UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

DURK PEARSON and SANDY SHAW,
401 Summa Hills
Tonopah, NV 89049;

AMERICAN PREVENTIVE MEDICAL ASSOCIATION,
9912 Georgetown Pike,
Suite D2,
Great Falls, VA 22066;

JULIAN M. WHITAKER, M.D.,
Whitaker Wellness Institute
4321 Birch Street, Suite 100,
Newport Beach, CA 92623;

PURE ENCAPSULATIONS, INC.,
490 Boston Post Road
Sudbury, MA 01776; and

XCEL MEDICAL PHARMACY, LTD.,
6016 Fallbrook Avenue, Suite 200,
Woodland Hills, CA 91367,

Plaintiffs,

v.

Case No. _____

DONNA E. SHALALA, SECRETARY, UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES,
Sixth Floor,
200 Independence Avenue, S.W.,
Washington, D.C. 20201;

UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES,
200 Independence Avenue, S.W.,
Washington, D.C. 20201;

JANE E. HENNEY, M.D., COMMISSIONER OF FOOD AND DRUGS, FOOD AND DRUG ADMINISTRATION,

5600 Fishers Lane, Room 1471,)
Rockville, MD 20857;)
)
FOOD AND DRUG)
ADMINISTRATION,)
5600 Fishers Lane,)
Rockville, MD 20857;)
)
and the UNITED STATES OF)
AMERICA,)
)
Defendants. **)**

COMPLAINT
SEEKING REVIEW OF ADMINISTRATIVE AGENCY ACTION,
DECLARATORY JUDGMENT,
AND
INJUNCTIVE RELIEF

Plaintiffs Durk Pearson and Sandy Shaw; the American Preventive Medical Association; Julian M. Whitaker, M.D.; Pure Encapsulations, Inc.; and XCEL Medical Pharmacy, Ltd. hereby sue Defendants Donna E. Shalala, Secretary, United States Department of Health and Human Services (in her official capacity only); the United States Department of Health and Human Services; Jane E. Henney, M.D., Commissioner of Food and Drugs, Food and Drug Administration (in her official capacity only); the Food and Drug Administration; and the United States of America. The Plaintiffs sue the government Defendants to obtain declaratory and injunctive relief against a Food and Drug Administration final action that (1) violates the Plaintiffs' First Amendment free speech rights and the constitutional mandate of the United States Court of Appeals in Pearson v. Shalala, 164 F.3d 650, 656 (D.C. Cir. 1999), *reh'g denied en banc*, 172 F.3d 72 (D.C. Cir 1999); (2) violates the Fifth Amendment Due Process Clause; (3) violates the Supremacy Clause; (4) violates the Food, Drug and Cosmetic Act, 21 U.S.C. §

343(r)(5)(D); and (5) violates the Administrative Procedure Act's prohibition on arbitrary and capricious agency action, 5 U.S.C. § 706(2)(A).

I. INTRODUCTION

This complaint arises from FDA's suppression of a health claim for folic acid-containing dietary supplements, an act held unconstitutional under the First Amendment in Pearson v. Shalala, 164 F.3d 650, 656 (D.C. Cir. 1999), *reh'g denied en banc,* 172 F.3d 72 (D.C. Cir 1999). In Pearson, the Court of Appeals held FDA's rule prohibiting the folic acid health claim, 21 C.F.R. § 101.79(c)(2)(i)(G), invalid under the First Amendment to the United States Constitution. That rule prohibited the following truthful and nonmisleading scientific claim which Pearson Plaintiffs Durk Pearson, Sandy Shaw, and the American Preventive Medical Association along with Plaintiffs Dr. Julian M. Whitaker, Pure Encapsulations, Inc., and XCEL Medical Pharmacy, Ltd. wish to make on the labels and in the labeling of dietary supplements that contain recommended daily doses of .8 mg of folic acid: **"0.8 mg of folic acid in a dietary supplement is more effective in reducing the risk of neural tube defects than a lower amount in foods in common form"** ("Folic Acid Claim"). The Court remanded the case to the agency for reconsideration of the Folic Acid Claim, among three other health claims the Court held unconstitutionally suppressed.

Although this Court issued the Pearson First Amendment mandate to the agency on April 20, 1999, the agency failed to issue its decision on reconsideration for 18 months (22 months after the date Pearson was decided). For those 18 months FDA continued to unconstitutionally suppress the claim. When FDA did act,on October 10,

2000, the Food and Drug Administration again suppressed the Folic Acid Claim ("FDA's Folic Acid Decision").

The scientific evidence confirms that the Folic Acid Claim is truthful and nonmisleading scientific speech of a very high order. The Plaintiffs ask this Court to declare the suppression of the Folic Acid Claim effected by FDA's Folic Acid Decision (1) invalid under the Freedom of Speech Clause of the First Amendment to the United States Constitution and a violation of the First Amendment mandate of the United States Court of Appeals in Pearson v. Shalala; (2) invalid under the Due Process Clause of the Fifth Amendment; (3) invalid under the Supremacy Clause of the United States Constitution; (4) invalid under the health claims provision of the Food, Drug, and Cosmetic Act, 21 U.S.C. § 343 (r)(5)(B); and (5) invalid under the Administrative Procedure Act's prohibition on arbitrary and capricious agency action. The Plaintiffs further ask this Court to enjoin FDA from taking any action that would prevent Plaintiffs from placing the Folic Acid Claim on labels and in labeling of their dietary supplement products that contain recommended daily doses of .8 mg of folic acid.

II. DESCRIPTION OF THE PARTIES

Durk Pearson and Sandy Shaw. Pearson and Shaw are scientists residing in Nevada. They design dietary supplement formulations and license them to manufacturing and retailing companies. They are authors of four books on aging and age-related diseases, including the #1, million plus copy best seller *Life Extension; A Practical Scientific Approach* (1982). They have also published three other health books, two of which were best sellers: *The Life Extension Companion* (1984); *The Life Extension Weight Loss Program* (1986); and *Freedom of Informed Choice—FDA Versus*

Nutrient Supplements (1993). Durk Pearson and Sandy Shaw were plaintiffs in Pearson v. Shalala. Pearson and Shaw license, and receive royalties from, two dietary supplements that contain a daily dose of 0.8 mg (i.e., 800 mcg) of folic acid. Pearson and Shaw wish to place the Folic Acid Claim on the labels and in the labeling of their folic acid dietary supplements and, but for FDA's bar on labeling use of the claim, would do so. They joined the other Plaintiffs in filing comments in response to FDA's request for comments following the remand of the Pearson case wherein they urged approval of the Folic Acid Claim, expressed a willingness to accept any disclaimer reasonably necessary to avoid a misleading connotation, and presented scientific evidence providing corroboration that the Folic Acid Claim was both truthful and nonmisleading. They also joined the other Plaintiffs in filing comments in response to FDA's significant scientific agreement Guidance Document, challenging FDA's failure therein to comply with the Pearson mandate. Pearson and Shaw are aggrieved by FDA's violation of their rights, both constitutional and statutory, to communicate the Folic Acid Claim on the labels and in the labeling of their folic acid dietary supplements.

American Preventive Medical Association. The American Preventive Medical Association (APMA) is a non-profit organization located in Great Falls, Virginia. APMA was founded in October of 1992 and is dedicated to ensuring consumer access to preventive therapies and the rights of health care providers to offer those therapies. APMA was a plaintiff in Pearson v. Shalala. Several APMA physicians, including all physician members of APMA's board of directors, sell to their patients dietary supplements that contain a daily dose of 0.8 mg of folic acid. APMA and its practitioner members (along with their hundreds of thousands of patients) would benefit from

approval of the Folic Acid Claim that is the subject of this proceeding because it would enable them to inform their patients of the superior effectiveness of dietary supplements they sell that contain 0.8 mg (i.e., 800 mcg) of folic acid (over foods in common form) in reducing the risk of NTDs. APMA joined the other Plaintiffs in filing comments in response to FDA's request for comments following the remand of the Pearson case, wherein APMA urged approval of the Folic Acid Claim, expressed a willingness to accept any disclaimer reasonably necessary to avoid a misleading connotation, and presented scientific evidence providing corroboration that the Folic Acid Claim was both truthful and nonmisleading. But for the FDA's ban on the Folic Acid Claim, APMA's physician members, including its physician board members, would place the claim on the labels and in the labeling of the dietary supplements they sell to their patients. APMA's physician members and board members are aggrieved by FDA's violation of their rights, both constitutional and statutory, to communicate the Folic Acid Claim on the labels and in the labeling of the folic acid dietary supplements they sell.

Julian M. Whitaker, M.D. Julian M. Whitaker, M.D. is a physician licensed to Practice medicine in the states of California and Washington. He graduated from Dartmouth College in 1966 with a B.S. degree and from Emory University in 1970 with an M.D. degree. He received additional training in surgery as a resident at the University of California Medical School. From 1975 to 1976 he worked as a physician at the Pritikin Institute in California. Since that time he has been the Clinical Director of the Whitaker Wellness Institute in Newport Beach, California. He is the author of five books: *Reversing Heart Disease* (1985); *Reversing Diabetes* (1987); *Reversing Health Risk* (1989); *Natural Healing* (1994); and *What Your doctor Won't Tell You About*

Bypass (1995). Since August of 1991 he has been the editor of *Health & Healing*, currently the nation's largest single editor health newsletter. In 1998, *Health & Healing* had over 500,000 subscribers. He receives royalties from the distribution and sale of several dietary supplements based on formulas he develops and licenses. Among the dietary supplements which Dr. Whitaker has formulated and licensed (and from which he receives royalty payments) are two containing folic acid, each with 0.8 mg (i.e., 800 mcg) of the acid per recommended daily dose. He wants to place the Folic Acid Claim on the labels and in the labeling of his folic acid dietary supplements and, but for FDA's bar on labeling use of the claim, he would do so. He joined the other Plaintiffs in filing comments in response to FDA's request for comments following the remand of the Pearson case wherein he urged approval of the Folic Acid Claim, expressed a willingness to accept any disclaimer reasonably necessary to avoid a misleading connotation, and presented scientific evidence providing corroboration that the Folic Acid Claim was both truthful and nonmisleading. He also joined the other Plaintiffs in filing comments in response to FDA's significant scientific agreement Guidance Document, challenging FDA's failure therein to comply with the Pearson mandate. Dr. Whitaker is aggrieved by FDA's violation of his rights, both constitutional and statutory, to communicate to the public (and to his patients) the Folic Acid Claim on the labels and in the labeling of his folic acid dietary supplements.

Pure Encapsulations, Inc. Pure Encapsulations, Inc. (Pure) is a Massachusetts corporation engaged in the business of manufacturing, distributing, and selling over 250 pharmaceutical grade dietary supplements for human and companion animal consumption. Eight of the dietary supplements manufactured and sold by Pure each

contain 0.8 mg (i.e., 800 mcg) of folic acid per recommended daily dose. Pure would like to place the Folic Acid Claim on the labels of, and in the labeling for, each of those eight dietary supplement products, and, but for FDA's bar on labeling use of the claim, would do so. Pure joined the other Plaintiffs in filing comments in response to FDA's request for comments following the remand of the Pearson case wherein Pure urged approval of the Folic Acid Claim, expressed a willingness to accept any disclaimer reasonably necessary to avoid a misleading connotation, and presented scientific evidence providing corroboration that the Folic Acid Claim was both truthful and nonmisleading. Pure also joined the other Plaintiffs in filing comments in response to FDA's significant scientific agreement Guidance Document, challenging FDA's failure therein to comply with the Pearson mandate. Pure is aggrieved by FDA's violation of its rights, both constitutional and statutory, to communicate the Folic Acid Claim on the labels and in the labeling of Pure's folic acid dietary supplements.

XCEL Medical Pharmacy, Ltd. d/b/a XCEL Health Care. XCEL Medical Pharmacy, Ltd. d/b/a XCEL Health Care (XCEL) is a California corporation engaged in the business of manufacturing, distributing, and selling pharmaceutical grade dietary supplements for human consumption. One of the supplements manufactured and sold by XCEL contains 0.8 mg (i.e., 800 mcg) of folic acid per daily recommended dose. XCEL would would like to place the Folic Acid Claim on the labels of, and in the labeling for, its folic acid dietary supplement, and, but for FDA's bar on labeling use of the claim, would do so. XCEL joined the other Plaintiffs in filing comments in response to FDA's request for comments following the remand of the Pearson case wherein XCEL urged approval of the Folic Acid Claim, expressed a willingness to accept any disclaimer

reasonably necessary to avoid a misleading connotation, and presented scientific evidence providing corroboration that the Folic Acid Claim was both truthful and nonmisleading. XCEL also joined the other Plaintiffs in filing comments in response to FDA's significant scientific agreement Guidance Document, challenging FDA's failure therein to comply with the Pearson mandate. XCEL is aggrieved by FDA's violation of its rights, both constitutional and statutory, to communicate the Folic Acid Claim on the labels and in the labeling of XCEL's folic acid dietary supplement.

Donna E. Shalala, Secretary, United States Department of Health and Human Services; United States Department of Health and Human Services; Jane E. Henney, M.D., Commissioner of Food and Drugs, Food and Drug Administration; United States Food and Drug Administration; and the United States of America. Donna E. Shalala (sued in her official capacity only) is the Secretary of the United States Department of Health and Human Services, the executive department having jurisdiction over the Food and Drug Administration. Jane E. Henney, M.D. (sued in her official capacity only) is the Commissioner of the Food and Drug Administration. The Food and Drug Administration is that administrative agency granted authority by Congress to regulate the interstate manufacture, sale, and distribution of foods, drugs, cosmetics, biologics, medical devices, and dietary supplements in the United States. The Department of Health and Human Services and the Food and Drug Administration are part of the executive branch of the government of the United States.

III. REQUEST FOR EXPEDITED REVIEW

The Plaintiffs respectfully request that the Court accord this Complaint expedited review. Two of the Plaintiffs first sought FDA approval of the Folic Acid Claim six (6)

years ago. The agency's suppression of the claim was held to violate the First Amendment to the United States Constitution in January of 1999. The claim continues to be suppressed by this agency, a civil rights violation in need of immediate rectification. The suppression of the claim produces immediate and profound adverse public health effects by causing fertile women unaware of the claim to bear unwittingly an unnecessary risk of having an NTD-affected birth. The Court of Appeals has already held FDA's rule suppressing the claim invalid, yet the agency has enacted a new rule prohibiting the very same claim following eighteen months of delay in reaching that decision, during which time FDA continued its suppression of the claim.

Each day of delay in reaching a decision on the merits is another in which fertile women continue to be deprived of information essential to lowering the risk of NTD-affected births. According to the CDC, each year there are approximately 4,000 live births and pregnancies afflicted with spina bifida and anencephaly. Access to the Folic Acid Claim is, thus, a public health imperative. FDA's refusal to approve the Folic Acid Claim ensures that women, particularly the poor who lack prenatal care, are denied access at the point of sale to information that could save them and their newborns from the horrible affliction of an NTD-affected birth. Without access to the Plaintiffs' truthful and direct claim, fertile women unaware of the superior bioavailability of folic acid in supplements are likely to experience a heightened risk of an NTD birth, a risk that could be averted were they simply made aware of the inexpensive expedient of daily ingesting .8 mg of folic acid in a dietary supplement. Indeed, FDA's current labeling regulations encourage misleading labeling: Foods in common form containing $1/10^{th}$ to $1/20^{th}$ of the minimum dose of folate officially estimated to be 50% effective at preventing NTDs may

nevertheless be labeled a "good source" of folate and carry an NTD risk reduction claim. No qualification is required that ten to twenty servings per day of such foods must be consumed to provide the promised risk reduction.

IV. BACKGROUND

A. Neural Tube Defects in the United States

1. Neural tube defects (NTDs), specifically spina bifida and anencephaly, affect approximately 4,000 live births and pregnancies each year in the United States. Of these, the Centers for Disease Control and Prevention (CDC) report that 1,500 afflicted infants are born with spina bifida, 1000 are born with anencephaly, and an estimated 1,500 NTD fetuses are aborted annually. NTDs are implicated in 1.3% of all infant deaths and are second only to cardiac defects as the leading cause of perinatal mortality from all birth defects. These spinal cord malformations are associated with serious developmental disabilities including muscle weakness and/or paralysis, bowel and bladder incontinence, and intellectual impairment. While infants with anencephaly usually die shortly after birth, those with spina bifida usually survive into adulthood with life-long impairments.

B. Folic Acid

2. Folic acid, also known as pteroylmonoglutamic acid, is a synthetic compound used in dietary supplements and fortified foods.

3. The term folate includes all compounds that have the vitamin properties of folic acid—including folic acid and naturally occurring compounds in food.

4. The average diet in the United States contains .2 mg (i.e., 200 mcg) of naturally occurring food folate. Naturally occurring food folate is one-half as bioavailable as folic acid, yielding in the average diet 100 mcg of folic acid per day.

5. Folic acid is a water soluble B-vitamin that has no known toxicity.

C. <u>Fertile Women Are Not Getting Enough Folic Acid in their Diets</u>

6. As many as 35-50% of pregnancies are unplanned. Folic acid must be taken from at least one month before through the first trimester of pregnancy in order to be effective in preventing NTDs; folic acid interventions will therefore be significantly less successful if targeted only to pregnant women or those planning a pregnancy. CDC, "Recommendations for the Use of Folic Acid to Reduce the Number of Cases of Spina Bifida and Other Neural Tube Defects," 41 *Morbidity and Mortality Weekly Reports*, 1-7, 1992.

7. The National Center for Health Statistics reports that women are not getting enough folic acid in their diets – on average, U.S. women of childbearing age (approximately 15 – 44 years of age) consume only about .2 mg (i.e., 200 mcg) of naturally occurring food folate per day, yielding only about .1 mg (i.e., 100 mcg) of folic acid per day. Only 66% of women report ever hearing of folic acid; only 16% report knowledge that it helps reduce birth defects; and only 9% report knowledge that it should be taken before pregnancy, according to a 1997 March of Dimes Birth Defects Foundation and CDC survey. National Folic Acid Program of the National Center for Environmental Health, Center for Disease Control and Prevention, Publication Number 99-0082 (1999).

8. Only 32% of American women of childbearing age are taking a multivitamin with folic acid on a daily basis. Centers for Disease Control and Prevention, *Knowledge and Use of Folic Acid by Women of Childbearing Age in the United States, 1995 and 1998*, 48 MORBIDITY MORTAL WEEKLY REPORTS, 325-7 (1999).

9. The majority of adult men and women in the U.S. consume less than the 1989 RDA for dietary folate (180-200 mcg/day). ALAIMO K. MCDOWELL, et al., NATIONAL CENTER FOR HEALTH STATISTICS, DIETARY INTAKE OF VITAMINS, MINERALS, AND FIBER OF PERSONS AGES 2 MONTHS AND OVER IN THE UNITED STATES: THIRD NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, PHASE 1, *1988-1991*(1994).

10. The CDC and the FDA accept that a reasonable estimate of the risk reduction achievable from .4 mg (i.e., 400 mcg) of folic acid is 50%. Centers for Disease Control, 41 *Morbidity and Mortality Weekly Report* (September 11, 1992); 21 C.F.R. § 101.79.

D. Folic Acid in Dietary Supplement Form Is More Bioavailable Than Folate in Foods in Common Form

11. In their comments to FDA, the Plaintiffs supplied FDA proof that other health agencies of the federal government recognized that dietary supplement (synthetic) folic acid is more bioavailable than food folate.

12. On April 30, 1999, the U.S. Centers for Disease Control and Prevention, the March of Dimes, and the National Council on Folic Acid stated, "Although it is possible to get enough folic acid from fortified foods, it is not easy. Most experts caution that it may be difficult to maintain the daily requirement without taking a folic acid pill or multivitamin."

13. The Food and Nutrition Board of the National Academy of Sciences has determined that the bioavailability of synthetic folic acid found in dietary supplements is

twice that of food folate. To account for the differences in bioavailability, the FNB has given its recommendations for folic acid in dietary folate equivalents (DFEs). One DFE = 1 mcg food folate = 0.6 mcg of folic acid (from fortified food or supplement) consumed with food, or one DFE = 0.5 mcg of synthetic (supplemental) folic acid taken on an empty stomach. FOOD AND NUTRITION BOARD, INSTITUTE OF MEDICINE, DIETARY REFERENCE INTAKES: THIAMIN, RIBOFLAVIN, NIACIN, VITAMIN B6, FOLATE, VITAMIN B12, PANTOTHENIC ACID, BIOTIN, AND CHOLINE 210 (1998).

14. In the National Folic Acid Program of the U.S. Centers for Disease Control and Prevention and of the National Center for Environmental Health, those two federal agencies state:

- "Folic acid is the synthetic B-vitamin form that is used in vitamin supplements and added to fortified foods.[1] **Synthetic folic acid is absorbed better than natural food folate."** (emphasis in original).
- "The bioavailability of synthetic folic acid is approximately twice that of food folate."
- "it has not been demonstrated that food folate protects against NTDs as well as synthetic folic acid."
- "synthetic folic acid is more easily absorbed than food folate (**0.5-0.6 mcg of folic acid equals one mcg of food folate**)." (emphasis in original).
- "To get the recommended amount of folic acid each day, most women will need to change their behaviors either to take vitamin supplements that contain folic acid or to consume sufficient amounts of . . . foods fortified with folic acid."
- "women capable of becoming pregnant who eat a healthy diet still need to take a vitamin supplement, eat a breakfast cereal containing 100% of the daily value of folic acid daily[2] or increase their consumption of foods fortified with folic acid to achieve the recommended amount of folic acid for the prevention of NTDs."

[1] Folic acid fortified foods are foods supplemented with synthetic folic acid. They are not foods in common form.
[2] This is possible only with a fortified cereal and not with a food in common form.

- "At this time the evidence for a protective effect from folate supplements is much stronger than that for food folate."

- "CDC and NCEH question whether food folate is effective in preventing NTD."

E. .8 mg of Folic Acid in a Supplement Reduces Risk of NTDs by a Greater Percentage than Lower Amounts in Foods in Common Form

15. The Folic Acid Claim compares .8 mg of folic acid in a dietary supplement with a lower amount in foods in common form.

16. A food in common form is not a fortified food.

17. Fortified foods are uncommon foods in that they are supplemented with synthetic folic acid. According to the Institute of Medicine of the National Academy of Sciences, the bioavailability of folic acid in a dietary supplement consumed on an empty stomach is greater than the bioavailability of folic acid in a fortified food.

18. Current folic acid fortification programs have not reduced the prevalence of NTDs in the United States.

19. Based upon its evaluation of scientific studies that have examined the comparative effectiveness of dietary folate and synthetic folic acid in reducing NTD risk, the Institute of Medicine and the Food and Nutrition Board concluded that only synthetic folic acid found in supplements and fortified foods has been shown to provide protection against NTD. FOOD AND NUTRITION BOARD, INSTITUTE OF MEDICINE, DIETARY REFERENCE INTAKES: THIAMIN, RIBOFLAVIN, NIACIN, VITAMIN B6, FOLATE, VITAMIN B12, PANTOTHENIC ACID, BIOTIN, AND CHOLINE 259 (1998).

20. Under 21 CFR §§ 136, 137 and 139, FDA has ordered all enriched cereal or grain products to be fortified at a level of .14 (i.e., 140 mcg) of folic acid per 100 grams of grain product.

21. No published peer-reviewed scientific study associates daily consumption of less than .1 mg (i.e., 100 mcg) of folic acid with ***any*** reduction in the risk of NTDs. By FDA's own admission, a reasonable estimate of a 50% reduction is attainable with consumption of .4 mg (i.e., 400 mcg) per day of folic acid. 21 C.F.R. § 101.79.

22. Scientific evidence does not confirm a single reasonable estimate of risk reduction attainable from consumption of less than 0.4 mg (i.e., 400 mcg) of folic acid. 21 C.F.R. § 101.79.

23. 0.8 mg (i.e., 800 mcg) of folic acid in a dietary supplement consumed daily by women of childbearing age has been shown in human clinical intervention trials (the FDA's so-called "gold-standard") to reduce the risk of NTD births by between 70% and 100%.

24. Women who have previously had one NTD-affected pregnancy are at a higher risk of a second NTD-affected pregnancy. Among U.S. couples who have had a child with an NTD, the recurrence risk is 2% to 3% in subsequent pregnancies.

25. The CDC recommends increasing the intake of folic acid to 4mg per day (i.e., 4,000 mcg) beginning at least 1 month before conception and continuing through the first trimester for all women who have had a prior NTD-affected pregnancy. CDC, "Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects," *Use of Folic Acid for Prevention of Spina Bifida and Other Neural Tube Defects 1983 and 1991,* 40 MORBIDITY MORTAL WEEKLY REPORTS

500, 513-516 (1991). CDC bases its recommendation on scientific proof that the higher amounts of folic acid supplementation correlate with a higher percentage of protection against NTD risk. Center for Disease Control and Prevention, *Recommendations for the Use of Folic Acid to Reduce the Number of Cases of Spina Bifida and Other Neural Tube Defects.* 40 MORBIDITY MORTAL WEEKLY REPORTS 1, 1-8 (1992).

26. The Institute of Medicine of the National Academy of Sciences has found the "best evidence" concerning the effect of folic acid on reduction in the risk of NTDs to come from four randomized clinical trials: Cziezel (1992, using 0.8 mg (i.e., 800 mcg) of folic acid in a multivitamin and finding complete, 100% protection against NTDs); Kirke (1992, found some protection against NTD using 0.36 mg (i.e., 360 mcg) of folic acid alone or in a multivitamin preparation); Laurence (1981, using 4.0 mg (i.e., 4000 mcg) of folic acid alone and finding 100% protection against NTDs); and Wald (1991, using 4.0 mg (i.e., 4,000 mcg) of folic acid alone and in a multivitamin and finding both to convey 72% protection against NTDs).

27. In approving its original NTD/folic acid claim, FDA relied upon seven studies involving use of folic acid in a multivitamin. In 58 Fed. Reg. 53254, approving the claim, FDA did not question the effectiveness of folic acid in a multivitamin preparation.

28. No peer reviewed scientific evidence exists to support the conclusion that folic acid is less effective in a multi-vitamin preparation than when taken as a single vitamin. To the contrary, peer reviewed scientific evidence exists to support the conclusion that folic acid is as effective in a multi-vitamin preparation as it is in a single vitamin (Bower and Stanley, 1989; Berry, 1999; Czeizel, 1992; Kirke, 1992; Milunsky, 1989; Mulinare, 1988; Smithells, 1983; Wald, 1991; Werler 1993). Despite that fact,

FDA has questioned the Cziezel study results demonstrating 100% effectiveness of a .8 mg folic acid supplement on the basis that the folic acid was in a multivitamin and that other vitamins in the multivitamin could have affected the outcome. No scientific evidence exists to corroborate FDA's suspicions.

V. PROCEDURAL HISTORY

29. On November 8, 1990, the President signed into law the Nutrition Labeling and Education Act ("NLEA"). 21 U.S.C. 331, *et seq*. Within the Act Congress ordered the FDA to examine 10 nutrient-disease relationships to determine whether health claims could be authorized for them. Among the 10 claims was one associating folic acid with neural tube defects. See Nutrition Labeling and Education Act § 3(b)(1)(A); 21 U.S.C.§ 331 (2000).

30. On November 27, 1991, the FDA published a proposed rule, where it proposed not to authorize any health claim linking folic acid with a reduction in the risk of neural tube defects. 56 Fed. Reg. 60610.

31. On September 11, 1992, the United States Centers for Disease Control and Prevention issued a public recommendation containing a claim FDA refused to authorize. The CDC published the following recommendation:

> All women of childbearing age in the United States who are capable of becoming pregnant should consume 0.4 mg of folic acid per day for the purpose of reducing their risk of having a pregnancy affected with spina bifida or [other neural tube defects].

Centers for Disease Control, 41 *Morbidity and Mortality Weekly Report* (September 11, 1992). The CDC estimated that this recommendation could reduce the number of cases of NTDs in the United States by 50 percent. Ironically the CDC recommendation was developed through a joint effort, coordinated by the Office of the Assistant Secretary for

Health, Department of Health and Human Services; by the CDC; by the Health and Resources and Services Administration; by the National Institutes of Health; and, indeed, by the FDA itself. See id. at 5.

32. On January 6, 1993, against the CDC's recommendation, FDA adopted a final rule prohibiting any claim associating folic acid with NTDs, 58 Fed. Reg. 2606 (January 6, 1993).

33. On October 14, 1993, just one week before Congressional hearings were scheduled to commence on FDA's refusal to allow a Folic Acid-NTD claim (see "Dietary Supplement Health and Education Act of 1994," Senate Report 103-410, October 8, 1994 (103d Cong., 2d Sess.) at 16), without any change in scientific evidence and after the Pearson Plaintiffs had sued the agency for its refusal, FDA reversed its position and proposed a claim associating folic acid with a reduction in the risk of NTDs, 58 Fed. Reg. 53254 (October 14, 1993). Three years later, FDA finally authorized claims to be made in final regulations, 61 Fed. Reg. 8752 (March 5, 1996).

34. The United States Senate Committee on Labor and Human Resources evaluated FDA's actions and concluded:

> Without appropriately accounting for the CDC recommendation, FDA promulgated a rule in January 1993, prohibiting claims concerning the relationship. In the wake of controversy concerning FDA's action, and despite the absence of any change in the scientific evidence, the Agency reversed course, proposing to authorize such claims in October, 1993. Final regulations authorizing the claim were promulgated in March 1996. ***Undoubtedly, many children suffered from preventable neural tube defects as a result of FDA's delay in authorizing health claims based on the 1992 CDC recommendation.***

"Food and Drug Administration Modernization and Accountability Act of 1997," Senate Report 105-43, July 1, 1997 (105th Cong., 1st Sess.) at 50 (emphasis added).

35. In its final rule of March 5, 1996, the FDA found that a reasonable estimate of reduction in the incidence of neural tube defects attainable from daily consumption of .4 mg (i.e., 400 mcg) of folic acid was 50% (the CDC estimate) and specified as its daily "target intake goal" that amount of folic acid. 21 C.F.R. §§ 101.79(b)(3); (c)(3)(iv).

36. FDA approved the following "model" health claims associating folic acid with a reduction in the risk of neural tube defects, 21 C.F.R. § 101.79(d)(1)-(3). Each conveys the misleading impression that food folate provides adequate protection against NTDs when scientific evidence fails to confirm any reduction in NTD risk from food folate alone:

> Example 1. Healthful diets with adequate folate may reduce a woman's risk of having a child with a brain or spinal cord birth defect.
>
> Example 2. Adequate folate in healthful diets may reduce a woman's risk of having a child with a brain or spinal cord birth defect.
>
> Example 3. Women who consume healthful diets with adequate folate throughout their childbearing years may reduce their risk of having a child with a birth defect of the brain or spinal cord. Sources of folate include fruits, vegetables, whole grain products, fortified cereals, and dietary supplements.
>
> Example 4. Women who consume healthful diets with adequate folate may reduce their risk of having a child with birth defects of the brain or spinal cord. Folate intake should not exceed 250% of the DV (1,000 mcg).

21 C.F.R. § 101.79.

37. Although FDA identified its daily "target intake goal" to be 400 mcg (the Recommended Daily Intake (RDI) for the vitamin), it authorized the above model claims to be made on foods containing as little as 10% of the RDI.[3] 21 C.F.R. § 101.79 (c)(2)(ii) cross-referencing 21 C.F.R. §101.54. That 10% of the RDI as food folate (the equivalent

[3] FDA's model claims do not disclose FDA's 400 mcg daily target intake goal.

of only 20 mcg of folic acid), has not been demonstrated to produce any reduction in NTD affected births.

38. In response to FDA's proposed and final rules not to allow a folic acid-NTD claim, Plaintiffs Durk Pearson and Sandy Shaw and Plaintiff American Preventive Medical Association (hereinafter the "Pearson Plaintiffs") filed comments urging FDA to authorize a claim associating consumption of folic acid with a reduction in the risk of NTDs and inviting FDA to use a "split label" approach wherein FDA would qualify the level, degree, quality, and quantity of scientific evidence supporting the claim in the disclaimer statement.

39. FDA at first rejected the Pearson Plaintiffs comments and refused to authorize any folic acid-NTD claim with or without disclaimer in its Final Rule, 58 Fed. Reg.2606 (1993). In response to that rule, the Pearson Plaintiffs filed suit against the agency on June 24, 1994. During the pendency of the suit, FDA reversed its position based on no change in the scientific evidence and authorized a claim. 58 Fed. Reg. 53254 (1993). In response to that agency action, the Plaintiffs withdrew their initial suit.

40. On January 28, 1994, the Pearson Plaintiffs filed new comments in response to FDA's rule of January 4, 1994, urging FDA to delete 21 C.F.R. § 101.79(c)(2)(i)(G), which read: "The claim shall not state that a specified amount of folate per serving from one source is more effective in reducing the risk of neural tube defects than a lower amount per serving from another source." In their comments, the Plaintiffs asked FDA to authorize the following claim for which they presented substantial scientific evidence in support: ".8 mg of folic acid in a dietary supplement is more effective in reducing the risk of neural tube defects than a lower amount in foods in common form" (hereinafter "Folic

Acid Claim"). They did so not only because they wished to place the claim on the labels and in the labeling of their .8 mg folic acid-containing dietary supplements but also because they regarded the Folic Acid Claim as a public health necessity.

41. In its final rule on a folic acid-NTD claim, 61 Fed. Reg. 8752; 21 C.F.R. § 101.79, FDA rejected the Pearson Plaintiffs requests (including their Folic Acid Claim), addressing them without reasoned analysis in a single sentence: "the scientific literature does not support the superiority of any one source [of folic acid] over others." 61 Fed. Reg. at 8760.

42. On January 28, 1994, the Pearson Plaintiffs filed an emergency petition to stay FDA's rule 21 C.F.R. § 101.79(c)(2)(i)(G), reciting the public health necessity of providing women of childbearing age information indispensable to reducing NTD risk. FDA ignored the petition.

43. In its final rule, the FDA authorized foods to carry any of the model claims in 21 C.F.R. § 101.79 on its labels and in its labeling if the food qualifies as a "good source" of folate, 21 C.F.R. §101.79(c)(2)(ii), as that term is defined in 21 C.F.R. § 101.54. Under the latter section, a food is a "good source" if it contains as little as 10% of the RDI for the nutrient in question per reference amount customarily consumed (typically, per serving). The RDI for folic acid is 400 mcg. 21 C.F.R. § 101.9 (c)(8)(iv). Therefore, FDA has authorized use of its model claims on foods containing per serving amounts of folate that are as little as 40 mcg of food folate (equivalent to 20 mcg of folic acid) an amount not demonstrated to reduce the risk of NTD-affected births.

44. No published peer-reviewed study associates daily consumption of less than 100 mcg of folic acid with ***any*** reduction in the risk of NTDs. By FDA's own admission,

a reasonable estimate of a 50% reduction is attainable with consumption of 400 mcg per day of folic acid. 21 C.F.R. § 101.79.

45. On November 16, 1995, the Pearson Plaintiffs sued the FDA on, *inter alia*, First Amendment and Administrative Procedure Act grounds, for denying and suppressing the Folic Acid Claim, asking the Court to hold FDA's action and rule, 21 C.F.R. § 101.79(c)(2)(i)(G), invalid under the First Amendment's free speech clause and the Administrative Procedure Act's prohibition on arbitrary and capricious agency action, abuse of agency discretion, and unlawful agency action.

46. On March 5, 1996, FDA ordered that all enriched cereal or grain products be fortified at a level of .14 mg (i.e., 140 mcg) of folic acid per 100 grams of grain product. 61 Fed. Reg. 8781; 21 C.F.R. §§ 136, 137 and 139.

47. On January 12, 1998, the United States District Court for the District of Columbia upheld FDA's speech ban. Pearson v. Shalala, 14 F. Supp. 2d 10 (D.D.C.1998).

48. On January 15, 1999, a unanimous panel of judges for the United States Court of Appeals for the D.C. Circuit reversed and remanded the case to the district court with instructions to remand in turn to the FDA for reconsideration of the Pearson Plaintiffs' health claim. See Pearson v. Shalala, 164 F.3d at 661. In particular, the Pearson Court held FDA's denial of each claim there in issue, including the Folic Acid Claim, a violation of the First Amendment to the United States Constitution, reasoning that none of the claims was "inherently misleading" such that they could be constitutionally suppressed. The Court held that each of the claims was, at worst,

potentially misleading and thus had to be evaluated to determine if qualifying statements could eliminate any potentially misleading connotations. See id. at 655.

49. The Pearson Court additionally agreed with the Pearson Plaintiffs that the FDA had violated the Administrative Procedure Act's prohibition on arbitrary and capricious agency action by not adequately defining its standard for review of health claims, i.e., "significant scientific agreement." See id. at 660. The Court reasoned:

> [I]t must be possible for the regulated class to perceive the principles which are guiding agency action. Accordingly, on remand, the FDA must explain what it means by significant scientific agreement or, at minimum, what it does not mean.

Id. at 661.

50. Concerning the denial of the Folic Acid Claim, the Court reasoned:

> The FDA's concern regarding the fourth claim—"0.8 mg of folic acid in a dietary supplement is more effective in reducing the risk of neural tube defects than a lower amount in foods in common form"—is different from its reservations regarding the first three claims; the agency simply concluded that "the scientific evidence does not support the superiority of any one source [of folic acid] over others." 61 Fed. Reg. at 8760. But it appears that credible evidence did support this claim, see, e.g., DIET AND HEALTH: IMPLICATIONS FOR REDUCING CHRONIC DISEASE RISK 67 (Committee on Diet and Health, Food and Nutrition Board 1989) (concluding that "[l]osses [of folic acid] in cooking and canning [foods] can be very high due to heat destruction") and we suspect that a clarifying disclaimer could be added to the effect that "the evidence in support of this claim is inconclusive." . . .

Pearson at 659.

51. The FDA sought rehearing en banc but was rebuffed in a 11-0 decision of the entire Court of Appeals. Pearson v. Shalala, 172 F.3d 72 (D.C. Cir. 1999). The Solicitor General of the United States declined to file a petition for certiorari, electing not to seek Supreme Court review.

52. On April 20, 1999, the United States District Court issued its mandate to the FDA to implement the Court of Appeals decision.

53. From April 20, 1999 until approximately April 7, 2000, FDA refused to announce any date certain by which it would act on the mandate. In letters dated July 19, 1999, September 23, 1999 and February 18, 2000, the Plaintiffs demanded that FDA adopt a date certain. In letters of October 5, 1999 and February 17, 2000, FDA refused to specify any date certain. In plaintiffs' letters, they asked the agency to allow, but FDA refused to permit, use of the Folic Acid Claim with the interim disclaimers presented in Pearson, i.e., "The FDA does not approve this claim" or "The evidence in support of this claim is inconclusive."

54. FDA refused to allow the Folic Acid Claim to be made with or without disclaimers between April 20, 1999 and October 10, 2000 (18 months). When FDA finally issued its decision on October 10, 2000, it continued to prohibit the Folic Acid Claim. It prohibits the claim to this day.

55. Although the Court of Appeals held FDA's folic acid regulation, 21 C.F.R. § 101.79(c)(2)(i)(G), invalid on January 15, 1999, FDA did not publish a revocation of that rule in the Federal Register until October 3, 2000 (22 months after that decision and 18 months after the constitutional mandate issued to FDA). Even then, although FDA revoked the rule, it simultaneously announced that it would continue to prohibit the Folic Acid Claim pending issuance of its decision on October 10, 2000 (and, on October 10, it again prohibited the claim and continues to prohibit the claim to this day).

56. Although the Court of Appeals held that FDA failed to satisfy its First Amendment burden of proof to justify suppression of the Folic Acid Claim, the FDA

continued to prohibit the claim after the mandate for implementation of the decision issued on April 20, 1999, after it revoked the rule on October 3, 2000, and to this day.

57. Prior to its Folic Acid Decision of October 10, 2000, the FDA never associated the term "foods in common form" with fortified foods. Folic acid fortified foods are uncommon in that they have synthetic folic acid added to them. FDA has authorized fortification of farina and certain other grain products with .14 mg (i.e., 140 mcg) of synthetic folic acid per 100 grams of grain product. Those foods are defined as "fortified foods" but not as "foods in common form." 21 C.F.R. § 137.

58. On December 22, 1999, FDA published a *Guidance for Industry: Significant Scientific Agreement in the Review of Health Claims for Conventional Foods and Dietary Supplements* (hereinafter "Guidance Document") meant to be a response to the Pearson Court's requirement that FDA define its standard for health claims review. The Guidance Document did not explain what level, quantity, quality, or kind of scientific evidence FDA expected as a condition precedent for health claims approval except to indicate that human clinical trials, so-called intervention studies, that it regarded as well-designed would be the best evidence in support of a claim and that causal proof of the relationship between a nutrient and a disease would have to be established to a near conclusive degree before a claim would be approved. FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, GUIDANCE FOR INDUSTRY: SIGNIFICANT SCIENTIFIC AGREEMENT IN THE REVIEW OF HEALTH CLAIMS FOR CONVENTIONAL FOODS AND DIETARY SUPPLEMENTS (1999). The latter is precisely the level of proof Congress intended not be required for foods and dietary supplements as evidenced by the plain

meaning of the language in, and as explained in the legislative history concerning, the health claims provisions of the Food, Drug and Cosmetic Act.

59. In the absence of an assurance from the agency of a specific date by which it would end its practice of suppressing the claims held unconstitutionally suppressed by the Pearson Court, the Pearson Plaintiffs filed with this Court an application for preliminary injunction against the agency on March 31, 2000.

60. On or about April 7, 2000, on the eve of filing its opposition to the Pearson Plaintiffs' application for preliminary injunction to block FDA from denying use of the claims, the FDA announced for the first time that it would issue a decision on the mandate by October 10, 2000.

61. On May 23, 2000, the United States District Court denied the application for preliminary injunction.

62. On September 8, 2000, the FDA invited parties to file additional scientific evidence on each of the four claims held unconstitutionally suppressed in Pearson. FDA pledged to re-evaluate the claims in light of all scientific evidence and issue its decision on whether to permit the claims under its still undefined "Significant Scientific Agreement" review approach or, if not, under the First Amendment standard articulated in Pearson, relying on disclaimers to cure potential misleadingness.

63. The Pearson Plaintiffs and Dr. Julian M. Whitaker, Pure Encapsulations, Inc., and XCEL Medical Pharmacy, Ltd. filed over 600 pages of scientific submissions on November 22, 1999, April 3, 2000, and August 9, 2000. The Pearson Plaintiffs had filed over 300 pages of scientific submissions in the rulemaking proceedings preceding Pearson.

64. In their comments, the Plaintiffs supplied documentary evidence providing strong scientific support from human clinical intervention trials (FDA's so-called "gold-standard") that .8 mg (i.e., 800 mcg) of folic acid in a dietary supplement is more effective in reducing the risk of neural tube defect births than a lower amount in foods in common form.

65. After informing the courts and Congress that it would issue its decisions on all four Pearson claims on October 10, 2000, the FDA issued decisions on two of the four decisions and postponed action on the remaining two until October 24, 2000. On October 24, 2000, FDA acted on one of the two remaining claims and postponed action on the fourth until November 30, 2000.

66. On October 6, 2000, the FDA published in the Federal Register, 65 Fed. Reg. 59,855, a notice explaining how it would evaluate each of the four Pearson claims. FDA stated that it would evaluate each in accordance with its Guidance Document to determine if its undefined "significant scientific agreement" standard had been satisfied and, if denied under that standard, would then determine whether the scientific evidence for the claim outweighed the scientific evidence against the claim. If FDA found the latter, FDA would publish a qualified claim, and FDA would not authorize the claim but would use its administrative discretion to avoid enforcing its rules against the claim for so long as it deemed the claim adequately supported. FDA stated that any claim allowed through exercise of enforcement discretion would violate its extant general health claims rule, 21 C.F.R. §§ 101.14 and 101.70, and that it would exercise enforcement discretion to avoid application of that rule.

67. On October 3, 2000, the FDA published in the Federal Register, 65 Fed. Reg. 58,917, 58,918, a notice that the four rules held invalid by the Court of Appeals on January 15, 1999, were being revoked effective that date— 18 months after the Court's mandate issued. Despite revoking the rules, the FDA prohibited any use of the claims held unconstitutionally suppressed pending completion of its re-evaluation of the claims.

68. On October 10, 2000, the FDA again denied the Pearson Plaintiffs' Folic Acid Claim (hereinafter "Folic Acid Decision"). FDA denied the Folic Acid Claim but permitted, through exercise of non-enforcement discretion, four (4) alternative claims:

> Example 1: Healthful diets with adequate folate may reduce a woman's risk of having a child with a brain or spinal cord birth defect. The Institute of Medicine of the National Academy of Sciences recommends that women capable of becoming pregnant consume 400 mcg folate daily from supplements, fortified foods, or both, in addition to consuming food folate from a varied diet.
>
> Example 2: Healthful diets with adequate folate may reduce a woman's risk of having a child with a brain or spinal cord birth defect. The scientific evidence that 400 mcg folic acid daily reduces the risk of such defects is stronger than the evidence for the effectiveness of lower amounts. This is because most such tests have not looked at amounts less than 400 mcg folic acid daily.
>
> Example 3: Healthful diets with adequate folate may reduce a woman's risk of having a child with a brain or spinal cord birth defect. Women capable of becoming pregnant should take 400 mcg folate/day from fortified foods and/or a supplement, in addition to food folate from a varied diet. It is not known whether the same level of protection can be achieved by using only food that is naturally rich in folate. Neither is it known whether lower intakes would be protective or whether there is a threshold below which no protection occurs.
>
> Example 4: Healthful diets with adequate folate may reduce a woman's risk of having a child with a brain or spinal cord birth defect. Women capable of becoming pregnant should take 400 mcg of folate per day from a supplement or fortified foods and consume food folate from a varied diet. It is not known whether the same level of protection can be achieved by using lower amounts.

None of the alternative claims informs consumers that .8 mg of folic acid in a dietary supplement is more effective in reducing the risk of neural tube defects than a lower amount in foods in common form. Each emphasizes dietary folate without explaining its

inferior effectiveness when compated to synthetic folic acid in dietary supplements. Moreover, none reveals that under FDA's fortification rule, 21 C.F.R. § 104.20, foods fortified with as little as .14 mg (i.e., 140 mcg) of folic acid per 100 grams of grain product can carry one of FDA's authorized folic acid-NTD claims. Furthermore, none reveals that no scientific evidence confirms any reliable NTD risk reduction through consumption of less than .4 mg (i.e., 400 mcg) of folic acid per day.

G. FDA's Folic Acid Decision

69. In FDA's Folic Acid Decision, FDA concluded that .8 mg (i.e., 800 mcg) of folic acid had not been proven more effective in reducing NTDs than .4 mg (i.e., 400 mcg) of folic acid, but the Folic Acid Claim does not compare the effectiveness of .8 mg of folic acid to .4 mg of folic acid, it compares .8 mg of folic acid with a lower amount in foods in common form. Food folate, not more bioavailable synthetic folic acid, is found in foods in common form.

70. In FDA's Folic Acid Decision, FDA concluded that dietary supplements had not been proven more effective in reducing NTDs than foods in common form, but it based that decision on a comparison of folic acid-containing supplements with foods fortified with the same amount of folic acid. The Folic Acid Claim does not compare folic acid containing supplements with fortified foods containing the same amount of folic acid, it compares .8 mg of folic acid in a dietary supplement with a lower amount in foods ***in common form***. A fortified food is not a food in common form, it is uncommon food supplemented with synthetic folic acid.

71. In FDA's Folic Acid Decision, FDA concluded that .4 mg (i.e., 400 mcg) of folic acid daily is a highly effective dose, but the Folic Acid Claim does not state

otherwise; rather, it states that .8 mg (800 mcg) of folic acid in a dietary supplement is more effective in reducing the risk of neural tube defects than a lesser amount in foods in common form. It is true, however, that .8 mg (i.e., 800 mcg) has been linked to a 100% reduction in NTDs, while .4 mg (i.e., 400 mcg) has not. Rather, CDC and FDA have concluded that a reasonable estimate of NTD risk reduction attainable from .4 mg (i.e., 400 mcg) of folic acid per day is 50%.

72. In FDA's Folic Acid Decision, FDA concluded that Plaintiffs' claim was not supported by "significant scientific agreement" within the meaning of its Guidance Document, but FDA failed to define its health claims review standard such that the regulated class, including the Plaintiffs, could perceive the principles guiding agency action or could discern what FDA means by "significant scientific agreement" or, at minimum, what it does not mean.

73. In FDA's Folic Acid Decision, FDA concluded that the weight of the scientific evidence was against the Folic Acid Claim, holding the claim "inherently misleading," but FDA failed to evaluate the actual claim submitted and, instead, evaluated two claims not submitted: (1) whether .8 mg (i.e., 800 mcg) of folic acid is more effective in reducing the risk of NTDs than .4 mg (i.e., 400 mcg) of folic acid and (2) whether folic acid in a dietary supplement is more effective in reducing the risk of NTDs than the same amount of folic acid in a fortified food.

74. FDA concluded that the Folic Acid Claim was "inherently misleading," but FDA did not undertake any First Amendment analysis required to reach that decision. FDA did not evaluate the claim under the three-part Central Hudson test presented in Pearson. FDA did not address, let alone establish, that it possessed a substantial state

interest for prohibiting the Folic Acid Claim. FDA did not address, let alone establish, that empirical evidence of actual, not speculative, harm supported its ban on the Folic Acid Claim. FDA did not address, let alone establish, that its ban on the Folic Acid Claim directly advanced its interest in a material way. FDA did not address, let alone establish, a reasonable fit between its ban on the Folic Acid Claim and its interest. FDA did not explain why disclaimers could not cure any potential misleadingness it deemed present in the Folic Acid Claim.

75. In its Folic Acid Decision, FDA states that the scientific evidence does not support the conclusion that specific sources of folate are more effective than others. But in 58 Fed. Reg. 53254 (Oct. 14, 1993), FDA concluded: "It is well recognized that the bioavailability of free folic acid, the form included in fortified foods and in dietary supplements, is several fold higher than that of naturally occurring food folates. Estimates of the increased bioavailability ('potency') of free folic acid relative to food folates range from at least twofold to fourfold or greater. . . The bioavailability of folates in foods ranges from approximately 25 to 75 percent depending upon a variety of factors that are incompletely understood. The majority of food folates occur as reduced pteroylpolyglumates (i.e., forms that contain a number of glutamate residues), and the glutamates must be cleaved by intestinal conjugase before absorption."

76. FDA concluded without a scientific basis that folate from conventional foods and synthetic folic acid from fortified foods and in dietary supplements were comparably bioavailable to synthetic folic acid in dietary supplements. Scientific evidence from the Institute of Medicine of the National Academy of Sciences contradicts those conclusions, finding supplement folic acid more bioavailable, more readily absorbed and not subject to

loss in food preparation. FDA ignored and failed to distinguish the scientific evidence presented and ignored its own prior determination that synthetic folic acid is more readily absorbed and more effectively increases serum folic acid levels than food folate.

77. FDA concluded that data were insufficient to provide a basis for stating that a specific amount of folate is more effective than another amount. The Institute of Medicine of the National Academy of Sciences contradicted that conclusion finding that amounts lower than .4 mg (i.e., 400 mcg) were not shown to be sufficiently protective against NTDs and that there did not exist evidence to demonstrate that food folate was as effective as synthetic folic acid (the kind found in dietary supplements and fortified foods).

78. Claiming to rely on the Institute of Medicine, FDA concluded that while proof existed of a quasilinear decrease in relative risk for NTDs from consumption of dietary folate in values between 100 mcg and 400 mcg, no further decreased risk had been observed for higher intake values. In context, FDA's citation is misplaced. The Institute of Medicine excerpt referred to by FDA concerns folate in foods in common form, not synthetic folic acid in dietary supplements or fortified foods. With regard to synthetic folic acid in dietary supplements, the Institute of Medicine concluded that "[a]t this time the evidence for a protective effect from . . . supplements is much stronger than that for food folate" and that women at higher risk of NTDs (such as those with a prior NTD birth) should take not .4 mg (i.e., 400 mcg) of folic acid per day in a dietary supplement but 4 mgs (i.e., 4,000 mcg) of folic acid per day in a dietary supplement, based on the superior effectiveness of that latter dose level in reducing NTDs. The CDC reached the same conclusion. Centers for Disease Control and Prevention, *Use of Folic Acid for*

Prevention of Spina Bifida and Other Neural Tube Defects 1983 and 1991, 40 MORBIDITY MORTAL WEEKLY REPORTS 500, 513-516 (1991).

79. In its Folic Acid Decision, FDA attributes to the following scientific studies, upon which it relies, conclusions nowhere found in those studies. FDA cites to Stevenson, R.E., et al., *Decline in prevalence of neural tube defects in a high-risk region of the United States*, 106 PEDIATRICS 670, 677-683 (2000), for the proposition that lesser amounts of folate from all sources is as effective in reducing NTD risk as 0.8mg (i.e., 800 mcg) of folic acid from dietary supplements or fortified foods. That proposition is not supported by the study. FDA cites to Berry, R.J., et al., *Prevention of neural tube defects with folic acid in China. China-U.S. Collaborative Project for Neural Tube Defect Prevention*, 341 NEW ENGLAND JOURNAL OF MEDICINE 1480, 1485-1490 (1999), for the proposition that other components of multivitamins rather than folic acid may be responsible for the reduction of NTD risk, but that proposition is not supported by the study.

80. In the Hungarian study (Cziezel, 1992), a human clinical intervention study (i.e., FDA's so-called "gold standard"), 0.8mg (i.e., 800 mcg)/day of folic acid was 100% protective against NTDs. FDA states that the results of the Hungarian study were not persuasive because the study used a preparation that combined folic acid with other vitamins in a multivitamin. FDA's conclusion is inconsistent with, and contrary to, its evaluation of the scientific evidence. In its Folic Acid Decision of October 10, 2000, FDA states that of the studies it evaluated, the results of the Multivitamin Research Council (MRC) study (Wald, 1991) were the most persuasive. The MRC study found periconceptional intake of folic acid (4.0 mg (i.e., 4,000 mcg)/day) reduced the risk of

recurrent NTDs by 72% in women with a history of prior NTD pregnancies. The MRC study examined the effect of 4.0 mg (i.e., 4000 mcg) of folic acid ***alone and in multivitamin preparations*** compared to multivitamin preparations without folic acid and to placebo, establishing that the risk reduction was due to increased folic acid intake, not other vitamins in the multivitamin preparation.

81. In its October 10, 2000 decision, FDA also relies upon the study published by Berry et al. (1999). This study examined the effect of folic acid in a multivitamin preparation. FDA relies upon this study in an effort to discount the results of the Hungarian study that showed greater protection with 0.8 mg (i.e., 800 mcg) of folic acid and to support the agency's position that vitamins other than folic acid may be responsible for the reduction of NTD risk. The authors, Berry, et al., are convinced, however, that the observed NTD risk reductions are due to folic acid supplementation, with or without other vitamins. In support of their conclusions the authors compare the similarity of their results to results of earlier studies that examined folic acid in multivitamin preparations: the MRC study; Cziezel (1992); Mulinare (1988); Milunsky (1989); Bower and Stanley (1989); and Shaw (1995).

III. JURISDICTION

82. This Court has jurisdiction over this matter pursuant to 5 U.S.C. §§ 702 and 706 (hereinafter the "Administrative Procedure Act") and 28 U.S.C. § 1331 (federal question jurisdiction).

IV. VENUE

83. This Court has venue over this action pursuant to 28 U.S.C. § 1391(e).

CAUSE OF ACTION I: VIOLATION OF THE FIRST AMENDMENT

84. Plaintiffs reallege and restate paragraphs 1 through 83 and incorporate them herein.

85. The Folic Acid Claim (".8 mg of folic acid in a dietary supplement is more effective in reducing the risk of neural tube defects than a lower amount in foods in common form") is truthful and nonmisleading scientific speech of a very high order. It is vital health information for all fertile women in the United States, indispensable to lowering their risk of NTD-affected births. Ignorance of it unnecessarily increases substantially the risk of NTD-affected births. Receipt of it can enable fertile women to reduce their risk of having an NTD-affected birth reliably, substantially, and safely.

86. The FDA's current authorized and permitted folic acid-NTD health claims mislead women into believing food folate a source of folic acid that can reliably and substantially reduce the risk of an NTD-affected birth when in fact no scientific evidence exists to confirm NTD risk reduction greater than 40% for foods in common form.

87. The government's current authorized folic acid-NTD health claims misleads women into believing fortified foods containing .14 mg (i.e., 140 mcg) of folic acid per 100 grams of grain product can reliably and substantially reduce the risk of an NTD-affected birth when in fact, by FDA's own admission, a reasonable estimate of a 50% NTD reduction is attainable by consuming .4 mg (i.e., 400 mcg) of folic acid per day and no scientific evidence exists to confirm that fortified foods have reduced NTD risks.

88. The logical effect of the authorized and permitted folic acid-NTD health claims, in the absence of the Folic Acid Claim, is to increase unnecessarily the number of NTD-affected births in the United States.

89. The Plaintiffs have agreed to accept any reasonable disclaimer to qualify the Folic Acid Claim in a way that may avoid a potentially misleading connotation. For example, they would readily accept a requirement that the Folic Acid Claim be accompanied by the following disclaimer: "Foods fortified with similar amounts of folic acid may be as effective as dietary supplements in reducing the risk of neural tube defects." Indeed, if the Folic Acid Claim is allowed by action of this Court, they will accompany it with this qualification wherever it appears.

90. The Folic Acid Claim is scientific speech or, if not, it is commercial speech protected from government suppression by the First Amendment to the United States Constitution.

91. FDA's Folic Acid Decision violates the First Amendment to the United States Constitution by suppressing the Folic Acid Claim without satisfying the government's First Amendment burden of proof and by favoring alternative claims that mislead fertile women and do not inform them of Plaintiffs' truthful and vital health message that .8 mg of folic acid in a dietary supplement is more effective in reducing the risk of neural tube defects than a lower amount in foods in common form.

CAUSE OF ACTION II: VIOLATION OF THE *PEARSON* DECISION

92. Plaintiffs reallege and restate paragraphs 1 through 83 and incorporate them herein.

93. In its Folic Acid Decision, the FDA failed to evaluate its restriction on speech under the constitutional test applicable to such restrictions and failed to implement the First Amendment principles, and comply with the First Amendment requirements, imposed upon the agency by the United States Court of Appeals in the Pearson decision.

As conditions precedent to suppression of the Folic Acid Claim, FDA failed to establish satisfaction of every element of the three-part *Central Hudson* test and failed to demonstrate that no disclaimer could suffice to cure potential misleadingness. The FDA thereby violated the Pearson v. Shalala decision.

CAUSE OF ACTION III: VIOLATION OF THE FIFTH AMENDMENT

94. Plaintiffs reallege and restate paragraphs 1 through 83 and incorporate them herein.

95. Plaintiffs' Folic Acid Claim is speech protected from suppression by the First Amendment to the United States Constitution.

96. Plaintiffs' protected speech is a liberty and property interest under the Due Process Clause of the Fifth Amendment to the United States Constitution. It is not only scientific speech Plaintiffs desire to communicate on labels and in labeling, it is also scientific speech that can lead consumers to purchase the dietary supplements Plaintiffs sell and recommend. That liberty and property interest may not be deprived without due process of law.

97. Process constitutionally due before deprivation of the protected speech requires, at minimum, that government define procedural safeguards upfront and adduce empirical evidence sufficient to satisfy its First Amendment burden of proof before it continues to suppress protected speech following a federal court order holding that government suppression unconstitutional.

98. In Pearson v. Shalala, the United States Court of Appeals for the D.C. Circuit held FDA's suppression of the Folic Acid Claim a violation of the First Amendment to the United States Constitution, finding that FDA failed to meets its First Amendment

burden of proof, invalidated FDA's rule that prohibited the Folic Acid Claim, and ordered FDA to reconsider the Folic Acid Claim in light of its decision.

99. At no time from the moment the Court's mandate issued until the present has FDA adduced empirical evidence necessary to satisfy its First Amendment burden of proof for suppression of the Folic Acid Claim. Despite that fact, FDA has prohibited, and continues to prohibit, the Folic Acid Claim.

100. At no time from the moment the Court's mandate issued until the present has FDA defined or adopted any procedural safeguards to avoid suppression of protected speech following the federal court decision holding that speech unconstitutionally suppressed.

101. The FDA violated the procedural due process rights of the Plaintiffs by failing to define and employ expeditiously those procedural safeguards necessary to protect Plaintiffs' liberty and property interests in their First Amendment rights from suppression and deprivation following the United States Court of Appeals' decision holding FDA's suppression of the Folic Acid Claim unconstitutional.

102. Procedural due process is violated when, as here, government continues to forbid protected speech for over a year and a half after a federal court has held suppression of that speech a violation of the First Amendment and without the government having adduced empirical evidence sufficient to justify speech suppression under the First Amendment.

103. Unless this Court holds that FDA violated the Fifth Amendment by failing to accord the protected speech here in issue the process it was due, the FDA is likely to delay action on health claims held unconstitutionally suppressed by federal courts in an

interminable bureaucratic loop of claim denial followed by Court review followed by lengthy agency reconsideration ending in further claim denial followed by further court review and on and on. That interminable loop entails continuous suppression of speech protected by the First Amendment to the United States Constitution. Thus, unless this Court holds FDA's process a violation of the Fifth Amendment on the facts present here that process of continuous suppression of speech is capable of repetition yet may evade judicial review.

104. When First Amendment rights have been held violated by a federal court, procedural due process requires government to eliminate that violation without delay. Eighteen months, the period of time spent between the issuance of the Court's mandate and FDA's Folic Acid Decision, is an unacceptable delay in acting on a federal court mandate to eliminate a First Amendment rights violation, and the violation continues indefinitely.

CAUSE OF ACTION IV: VIOLATION OF THE SUPREMACY CLAUSE

105. Plaintiffs reallege and restate paragraphs 1 through 83 and incorporate them herein.

106. Under the Supremacy Clause of the United States Constitution, U.S. Const. Art. VI, Cl. 2, the Constitution and the laws in pursuance thereof, are the supreme Law of the Land. In Pearson v. Shalala, the United States Court of Appeals held FDA's interpretation of its general health claims regulation, 21 C.F.R. § 101.14 and 101.70, invalid under the First Amendment to the United States Constitution.

107. Despite that holding, the FDA refuses to interpret its general health claims regulation consistent with the First Amendment to the United States Constitution. FDA

interprets its general health claims regulation to prohibit authorization of any health claim, even if truthful and nonmisleading, unless it finds that the underlying relationship between the nutrient and the disease is established to a near conclusive degree. That interpretation causes the rule to violate the First Amendment, as explained in Pearson v. Shalala.

108. Under the Supremacy Clause of the United States Constitution, the First Amendment is law supreme to contrary administrative law. Consistent with the canons of construction, FDA may not lawfully interpret its general health claims rule to effect an unconstitutional outcome if that rule may be interpreted in a manner consistent with the higher law.

109. The general health claims rule, 21 C.F.R. §§ 101.14 and 101.70, codifies for dietary supplements the same standard of review contained in the Food Drug and Cosmetic Act for foods, 21 U.S.C.A. § 343(r)(3)(B)(i). That Section requires FDA to determine as a condition precedent to health claim authorization whether a health "claim is supported by [scientific] evidence," i.e., whether it truthfully describes the present state of scientific understanding not whether the nutrient-disease relationship underlying the claim is established to a near conclusive degree. The latter is FDA's interpretation of the language. The plain and intended meaning of the statutory language comports with the First Amendment. The FDA's interpretation of it does not. Under the plain and intended meaning of the statutory language, FDA should have approved the Folic Acid Claim under the health claims general rule. Under the FDA's interpretation of the language, it did not approve the claim, thus violating the First Amendment and the Supremacy Clause to the United States Constitution (by deeming legal and binding its

interpretation of the health claims general rule in disregard of the contrary requirements of the statute, of the Pearson court, and of the First Amendment to the United States Constitution).

CAUSE OF ACTION V: VIOLATION OF THE FOOD, DRUG, AND COSMETIC ACT

110. Plaintiffs reallege and restate paragraphs 1 through 83 and incorporate them herein.

111. The FDA violated 21 U.S.C. § 343(r)(5)(D) and the order of the Pearson Court compelling FDA to define comprehensibly a health claims standard through articulation of the principles guiding agency action and through elucidation of the meaning of "significant scientific agreement." FDA has not defined "significant scientific agreement" in a way that enables the regulated class, including the Plaintiffs, to discern what scientific evidence, other than that necessary to approve a new drug, FDA will accept to permit health claim authorization. The Congress of the United States has forbade FDA from requiring the same level of proof required to authorize the marketing of a new drug as a condition precedent for authorization of a health claim on a food or a dietary supplement.

112. Although FDA purports to have adopted for dietary supplement health claims the same standard of review used for food health claims (articulated in 21 U.S.C.A. § 343(r)(3)(B)(i)), it in fact evaluates not whether a dietary supplement health "claim is supported by [scientific] evidence," as required by Section 343(r)(3)(B)(i), but whether the nutrient-disease relationship underlying the claim is established to a near conclusive degree, a level of proof comparable to that required for pre-market authorization of a new drug. That latter interpretation of the general health claims rule,

21 C.F.R. § 101.14, is not prescribed for foods in common form by the Act and denies authorization to truthful and nonmisleading health claims for dietary supplements in violation of the intentions of Congress in enacting the health claims provisions of the Nutrition Labeling and Education Act and the First Amendment as explained in Pearson v. Shalala.

CAUSE OF ACTION VI: VIOLATION OF THE ADMINISTRATIVE PROCEDURE ACT

113. Plaintiffs reallege and restate paragraphs 1 through 83 and incorporate them herein.

114. Under the Administrative Procedure Act, 5 U.S.C. § 706, the FDA may not take an agency action that is arbitrary, capricious, an abuse of discretion, or contrary to law.

115. Plaintiffs reassert paragraph 112 herein.

116. In Pearson, the Court of Appeals held FDA to have violated the Administrative Procedure Act by not defining its health claims review standard in a manner that would enable the regulated class, including the Plaintiffs, to perceive the principles which guide agency action. On remand, FDA was to explain what it meant by significant scientific agreement or, at minimum, what it did not mean.

117. On remand, the FDA has failed to explain the principles which guide its actions (indeed no coherent principle is discernible) and has not explained what it means by significant scientific agreement or what it does not mean, thus violating the Pearson Court decision and the Administrative Procedure Act's prohibition on arbitrary and capricious agency action. When acting on a case by case basis, FDA has failed to present

any discernible or consistent evaluative criteria in review of scientific evidence supporting health claims.

118. In addition, the agency—while prohibiting Plaintiffs' truthful Folic Acid Claim—allows foods in common form containing as little as 10% of the RDI of folate (i.e., the equivalent of 20 mcg of folic acid) to carry NTD risk reduction claims despite the absence of any scientific proof of any NTD risk reduction from such low amounts.

RELIEF REQUESTED

The Plaintiffs respectfully request that this Honorable Court:

Declare in accordance with 28 U.S.C. § 2201 (the Declaratory Judgment Act) that the FDA's October 10, 2000 denial of the Folic Acid Claim is invalid; in particular, they request that this Court declare:

(a) that the FDA's October 10, 2000 denial of the Folic Acid Claim violates the free speech clause of the First Amendment to the United States Constitution and the decision of the United States Court of Appeals in Pearson v. Shalala;

(b) that the FDA's failure to adopt procedural safeguards to protect the Folic Acid Claim from suppression following the Pearson Court's invalidation of FDA's rule suppressing that claim and its failure to act on the claim for eighteen months after this Court's mandate had issued violates the due process clause of the Fifth Amendment to the United States Constitution;

(c) that the FDA's failure to interpret its general health claims rule, 21 U.S.C. § 101.14, consistent with the requirements of the First Amendment to the

United States Constitution violates the Supremacy Clause of the United States Constitution;

(d) that FDA has violated the Food, Drug, and Cosmetic Act, 21 U.S.C. § 343(r)(5)(D), and the order of the Pearson Court, by failing to define comprehensibly a health claims standard through articulation of the principles guiding agency action and through elucidation of the meaning of "significant scientific agreement;" and

(e) that FDA has violated the Administrative Procedure Act, 5 U.S.C. § 706(2)(A), and the Pearson Court decision by not defining its health claims review standard in a manner that would enable the regulated class, including the Plaintiffs, to perceive the principles which guide agency action and by not explaining what it means by significant scientific agreement or, at minimum, what it does not mean, thus engaging in arbitrary and capricious agency action, abusing its discretion, and violating the law.

Order FDA to refrain from taking any action that would preclude the Plaintiffs from placing the following health claim on the labels and in the labeling of their dietary supplements that contain .8 mg of folic acid: "0.8 mg of folic acid in a dietary supplement is more effective in reducing the risk of neural tube defects than a lower amount in foods in common form."

Enjoin through a permanent injunction FDA from taking any action that would preclude the Plaintiffs from placing the following health claim on the labels and in the

labeling of their dietary supplements that contain recommended daily doses of 0.8 mg of folic acid: "0.8 mg of folic acid in a dietary supplement is more effective in reducing the risk of neural tube defects than a lower amount in foods in common form."

Respectfully submitted,

_____

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