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Testimony and Written Comments for the Food and Drug Administration

about

Safety Issues Associated With Dietary Supplement Use During Pregnancy

at a

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by

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Good afternoon. I am Godfrey Oakley. I am currently a Visiting Professor of Epidemiology of the Rollins School of Public Health of Emory University. I am a pediatrician, epidemiologist and geneticist who has worked in birth defects prevention, research, and policy for most of my professional career. Thank you for the opportunity to present to you. I start my presentation by stating the main point.

**Main Point:**

The United States Preventive Services Task Force has produced two Clinical Guides to Preventive Services and scored each possible preventive service based on the quality of the evidence for that service. I have placed this scoring system on the overhead and it is on page 6 of my written comments. I believe the evaluation of herbs and supplements would be vastly improved were this quality of evidence approach taken. I suggest that FDA and industry make this quality of evidence approach the basis for substantiating health and structure/function claims under DSHEA.

We are here today to address safety issues associated with dietary supplement use during pregnancy. In my opinion, the current regulatory policies and practice regarding dietary supplements are not in the best interest of the public. There is great distrust among the academic medical and nutrition communities, the regulatory agencies and industry. This distrust goes beyond the safety of dietary supplement use during pregnancy and has

undermined the public health. This distrust is in contrast to the trust among most of these same communities in the vaccine industrial complex. There is a public health need for a better way to manage herbs and dietary supplements.

I call to attention recent rulings that suggest to me that the current system is broken and needs fixing. In one instance, the FDA position harms the public health by denying a health claim and, in the other, by permitting, if not encouraging, the unnecessary use of supplements and herbs during pregnancy.

There are now hundreds of controlled studies performed at the leading universities in the world showing that homocysteine is a powerful risk factor for heart attacks and strokes. The most recent NHANES study showed that essentially all Americans who do not consume a multivitamin have blood folate concentrations associated with elevated homocysteine. Randomized controlled trials have shown, among those not taking folic acid supplements, that consuming the amount of synthetic folic acid--400 micrograms a day--in a multivitamin will substantially reduce homocysteine concentration. The evidence that the homocysteine-cardiovascular link is causal is very strong. The evidence that increased consumption could prevent an estimated 50,000 deaths from heart attacks annually is strong. In spite of these strong data, the FDA turned down the following health claim for a product with 400 micrograms of folic acid: "**As part of a well-balanced diet, rich in fresh whole fruits and vegetables, daily intake of at least 400 µg of folic acid, 3 mg of vitamin B6, and 5 µg of vitamin B12 may reduce the risk of vascular disease.**" The rationale for the denial was that there was not "significant

scientific agreement". After reading the long document, I inferred that the FDA denied the claim because it had not met the drug standard for multiple randomized controlled trials showing efficacy.

The second example of how the process is broken is the reason we are here today. The FDA issued a regulation on Jan 6th that opened the door for pregnant women to be exposed to increased consumption of herbs and supplements for which there are few, if any, data about safety for the embryo or efficacy for the pregnant woman. We know from tragic experience that rubella (which causes mild disease in adults), thalidomide (a safe and effective sleeping medicine for adults), and alcohol (at social drinking levels) can cause death or permanent disability of infants that were exposed in utero. Thus, any regulation that promotes the use of untested substances in pregnancy sets the stage for the tragic induction of birth defects.

I believe that these two types of errors that I have been discussing could have been reduced considerably if a grading protocol based on the quality of the data had been used. A useful prototype is available from the work of The United States Preventive Services Task Force. This Department of Health and Human Services task force has now published two editions of the Guide to Clinical Preventive Services. The second edition notes that the report "...provides recommendations for clinical practice on preventive interventions—screening tests, counseling interventions, immunizations and chemoprophylactic regimens—for the prevention of more than 80 target conditions." It further notes: "The recommendations in each chapter reflect a standardized review of

current scientific evidence and include a summary of published clinical research regarding the clinical effectiveness of each preventive service.” They had to deal with hundreds of potential tests and with various amounts of and quality of data. In the end, they decided to rate each test on the quality of the evidence supporting its use in clinical medicine. They created a scale of the quality of the evidence that decreased from randomized controlled trials to anecdotal/testimonial data. Attachment A describes the Task Force ratings and shows a few examples of the ratings for specific preventive services candidates. The quality of evidence scale follows:

## **“Quality of Evidence**

- I. Evidence obtained from at least one properly randomized controlled trial**
  
- II-1 Evidence obtained from well-designed controlled trials without randomization.**
  
- II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.**
  
- II-3 Evidence obtained from multiple time series with or without the intervention.**
  
- III Opinions of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.”**

I believe that this system that has been used by DHHS for many years could be very helpful in improving the way we deal with supplements and herbs. If there is proof of effectiveness from randomized controlled trials--a standard high enough for drug approval--it should be reported in a way that consumers can understand. An herb (in a consistently formulated form) or a supplement with such high quality data would receive the highest rating--Grade A, for example. Placing the grade on the package could be a quick way to inform consumers about the strength of the evidence for this product. Folic acid-containing multivitamins for the prevention of spina bifida would receive a Grade A. Multivitamins containing folic acid or folic acid and B12 and B6 for the prevention (reduction of the risk) of cardiovascular disease would receive at least Grade B (there is one randomized controlled trial showing stroke prevention). It would certainly become Grade A if additional randomized trials demonstrate benefit. Herbs or supplements for which there are no controlled data on efficacy would receive a Grade F. Considerable judgment would be required for the intermediate grades, of course.

A scoring system such as I suggest here, I think, could go a long way to reduce the risk to the public health that the current situation brings. DSHEA requires "substantiation". An evidence based scoring system such as I have mentioned could be the foundation for policy and practices for substantiation. Such a system could provide industry, the FDA and consumers the best interpretation of the existing data. Assuming that Grade A products sold better than Grade F products, there would a market-driven reason for industry to support

studies that would improve the quality of the data available for setting the grade.

Who would conduct such a scoring system, I think, is open to discussion. The key is that the body would be independent and that it would provide an objective, science based review of the effectiveness and safety of herbs and supplements. It could be entirely supported by industry, jointly supported by industry and government or supported by government alone. There may be other possibilities. Again, wherever and however it is supported, it must be independent and perceived as a source for independent, reliable, trustworthy interpretations of the existing data.

I hope that these comments are of help to the FDA, industry, the academic community, and the new Commission on Alternative and Complementary Medicine recently announced by President Clinton.