra, is a plant product that is commonly found in herbal supplements currently promoted for cough and colds--indeed, only last week I heard an advertisement for a Tom's of Maine cold product that contained pseudoephedrine but was safer than other products because it did not contain alcohol!

It is particularly ironic that the FDA recently approved thalidomide for marketing in the U.S., but did so only after developing, in concert with the manufacturer, a uniquely and extremely carefully thought-out restricted distribution system designed to protect the fetus from exposure to this agent. It is hard to conceive that the FDA would so carefully implement unprecedented steps to protect the fetus from thalidomide teratogenesis but at the same time allow the fetus to be exposed to unproven and untested agents that may well be teratogenic.

The fact that the agency retains the ability to remove a product if it finds it to be unsafe (i.e., teratogenic) is little comfort. Unlike most drug risks, evidence of human teratogenesis comes almost entirely from human exposures and tragedies. I have spent my career investigating how to identify drugs that cause birth defects in humans, and I am painfully aware of our limited abilities to rapidly identify new teratogens. This is particularly problematic for supplements whose efficacy is unproven and whose constituents might not be accurately known.

Based on existing teratogenic concerns surrounding certain vitamins (e.g., vitamin A) and plant-derived agents in dietary supplements (e.g., pseudoephedrine), there is little doubt that some dietary supplements carry the strong potential to be human teratogens. Allowing their promotion for treatment of a disease directly associated with the early stages of pregnancy serves to encourage their use, particularly since pregnant women will be led to believe that dietary supplements represent a "safe" alternative to prescribed or OTC medications.

We as a society and FDA as a regulatory agency must not forget the lessons of the thalidomide tragedy. To maintain the above-cited rule is to invite a medical, moral, and public health disaster that could, with simple revision of that rule, be averted.

Sincerely,



Allen A. Mitchell, M.D.

Director, Slone Epidemiology Unit

Professor of Public Health & Pediatrics

Boston University Schools of Public Health & Medicine