FDA Public Meeting On Safety Issues Associated With Dietary Supplement Use During Pregnancy (Gaithersburg Hilton, Gaithersburg, MD, March 30, 2000)

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I very much appreciate having the opportunity to be here today to give my perspective on the safety issues associated with diet supplement use during pregnancy.

For the record, I am Director of the Slone Epidemiology Unit of Boston University Schools of Public Health and Medicine, where I am Professor of Public Health and Pediatrics. I was trained in pediatrics and for more than three decades have devoted myself to studying the risks and safety of medications used in pregnancy.

I have come here to ask that you immediately reconsider the final rule regarding uses of dietary supplements during pregnancy, published on January 6, 2000; this rule allows dietary supplement manufacturers to promote their products for treatment of pregnancy-related conditions, without first proving that the products are safe and effective.

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—a reputation that is well deserved.

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, changed that view-- dramatically, instantly, and, we hope, forever.

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 in 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, as a result of Dr. Kelsey's careful review of safety data, demanded more information before it would approve the drug for marketing. Though the U.S. population was spared, other countries were less fortunate. The lesson was not lost on Americans, however: Indeed, it was specifically the thalidomide disaster in the early 1960's--*and the public's demand to be protected from unsafe drugs*--that led to a strengthening of FDA's regulatory authority and responsibilities.

These changes created public confidence in the general safety of regulated drug products, and this confidence has, I believe, spilled over to include unregulated dietary supplements. The notion that dietary supplements are safe may be debated, but when it comes to the fetus, assumptions of safety are without foundation. The truth is that we simply do not know the fetal effects of the vast majority of dietary supplements, and we <u>certainly</u> do not know that they are safe—that is, that they carry *no* risk to the fetus. The few studies that have been conducted do not offer reassurance; on the other hand, evidence is emerging that argues for caution. I will

briefly cite just three examples.

In 1999, researchers studying donor human sperm and hamster oocytes reported that "St. John's wort, ginko, and echinacea in high concentrations damage reproductive cells" and that "St. John's wort was mutagenic to sperm cells." (1)

Vitamins taken in large doses also have raised concerns. Some studies suggest that high-dose vitamin A causes birth defects. Though these results are not universally accepted, there is biologic reason to worry about high-dose vitamin A since it is a congener, or close cousin, of the acne drug isotretinoin (Accutane), which is a classic and very potent human teratogen.

Finally, we and others have raised questions about whether pseudoephedrine may be responsible for an increased risk of a rare but serious birth defect called gastroschisis (2,3). Most will recognize pseudoephedrine as a common ingredient in over-the-counter medications sold for the treatment of colds, allergies, and sinus congestion. However, it is critically important to recognize that pseudoephedrine, which is derived from ephedra, is a “natural” plant product—and it is also found in a number of herbal supplements that are promoted for the treatment of colds, allergies, and sinus congestion. If the concern were proven real, and OTC pseudoephedrine caused birth defects in humans, wouldn’t “herbal” pseudoephedrine similarly cause birth defects? If this “natural” product caused birth defects, what fetal harm might be caused by other dietary supplements?

In its long history of concern about the fetal risks that might result from medications used by

pregnant women, FDA just yesterday completed another meeting of a subcommittee that is assisting the agency in seeking ways to apply pregnancy registries and other approaches to learn, as rapidly as possible, about the teratogenic effects of new medications. This is a part of a remarkable effort focused on drug products that have already passed FDA-mandated animal testing for fetal safety before they are approved for marketing. Without the benefit of similar testing before human use, and based on existing information about certain vitamins and plant-derived agents in dietary supplements, there is indeed reason for concern 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.

The fact that FDA retains the ability to remove a product if it finds it to be unsafe (i.e., teratogenic) provides little comfort. Unlike most drug risks, definitive evidence of human teratogenesis comes only after there have been human exposures and human tragedies. Given our ignorance at this time, can we honestly judge that the benefits of dietary supplements to pregnant women are so compelling and unique that we should allow their promotion, even at the risk of permitting another thalidomide?

Because of the FDA, the population of this country escaped the thalidomide disaster. We must not forget the lessons of that defining episode. To maintain the current rule is to almost certainly invite medical, moral, and public health disasters that could, with simple revision of that rule, be

averted.

I thank you for your consideration.

1. Ondrizek RR, Chan PJ, Patton WC, King A: An alternative medicine study of herbal effects on the penetration of zona-free hamster oocytes and the integrity of sperm deoxyribonucleic acid. Fertil Steril 1999; 71:517-22.

2. Werler MM, Mitchell AA, Shapiro S. First trimester maternal medication use in relation to gastroschisis. Teratology 1992;45:361-367.

2. 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.