UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

WESTON A. PRICE FOUNDATION 4200 Wisconsin Avenue, NW Washington, DC 20016, *Plaintiff*, v. UNITED STATES FOOD AND DRUG ADMINISTRATION 10903 New Hampshire Avenue Silver Spring, MD 20993, MARGARET A. HAMBURG, in her official capacity as Commissioner of the United States Food and Drug Administration 10903 New Hampshire Avenue Silver Spring, MD 20993, KATHLEEN SEBELIUS, in her official capacity as Secretary of Health and Human Services 200 Independence Avenue, S.W. Washington, DC 20201, *Defendants*.	Case No. 14-cv-2132

COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

INTRODUCTION

1. Plaintiff WESTON A. PRICE FOUNDATION brings this action pursuant to the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. §§ 301–399f, and the Administrative Procedure Act ("APA"), 5 U.S.C. § 551-559, 701-706, to compel the United States Food and Drug Administration and Margaret A. Hamburg, in her official capacity as Commissioner of the United States Food and Drug Administration (collectively, "FDA"), to render a decision on the Plaintiff's citizen petition (the "Citizen Petition") filed on August 8,

2008, which requests FDA to revoke its Final Rule, effective October 26, 1999, that allows heart health claims to be made in connection with foods containing soy protein.

2. The totality of scientific research shows that the benefits of consuming soy protein are putative and unproven. In fact, studies published since 1999 undermine the conclusions of key studies relied on by FDA when it approved the health claim in 1999. Studies cited in the Citizen Petition show that soy protein can actually contribute to or cause heart disease, including endothelial damage (especially in women), heart arrhythmias and cardiomyopathy, an increasingly prevalent condition that afflicts 1 in 500 Americans. Soy protein isolate contains a number of toxins and carcinogens, which are introduced into the product through its manufacturing process using high temperatures, high pressures, and harmful chemicals. Additional recent studies have failed to demonstrate that soy has beneficial effects on heart disease factors.

3. FDA's Final Rule placed consumers at risk because it helped establish the image of soy protein as heart healthy and contributed to an increase in consumption of soy protein in the United States from an average of 0.78 grams per day in 1999 to 2.23 grams per day in 2004. As a direct result of the health claim, many people who would not otherwise choose soy have consciously added more soy foods carrying the heart disease health claim to their diets. Many of these people consume amounts well in excess of the average. Populations at greatest risk are infants on soy formula, vegetarians and vegans who consume soy as both meat and dairy replacements, and adults who believe that they can prevent heart disease by consuming large amounts of soy products.

4. On August 8, 2008, Plaintiff submitted its Citizen Petition, requesting FDA to revoke its Final Rule on Food Labeling: Health Claims; Soy Protein and Coronary Heart Disease (effective October 26, 1999).

5. On August 14, 2008, FDA received and posted the Citizen Petition and assigned it a docket number (FDA-2008-P-0452-0001).

6. 21 C.F.R. § 10.30(e)(2) requires FDA to respond to citizen petitions "within 180 days of receipt of the petition." FDA's response must "[a]pprove the petition," "[d]eny the petition," or "[p]rovide a tentative response, indicating why the agency has been unable to reach a decision on the petition[.]" § 10.30(e)(2).

7. Under 21 C.F.R. § 10.30(e)(2), FDA's response was due by February 10, 2009.

8. By a letter file-stamped February 18, 2009 (but dated February 6, 2009), FDA responded that it has "not been able to reach a decision on [the] petition within the first 180 days of its receipt because of other agency priorities and the limited availability of resources," and that FDA "will complete [its] review of [the] petition and consider any amendments in [its] regulations as warranted and in the context of other program priorities within the Center."

9. On February 19, 2009, James S. Turner, Attorney for Plaintiff in the present matter, submitted a letter to FDA (file-stamped February 24, 2009), reminding FDA of the Citizen Petition and noting that more than six months had passed and FDA has provided no substantive response. James S. Turner's letter also formally requested a hearing on the substance of the Citizen Petition, and requested FDA's written response thereto.

10. Plaintiff has received no communication from FDA since the February 18, 2009 letter. FDA has neither granted nor denied the Citizen Petition, has provided no additional reasons for its failure to issue a decision, and has provided no information on when it intends to

issue a decision or take any other action in connection with the Citizen Petition. FDA has provided no response to James S. Turner's letter dated February 19, 2009. FDA has provided no hearing to Plaintiff.

11. Meanwhile, consumers continue to be misled about the connection between soy protein and heart health because they are told, based on the Final Rule, that soy protein is heart healthy, while scientific studies continue to show that the connection between soy protein and heart health is unclear, and even that soy protein may cause certain heart problems. See Exhibits.

12. Plaintiffs hereby seek declaratory and injunctive relief, and any other relief the Court deems proper, requiring FDA to issue a final decision on the Citizen Petition by a deadline ordered by this Court.

JURISDICTION AND VENUE

13. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. § 1331 (federal question). This action arises under the laws of the United States, specifically, the FDCA (21 U.S.C. §§ 301–399f) and the APA (5 U.S.C. § 551–559, 701–706). Plaintiff seeks judicial review under the APA, 5 U.S.C. § 706(1).

14. This Court also has subject matter jurisdiction over the claims in this action pursuant to 28 U.S.C. § 1346 (United States as Defendant).

15. Venue properly lies in this Court under 28 U.S.C. § 1391(e) on the following three independent bases: the Defendants reside in this judicial district, the Defendants' failure to act occurred in this judicial district, and the Plaintiff resides in this judicial district.

PARTIES

16. Plaintiff Weston A. Price Foundation is a nonprofit, tax-exempt charity founded in 1999 to disseminate the research of nutrition pioneer, Dr. Weston A. Price, whose studies of

isolated non-industrialized peoples established the parameters of human health and determined the optimum characteristics of human diets. Weston A. Price Foundation is dedicated to restoring nutrient-dense foods to the human diet through education, research, and activism. It supports a number of movements that contribute to this objective including accurate nutrition instruction, organic and biodynamic farming, pasture-feeding of livestock, community-supported farms, honest and informative labeling, prepared parenting and nurturing therapies. Weston A. Price Foundation has thousands of members, and over 600 local chapters throughout all fifty states, the District of Columbia, Puerto Rico, and thirty-four other countries, dedicated to advancing the ability of consumers to obtain healthy, nutritious food.

17. Defendant FDA is the agency responsible for "protect[ing] the public health by ensuring that . . . foods are safe, wholesome, sanitary, and properly labeled." 21 U.S.C. § 393(b)(2). This includes the responsibility of requiring information on food labels to prevent adulteration and misbranding, and to enable consumers to make informed choices about food. Additionally, FDA has statutory obligations to substantively respond to properly submitted citizen petitions.

18. Defendant Margaret A. Hamburg, in her official capacity as Commissioner of FDA, is responsible for FDA's administration and implementation of its legal duties, and for executing the FDCA.

19. Defendant Kathleen Sebelius, in her official capacity as Secretary of Health and Human Services, has delegated to FDA the authority to administer the relevant provisions of the FDCA.

STATUTORY FRAMEWORK

20. Congress passed the FDCA in 1938 "[t]o prohibit the movement in interstate commerce of adulterated and misbranded food, drugs, devices, and cosmetics[.]" Pub. L. No. 75-717, 52 Stat. 1040 (current version at 21 U.S.C. §§ 301-399(f)). Among other things, the Act mandates food and food packaging standards to ensure food integrity for the protection of consumers.

21. FDA is the agency responsible for enforcing the FDCA. 21 U.S.C. § 393. This responsibility includes "protect[ing] the public health by ensuring that . . . foods are safe, wholesome, sanitary, and properly labeled." § 393(b)(2).

22. The FDCA prohibits "[t]he receipt in interstate commerce of any food, drug, device, tobacco product, or cosmetic that is adulterated or misbranded, and the delivery or proffered delivery thereof for pay or otherwise." 21 U.S.C. § 331(c). A food is deemed adulterated "[i]f it bears or contains any poisonous or deleterious substance which may render it injurious to health." § 342(a)(1). A food is deemed misbranded if "its labeling is false or misleading in any particular," or if "the labeling or advertising fails to reveal facts . . . material with respect to consequences which may result from the use of the article . . . under such conditions of use as are customary or usual." §§ 343(a)(1); 321(n).

23. The FDCA and its regulations provide that FDA shall authorize a health claim "only if the Secretary determines, based on the totality of publicly available scientific evidence (including evidence from well-designed studies conducted in a manner which is consistent with generally recognized scientific procedures and principles), that there is significant scientific agreement, among experts qualified by scientific training and experience to evaluate such claims, that the claim is supported by such evidence." 21 U.S.C. § 343(r)(3)(B)(i); see 21 C.F.R. 101.14.

24. The APA mandates that "[e]ach agency shall give an interested person the right to petition for the issuance, amendment, or repeal of a rule." 5 U.S.C. § 553(e).

25. FDA regulations provide that citizens have the right to petition FDA to "issue . . . a regulation or order" through a citizen petition. 21 C.F.R. § 10.25(a)(2).

26. FDA regulations provide that "[t]he Commissioner shall . . . rule upon each petition filed under [21 C.F.R. 10.30(c)], taking into consideration (i) available agency resources for the category of subject matter, (ii) the priority assigned to the petition considering both the category of subject matter involved and the overall work of the agency, and (iii) time requirements established by statute." 21 C.F.R. § 10.30(e)(1).

27. In any case, within 180 days of receiving a petition, "the Commissioner shall furnish a response to each petitioner." 21 C.F.R. § 10.30(e)(2). The Commissioner's response must "[a]pprove the petition," "[d]eny the petition," or "[p]rovide a tentative response, indicating why the agency has been unable to reach a decision on the petition." *Id*.

FACTUAL BACKGROUND

28. Soy protein is not soy in its natural form. Soy protein concentrate and soy protein isolate are highly processed products that are precisely manufactured under industrial conditions in chemical factories, not kitchens. The basic procedure begins with defatted soybean meal, which is mixed with a caustic alkaline solution to remove the fiber, then washed in an acid solution to coagulate the protein. The protein curds are then dipped into yet another alkaline solution and spray-dried at high temperatures.

29. Soy protein isolates are a component of numerous food products today, including energy bars, shake powders, pasta sauces, burgers and hot dogs. Soy protein isolate is also the major ingredient in most of today's soy infant formulas.

Soy Protein Ingredients Are Adulterated and May Be Unsafe for Consumption

30. Products containing soy protein are adulterated because they contain a "poisonous or deleterious substance which may render … [them] injurious to health." 21 U.S.C. § 342(a)(1).

31. Toxicologists, endocrinologists and other expert scientists have questioned the safety of soy protein because of the known presence of antinutrients (protease inhibitors, phytates, lectins, saponins and oxalates) as well as the plant hormones known as phytoestrogens. A large body of research exists, documenting these hazards and refuting industry claims that there are no known safety hazards associated with soy protein.

32. Nitrates occur naturally in vegetables, water and many foods and beverages, including those containing soy. Nitrate is harmless until reduced to nitrite, which occurs through the processing methods used to manufacture soy protein isolate (SPI), casein and other fractionated food products. Nitrites are very reactive chemically and lead to nitrosamine formation in processed foods. Preformed nitrosamines are especially likely to be found in soy protein isolates and other soy products that have undergone acid washes, flame drying or other high temperature spraydrying processes. USDA studies from the 1980s showed that soy protein isolate contained almost twice the nitrite levels contained in other soy protein products. They also found in soy protein levels of 1.5 parts per billion of a potent nitrosamine known as N-nitrosodimethylamine (NDMA). Scientists have known since 1937 that nitrosamines damage the liver; and since 1956 that nitrosamines are mutagens and carcinogens.

33. The 1979 Select Committee of GRAS Substances (SCOGS) report examined safety issues pertaining to the manufacture of soy protein isolate and recommended the establishment of acceptable limits on the levels of lysinoalanine, nitrites, and nitrosamines. To this date, FDA

has not established safe levels for these toxins in soy protein and no agency is monitoring amounts of these toxins in food.

34. SCOGS had determined that 150 mg per day of soy protein is the maximum safe amount, which is less than 1/166th of the 25 grams per day of soy protein required by the Final Rule for the health claim at issue.

35. The following issues have not been satisfactorily addressed by FDA, and remain unresolved:

a. Soy protein may contain nitrites, which may form nitrosamines in vivo, which have been shown to be carcinogenic in experimental animals.

b. Modern heat treatment and other processing do not entirely eliminate the activity of trypsin inhibitors in products containing soy protein. The mechanism of feedback regulation of pancreatic enzyme secretion may be responsible for deleterious effects on the pancreas – hyperplasia and formation of nodules – seen in animal studies. Further, infusion of high levels of isolated trypsin inhibitor in humans can evoke this mechanism, but further research is needed to assess whether frequent exposures to low levels of trypsin inhibitors consumed in the diet could have the same effect.

c. Soy protein contains phytate, which is the salt of phytic acid or inositol hexakisphosphate and is a natural plant constituent containing six negatively charged phosphate groups that can form strong complexes with divalent cations such as calcium, magnesium, iron, zinc, and copper.

d. Soy protein may hinder absorption of certain minerals and may cause deficiencies of those minerals in the body. A soy protein-based purified diet

has been shown to induce iron deficiency in monkeys. One human study found inhibition of the absorption of nonheme iron from both semisynthetic meals and meals comprising conventional foods by various soy protein-containing ingredients. Another human study found increasing inhibition of nonheme iron absorption with increasing amounts of phytate in liquid formula meals that contained soy protein isolates.

e. Soy protein contains isoflavones, which have been found to have estrogenic and goitrogenic effects.

36. Both soy protein isolate and soy protein concentrate contain glutamate, a potent excitatory neurotransmitter. FDA requires no disclosure of its actual concentration.

37. Soy protein isolate was incorrectly determined to be Generally Recognized as Safe (GRAS) in a self-determination by Protein Technologies International, the petitioner of the Final Rule. Soy protein does not have a long history of safe use in the food supply. Unlike other GRAS substances in use prior to 1958, soy protein isolate was not originally developed as a food but as an industrial product to bind and seal paper products.

38. Soy is now one of the top eight allergens, a fact acknowledged by the Food Allergen Labeling and Consumer Protection Act (S. 741) that went into effect January 2006. In fact, soy allergies are increasing, and may already be in the top six, with some experts predicting that they will soon be in the top four. Many allergy experts believe that the increased use of soy protein ingredients in food products has increased exposure and the potential for sensitization.

The Significant-Scientific-Agreement Standard Has Not Been Met for the Soy/Heart Health Claim

39. Products containing soy protein, and that make the health claim about soy and coronary heart disease, are misbranded because their labeling "fails to reveal facts . . . material

with respect to consequences which may result from the use of the article . . . under such conditions of use as are customary or usual." 21 U.S.C. §§ 321(n); 343(a)(1).

40. The standard set out in 21 U.S.C. § 343(r)(3)(B)(i) and 21 C.F.R. 101.14(c), requiring significant scientific agreement, was not met for the health claim about soy and coronary heart disease at the time FDA made the determination for the Final Rule. Furthermore, scientific evidence since FDA's determination in 1999 has shown that the soy health claim is not supported by significant scientific agreement.

41. No significant scientific agreement currently exists that consuming 25 grams or more per day of soy protein has a significant effect on reducing the risk of coronary heart disease.

42. No significant scientific agreement currently exists that consuming 25 grams or more per day of soy protein has a significant effect on blood cholesterol or on blood total and LDL cholesterol.

43. The totality of the data on soy and cholesterol are inconsistent and contradictory at best, with some studies showing that soy can lower total and/or LDL cholesterol and other studies showing that it can raise or have no effect on total and/or LDL cholesterol.

44. A key study relied on by FDA to arrive at its decision to approve the 1999 health claim was a meta-analysis funded by the petitioner, Protein Technologies International, and conducted by James W. Anderson, MD in 1995.

45. Subsequent research has shown the 1995 study by Dr. Anderson to be deeply flawed.

46. The US Agency for Healthcare Reform and Quality criticized Anderson's 1995 study. In its August 2005 report, the Agency noted that Anderson's meta-analysis used looser inclusion criteria, including nonrandomized trials, studies of children, very small sample sizes,

and short intervention durations. The Agency further concluded that much of the research carried out on soy is inconclusive, that soy products appear to exert a small benefit on LDL cholesterol and triglycerides but that those effects may be of small clinical effect in individuals. (US Agency for Healthcare Research and Quality. *Effects of Soy on Health Outcomes.* Evidence Report/Technology Assessment, Number 126, Prepared by Tufts-New England Medical Center Evidence-based Practice Center, Boston, MA. August 2005.)

47. In November 2005, Dr. Anderson, the lead researcher of the 1995 study, himself stated that most studies since 1995 have reported less impressive results. Dr. Anderson further announced that soy protein extraction or baking may fragment the most active hypocholsterolemic peptides.

48. In January 2006, the American Heart Association (AHA) contradicted Dr. Anderson's 1995 findings, when it announced in its journal, *Circulation,* that soy protein and isoflavones have little effect on cholesterol levels or other lipids. (Sachs, FM, Lichtenstein A, et al. Soy protein, isoflavones and cardiovascular health: an American Heart Association Science Advisory for professionals from the Nutrition Committee. C*irculation*, 2006, 113, 7, 1023-44.)

49. A study in 2007 made the same findings as Dr. Anderson that soy protein may lower cholesterol in hypercholesterolemic individuals. However, the majority of the population is not hypercholesterolemic, and soy protein has not been shown to consistently or significantly lower cholesterol in the general population.

50. The current soy/heart health claims allowed by FDA mislead the public by implying that soy lowers LDL and total cholesterol in the general population.

51. Additionally, most of the studies relied upon by FDA in approving the soy protein health claim are highly flawed because of their use of casein as the control. Casein is a

fractionated milk protein product that is high in methionine and highly deficient in cysteine. Research at the Faculty of Agriculture, Shizuoka University, Japan, has shown that -- compared to other proteins -- casein will significantly raise total cholesterol levels and lower HDL levels.

52. Furthermore, soy protein does not have a consistently and demonstrably better effect on cholesterol compared to casein. In a 2007 study, soy performed worse than the casein control in numerous categories. (Anderson JW, Fuller J, Patterson K, Blair R, Tabor A. Soy compared to casein meal replacement shakes with energy-restricted diets for obese women: randomized controlled trial. *Metabolism.* 2007 Feb;56(2):280-8.)

53. Research has not established that soy protein is safe and has not identified the mechanism for its lowering of cholesterol, if any.

54. To date, the most accepted explanation for soy protein's cholesterol lowering potential, if and when cholesterol lowering occurs, posits stimulation of LDL-receptor activity, causing alterations in LDL receptor quantity and/or activities. This mechanism may serve as compensation for a soy-dependent increase in bile acid excretion. This increase in bile acid excretion would be accompanied by losses of fat-soluble thyroid and steroid hormones, and of fat-soluble vitamins, thereby potentially altering liver function homeostasis.

55. Soy protein’s effect on other cardiovascular risk factors is unclear. A considerable body of evidence suggests that homocysteine level is a far better marker of heart disease risk than cholesterol. Soy protein has not shown a consistent and significant effect on lowering homocysteine levels.

56. Homocysteine is a non-protein amino acid that is biosynthesized from methionine. High levels of homocysteine in the body have been linked to cardiovascular disease.

57. Because the cysteine in soy protein is either biounavailable or damaged by modern processing methods, soy protein is likely to raise the body's homocysteine levels.

58. Low levels of cysteine may also decrease the body's ability to respond to infections, cancer, and other immune system challenges.

59. Soy protein is devoid of B12 and may increase the body's requirements for B12. Although FDA-mandated B12 fortification may reduce soy protein's contribution to elevated homocysteine levels, fortification alone cannot make soy protein a "heart healthy" substance because of and not limited to the following: compromised availability of cysteine, cystine and methionine; the incomplete digestion of soy protein due to the action of protease inhibitors and other factors; and the toxic accumulations of ornithine and metal toxins which result from the processing of soy protein.

60. Ingestion of soy protein products causes, or has been associated with, increased HMG-Coenzyme A reductase activity along with bile acid synthesis and secretion, thyroid disruption including decreases in T4 and increases in T3, steroid hormone imbalances, and dangerous accumulations of homocysteine, especially homocysteine thiolactone. Many of these soy protein-induced changes have been associated with cancer, thyroid and steroid hormone disruption, humoral immune suppression, thymus atrophy, and cardiovascular disease such as atherosclerosis.

Soy Protein May Have Detrimental Effects on Other Cardiovascular Risk Factors

61. The US Agency for Healthcare Research and Quality, in its 2005 report, found insufficient evidence to recommend soy for improving cardiovascular risk factors, including HDL, triglycerides, lipoprotein (a), c-reactive protein, endothelial function, systemic arterial compliance, oxidized LDL or blood pressure.

62. One study concluded as follows:

> *The results of this trial do not support the hypothesis that soy protein containing isoflavones have beneficial effects on vascular function in older postmenopausal women. Whether certain subgroups of women (eg, equol producers) do benefit from the intervention remains to be elucidated.*
>
> Kreijkamp-Kaspers S, Kok L, et al. Randomized controlled trial of the effects of soy protein containing isoflavones on vascular function in postmenopausal women. *Am J Clin Nutr.* 2005 Jan;81(1):189-95

63. Soy protein could have a detrimental effect on cardiovascular risk factors, such as arrhythmias and cardiomyopathy.

64. Cardiomyopathy is an increasingly prevalent heart condition that affects 1 in 500 Americans and is the leading cause of death in young athletes. Research from the University of Colorado shows that dietary modification from a soy-based diet to a casein-based diet radically improves disease indicators and cardiac function in a transgenic mouse model of hypertrophic cardiomyopathy. *See* Stauffer BL, Konhilas JP, Luczak ED, Leinwand LA. Soy diet worsens heart disease in mice. J Clin Invest. 2006, 116, 1, 209-216.

65. Another study concluded as follows:

> *In normotensive men and postmenopausal women, soy improved BP and lipids but, overall, did not improve vascular function. Potential adverse effects were noted, with a decline in endothelial function (in males only) and an increase in Lp(a).* Further research in hypertensive and hyperlipidemic populations is needed.
>
> Teede JH, Dalais FS et al. Dietary soy has both beneficial and potentially adverse cardiovascular effects: a placebo-controlled study in men and postmenopausal women. *J Clin Endocrinol Metab,* 2001, 86, 7, 3053-3060.

66. Another study concluded as follows:

> *These findings indicate that soy protein may have an Lp(a)-raising effect, potentially detrimental to its use in antiatherogenic diets._*

Nilausen K, Meinertz H. Lipoprotein(a) and dietary proteins: casein lowers lipoprotein(a) concentrations as compared with soy protein. *Am J Clin Nutr*. 1999, 69, 3, 419-25.

67. Another study concluded as follows:

In women with suspected myocardial ischemia, higher genistein blood levels are associated with impaired nonendothelial-dependent and endothelial-dependent coronary microvascular function.

Pepine CJ, von Mering GO, et al. Phytoestrogens and coronary microvascular function in women with suspected myocardial ischemia: a report from the Women's Ischemia Syndrome Evaluation (WISE) Study. *J Womens Health* (Larchmt). 2007 May;16(4):481-8

68. All soy protein products naturally contain isoflavones, often at high levels.

69. A 2002 study suggests that genistein, a soy isoflavone, "directly blocks the inward rectifying K(+) current in ventricular myocytes, and one should be cautious of its pro-arrhythmic effect in clinical use." Chiang CE, Luk HN, Chen LL, Wang TM, Ding PY.Genistein inhibits the inward rectifying potassium current in guinea pig ventricular myocytes. *J Biomed Sci*. 2002, 9, 4 321-326.

New Scientific Evidence Does Not Establish Benefits of Soy to Heart Health

70. Studies published since the filing of the Citizen Petition have not shown benefits to heart health from soy consumption.

71. A 2014 study concluded that "soy intake was not significantly associated with risk of cardiovascular disease mortality in the Chinese population. However, a slightly increased risk associated with high soy protein intake in men cannot be excluded and requires further investigation." J Nutr. 2014 Jun;144(6):921-8. doi: 10.3945/jn.114.190454. Epub 2014 Apr 3. Dietary soy intake is not associated with risk of cardiovascular disease mortality in Singapore

Chinese adults. Talaei M1, Koh WP2, van Dam RM3, Yuan JM4, Pan A5. (Abstract of article attached as Exhibit A.)

72. A 2013 study concluded the following: "Soy protein and isoflavone (either alone or together) did not impact serum lipids or inflammatory markers. Therefore, they should not be considered an effective intervention to prevent cardiovascular disease because of lipid modification in healthy late postmenopausal women lacking the ability to produce equol." Nutr Res. 2013 Dec;33(12):1026-33. doi: 10.1016/j.nutres.2013.08.009. Epub 2013 Sep 18. Soy proteins and isoflavones reduce interleukin-6 but not serum lipids in older women: a randomized controlled trial. Mangano KM1, Hutchins-Wiese HL, Kenny AM, Walsh SJ, Abourizk RH, Bruno RS, Lipcius R, Fall P, Kleppinger A, Kenyon-Pesce L, Prestwood KM, Kerstetter JE. (Abstract of article attached as Exhibit B.)

73. A 2012 study concluded: "Hypertrophic cardiomyopathy (HCM) is more severe in male than female mice eating a soy-based diet. … Somewhat surprisingly, estrogen was not protective in male or female mice with HCM and, in fact, was lethal in phytoestrogen-fed male mice with HCM. … Finally, we show that phytoestrogens led to distinct programs of gene expression in hearts from males vs. females with HCM, suggesting mechanisms by which males are more sensitive to the detrimental effects of phytoestrogens and females are protected. These results implicate the phytoestrogen genistein in mediating cardiac pathology in males with HCM and, importantly, establish that estrogen is not protective in the setting of HCM." Endocrinology. 2012 Sep;153(9):4470-9. doi: 10.1210/en.2012-1391. Epub 2012 Jul 9. Estrogenic compounds are not always cardioprotective and can be lethal in males with genetic heart disease. Haines CD1, Harvey PA, Luczak ED, Barthel KK, Konhilas JP, Watson PA, Stauffer BL, Leinwand LA. (Abstract of article attached as Exhibit C.)

74. A 2014 study concluded: "The use of dietary soy supplement did not show any significant favorable effect on cardiovascular health biomarkers compared with HT [low dose hormone therapy]." Rev Bras Ginecol Obstet. 2014 Jun;36(6):251-8. The effect of soy dietary supplement and low dose of hormone therapy on main cardiovascular health biomarkers: a randomized controlled trial. Carmignani LO, Pedro AO, da Costa-Paiva LH, Pinto-Neto AM. (Abstract of article attached as Exhibit D.)

75. A 2013 study concluded: "We found no evidence for effects of isoflavones on patient-important outcomes or lowering of cholesterol levels in people with hypercholesterolaemia. Our findings have to be interpreted with caution due to high or unclear risk of bias in several risk of bias domains, and low number of participants in trials." Cochrane Database Syst Rev. 2013 Jun 6;6:CD009518. doi: 10.1002/14651858.CD009518.pub2. Isoflavones for hypercholesterolaemia in adults. Qin Y1, Niu K, Zeng Y, Liu P, Yi L, Zhang T, Zhang QY, Zhu JD, Mi MT. (Abstract of article attached as Exhibit E.)

76. A 2011 study concluded: "Strong evidence suggests that C-reactive protein (CRP) is a novel risk factor for cardiovascular disease. We aimed to examine the effect of soy isoflavones on circulating CRP concentrations in postmenopausal women by conducting a meta-analysis of randomized controlled trials. … The present meta-analysis found insufficient evidence that soy isoflavones significantly reduce CRP concentrations in postmenopausal women. However, soy isoflavones may produce a significant reduction in CRP among postmenopausal women with elevated CRP." Menopause. 2011 Nov;18(11):1256-62. doi: 10.1097/gme.0b013e31821bfa24. Effect of soy isoflavones on circulating C-reactive protein in postmenopausal women: meta-analysis of randomized controlled trials. Dong JY1, Wang P, He K, Qin LQ. (Abstract of article attached as Exhibit F.)

77. A 2010 study concluded: "Soy protein with isoflavones or isoflavones alone at the provided dosage showed no significantly beneficial effects on measured cardiovascular risk factors in postmenopausal Chinese women with early hyperglycaemia." Nutr Metab Cardiovasc Dis. 2012 Sep;22(9):712-9. doi: 10.1016/j.numecd.2010.11.002. Epub 2011 Mar 22. The effects of isoflavones combined with soy protein on lipid profiles, C-reactive protein and cardiovascular risk among postmenopausal Chinese women. Liu ZM1, Ho SC, Chen YM, Ho YP. (Abstract of article attached as Exhibit G.)

78. A 2010 study concluded: "Our data indicate that 1-year soy protein supplementation did not confer cardiovascular benefits, in terms of favorable alterations in the lipid profile, in this cohort of postmenopausal women. These findings, as well as those from other studies, lend credence to the decision of the Food and Drug Administration to reevaluate the soy protein health claim issued a decade ago." Menopause. 2010 May-Jun;17(3):587-93. doi: 10.1097/gme.0b013e3181cb85d3. One-year soy protein supplementation does not improve lipid profile in postmenopausal women. Campbell SC1, Khalil DA, Payton ME, Arjmandi BH. (Abstract of article attached as Exhibit H.)

CLAIM FOR RELIEF

1. Plaintiff re-alleges and incorporates by reference each and every allegation contained in paragraphs 1 – 78 of this Complaint.

2. The APA mandates the right of a person to petition any agency for the issuance, amendment, or repeal of a rule (5 U.S.C. 553(e)), and for the agency to "within a reasonable time . . . conclude a matter presented to it" (5 U.S.C. § 555(b)). FDA regulations provide that within 180 days of receipt, "[t]he Commissioner shall . . . rule upon each petition filed under [21

C.F.R. § 10.30(c)]." 21 C.F.R. § 10.30(e)(1). The APA further mandates that the Court "shall . . . compel agency action unlawfully withheld or unreasonably delayed." 5 U.S.C. § 706(1).

3. FDA has unlawfully withheld and/or unreasonably delayed agency action by failing to issue a final response to Plaintiffs' August 8, 2008 Petition, in violation of the APA (5 U.S.C. §§ 553(e), 555(b)), and the FDCA and its implementing regulations (21 U.S.C. §§ 301-399(f); 21 C.F.R. § 10.30(e)).

4. As the petitioner, Plaintiff has a statutory right to receive FDA's substantive response to the Citizen Petition, which right has been infringed as a result of FDA's failure to respond. FDA's failure deprives Plaintiff of a decision on the merits of the Citizen Petition, and the opportunity to seek judicial review of a final agency action, if necessary.

5. Additionally, FDA's failure to respond to the Citizen Petition places Plaintiff's members and the general public at risk by continuing to allow misleading claims to be made about the relationship between soy protein and heart health, thereby preventing Plaintiff's members and the general public from making more informed decisions in consuming products containing soy protein.

6. The new scientific evidence showing no benefit to heart health from soy consumption, published after the implementation of the Final Rule at issue, show the increasingly pressing need for FDA to provide a substantive response to the Citizen Petition.

7. In light of FDA's unlawful failure to respond and its unreasonable delay, a court-ordered deadline is necessary to ensure that FDA provides a timely, substantive response to the Citizen Petition.

RELIEF REQUESTED

WHEREFORE, Plaintiff respectfully requests that the Court:

(1) Enter a declaratory judgment that FDA's failure to provide a substantive response to the Citizen Petition is unlawful, is unreasonable delay, and violates the APA and FDCA;

(2) Enter an order compelling FDA to issue a final and substantive response to the Citizen Petition by a deadline imposed by the Court;

(3) Retain jurisdiction of this matter until FDA fulfills its legal and court-ordered obligations as set forth in this Complaint;

(4) Award Plaintiff the costs of this litigation, including reasonable attorney and expert witness fees ; and

(5) Grant such other and further relief as this Court deems just and proper.

DATED: December 17, 2014

Respectfully submitted,

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