UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

JULIAN M. WHITAKER, M.D., et al.,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	**Civil Action No. 99-3247 (GK)**
	)	
TOMMY G. THOMPSON, SECRETARY, et al.,	)	
	)	
Defendants.	)	

PLAINTIFFS' REPLY TO OPPOSITION TO MOTION FOR SUMMARY JUDGMENT

Plaintiffs hereby submit their reply to Defendants' Opposition ("Opp.") to Plaintiffs' Motion for Summary Judgment.[1] FDA's position is legally untenable. (1) FDA's reclassification of Plaintiffs' claim for saw palmetto extract, an unpatentable nutrient, from the dietary supplement to the drug category imposes on Plaintiffs' protected speech a prohibitive economic burden in violation of the First Amendment.[2] (2)

[1]The Defendants have left substantively unrebutted Plaintiffs arguments on (1) the costs of the drug approval process and the inability of the Plaintiffs (or other supplement companies) to afford those costs (SJ Mem. at 14; 32-33); (2) the unpatentability of saw palmetto (SJ Mem. at 14; 32-33); (3) the truthfulness of Plaintiffs' claim and its protected status under the First Amendment (SJ Mem. at 34-35); (4) the necessity for FDA to satisfy the Central Hudson test as prescribed in the Pearson I and II (SJ Mem. at 36-40); (5) the fact that saw palmetto has no serious side effects and has been consumed safely as a food and dietary supplement (SJ Mem. at 6; 19-20); (6) the fact that Congress aware of FDA's 1990 reproposed rule (55 Fed Reg 5176, 5192 (1990) (containing the definition of health claim FDA argues for here) did not adopt that language but adopted the broader language contained in the statute, i.e., "characterizes the relationship of any nutrient . . . to a disease or health-related condition," in 21 U.S.C. § 343(r)(1)(B); FDA thereafter followed suit also adopting that broader language (56 Fed. Reg. 60537, 60538 (1991); 21 C.F.R. § 101.14(a)(1)) (SJ Mem. at 28-29); (7) the NLEA's purpose being "to assure that the public would be provided with clear information about the relationship of nutrition to disease" "without having to wait until the degree of scientific certainty contemplated by the drug standard has been achieved;" (SJ Mem. at 30); (8) FDA's admission in 52 Fed Reg 28843, 28845 (1987) that dietary supplements "are not likely to be able to meet the adequate directions for use requirement or to have disease prevention claims substantiated in a manner necessary for approval of a new drug application" (SJ Mem. at 31); and (9) the utility of a disclosure statement as a less restrictive alternative to outright suppression of Plaintiffs' claim (SJ Mem. at 6)

[2] Even were there no prohibitive cost, the reclassification would produce total suppression of the claim due to FDA's insistence that saw palmetto poses a safety problem not curable by any drug disclosure statement

Despite the fact that Congress did not forbid health claims that include "an effect on an existing disease" and, indeed, expected health claims "characteriz[ing] the relationship of a nutrient . . . to a disease or a health-related condition," 21 U.S.C. § 343(r)(1)(B), to be approvable, the FDA has interpreted the statute to preclude health claims concerning "an effect on an existing disease." Even were one to ignore the statutory language (and the legislative history) and presume FDA's interpretation consistent with congressional intent and purpose, FDA's interpretation would still be wholly irrational and impermissible because it causes the statute to be construed to effect an unconstitutional outcome in this case: the suppression of Plaintiffs' protected commercial speech through the imposition of a prohibitive burden on an unpatentable nutrient. FDA's speech suppression is untenable for the additional reason that the NLEA health claims provision can be interpreted to effect a constitutional outcome (one fully consistent with congressional intent and purpose).[3] As such, that constitutional interpretation is legally required.[4] (3) FDA's attempt to define a distinction between "prevention" and "treatment" claims fails because the distinction is illusive, admittedly includes overlap (which is in fact substantial), is irrational, and is not the product of any consistent agency decisionmaking in its *ex ante* claims review. To be sure, FDA has not even adhered to its argued-for distinction in its assessment of Plaintiffs' claim, as explained below. (4) FDA's

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(see 55 Fed. Reg. 6926, 6929 (1990); Opp. at 7), to wit that the claim would delay treatment of prostate cancer (an unsubstantiated charge). Thus, even were there no cost barrier, FDA's position still ensures suppression of the claim.

[3] If the Court construes the NLEA health claims provision as Defendants' demand, it would cause that provision to be unconstitutional as applied to Plaintiffs' claim (because it would assure suppression of protected speech), thereby rendering FDA's decision unenforceable nonetheless.

[4] See United States v. Rumely, 345 U.S. 41, 45 (1953) (When a statute is subject to a choice of fair alternatives, one of which may raise serious Constitutional questions, the Court must favor the alternative that is Constitutionally permissible); see also DeBartolo Corp. v. Florida Gulf Coast Bldg. & Const. Trades Council, 485 U.S. 568 (1988); United States v. Thompson, 452 F.2d 1333, 1337 (D.C. Cir. 1971) (if

argument that approval of Plaintiffs' claim will cause all plant-based drugs to become dietary supplements eligible for health claims is a slippery slope, ignoring the statutory provisions that unequivocally prohibit such a reclassification. (5) FDA's argument that allowing Plaintiffs' claim will delay prostate cancer diagnosis is wholly unfounded because no evidence exists that saw palmetto obscures or prevents prostate cancer diagnosis and, consistent with Pearson I[5], the constitutional resolution of this issue is not to deprive consumers of accurate health information but to require more speech, a disclosure statement, such as: "If you suffer from any prostate problem you should promptly see a physician and obtain a regular prostate cancer screening exam." Plaintiffs accept and are willing to use such a statement.[6]

As explained below, FDA's latest attempt to avoid accountability under the First Amendment for a speech suppressive act once again fails. This Court should declare the constitutional violations present and order FDA to review Plaintiffs' claim under the health claims provisions of the NLEA and in accordance with Pearson I and II.

I. FDA'S CLAIM RECLASSIFICATION IMPOSES AN EXCESSIVE BURDEN ON PROTECTED SPEECH IN VIOLATION OF THE FIRST AMENDMENT

A. PLAINTIFFS' PROOF OF THAT BURDEN IS PROPERLY BEFORE THIS COURT

The Defendants err fundamentally by presuming that Plaintiffs' Summary

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interpretation of "Act would produce an unconstitutional result, there is at least a strong prima facie argument that the interpretation is erroneous").

[5] Herein Pearson I refers to 164 F.3d 650 (D.C. Cir. 1999) reh'g denied en banc, 172 F.3d 72 (D.C. Cir. 1999); Pearson II refers to No. 00-2724, 2001 U.S. Dist. LEXIS 1253.

[6] Plaintiffs have agreed to use any reasonable disclaimer. See SJ at 7.

Judgment Exhibits (hereinafter "SJ Exh.") 5, 7-14, and 16 all pertain to the APA issue. In fact, all but three[7] pertain to the First Amendment issue in this case[8] and, thus, are appropriately received as part of the de novo review this Court performs on constitutional challenges to agency action.[9]

[7] All three are admissible. SJ Exh. 12 (law review articles on the high costs of the drug approval process and the role of patentability in recouping those costs) is not submitted as evidence but as persuasive non-binding legal authority. Use of law review articles for that purpose is well-accepted. See, e.g., Nez Perce Tribe v. Idaho Power Company, 847 F.Supp. 791, 808 (D. Idaho 1993) (stating that a law review article is persuasive, non-binding legal authority); United States v. Cree, 778 F.2d 474, 500 (8th Cir. 1985) (stating that a law review article is legal authority). SJ Exh. 13 is a recent news account of the relative wealth of the dietary supplement industry. It may be the subject of judicial notice (see Judge Kessler's Order denying Motion for Preliminary Injunction on Pearson remand, 8 at note 2); SJ Exh. 14 is a letter (FDA to Chairman, House Subcommittee on National Economic Growth, Natural Resources, and Regulatory Affairs) explaining FDA's response to Pearson. An exception to the "final record" rule exists when an agency considered evidence which it failed to include in the record. See Esch v. Yeutter, 876 F.2d 976, 991 (D.C. Cir. 1989). FDA's letter includes a breakdown of the process FDA used in evaluating the claim at issue and therefore fits within this exception.

[8] See United States v. Popa, 187 F.3d 672, 674 (D.C. Cir. 1999) (First Amendment challenges are reviewed de novo). The First Amendment forbids impositions of prohibitive costs on protected speech. See, e.g., Simon & Schuster, Inc. v. Members of the New York State Crime Victims Board, 502 U.S. 105, 115 (1991), citing Leathers v. Medlock, 499 U.S. 439, 447 (1991) ("A statute is presumptively inconsistent with the First Amendment if it imposes a financial burden on speakers because of the content of their speech"). The law on point defines as admissible through summary judgment affidavits all evidence germane to a constitutional challenge, separate and apart from the APA exception discussed below. Across jurisdictions, when constitutional challenges to agency action are squarely presented, information pertinent to those challenges are found admissible. The Courts have not allowed the "raise-or-waive" doctrine to preclude consideration of such evidence. See Massachusetts v. Secretary of Agriculture, 984 F.2d 514, 524 (1st Cir. 1993); Facchiano v. United States Dept. of Labor, 859 F.2d 1163, 1167-68 (3d Cir. 1988) (courts have declined to require exhaustion when the challenged agency action presents a violation of constitutional rights); see also Republic Industries, Inc. v. Central Pa. Teamsters Pension Fund, 693 F.2d 290, 293 (3d Cir. 1982) (when the nonjudicial remedy would violate constitutional rights, the court may overlook the exhaustion doctrine to prevent irreparable injury); Reid v. Engen, 765 F.2d 1457, 1461 (9th Cir. 1985) (there is an exception to the raise-or-waive doctrine when a party challenges the constitutionality of a regulation proffered by the agency); see also Arctic Express, Inc. v. United States Dept. of Trans., 194 F.3d 767, 769 (6th Cir. 1999) ("courts have waived the exhaustion requirement when constitutional issues are asserted").

[9] SJ Exh. 5 (affidavit from Dr. Harry G. Preuss including a review of the "Costs in Obtaining FDA Approval for a New Drug") is admissible because it directly concerns the First Amendment issue. Safety information forms the remaining part of Dr. Preuss's affidavit. That information is also germane under the First Amendment and is admissible therefore. SJ Exh. 7 is an affidavit from Paul H. Rubin, Ph.D., economist, on the cost of the drug approval process for saw palmetto. That affidavit is directly germane to the First Amendment issue. SJ Exhs. 8-11 (affidavits from the Plaintiffs confirming that none of them has the financial wherewithal to pay the high cost of the drug approval process and none could recoup a new drug investment because saw palmetto is unpatentable) are directly germane to the First Amendment issue. SJ Exh. 16 (an affidavit from patent attorney Arlie Amando on the unpatentability of saw palmetto extract) is directly germane to the First Amendment issue.

Plaintiffs were not required to present that evidence to the agency below nor could they, reasonably, because FDA did not solicit any supplement health claim/drug approval process cost comparison in its rulemaking proceeding. FDA nevertheless addressed that subject in its May 26, 2000 letter ruling on Plaintiffs' claim (hereinafter "May 26 Ruling").

Even were the affidavits rejected, the underlying point that drug approval entails extraordinary costs is an unremarkable one – essentially admitted in FDA's May 26 Ruling (AR at 721) and reported in law review articles submitted not as evidence (as FDA erroneously presumes) but as non-binding legal authority. SJ Exh. 12.[10] In SJ Exh. 7, Economist Paul Rubin explains that satisfying FDA's drug approval requirements for the saw palmetto claim would cost approximately $58 million in 1999; that saw palmetto is unpatentable (a fact confirmed by SJ Exh. 16, the affidavit from patent attorney Arlie Amando); and that as a practical matter no U.S. company, and certainly none in the dietary supplement industry, could afford drug approval because none could recoup costs in post-approval sales.

The Defendants would have this Court exclude Plaintiffs' cost evidence as extra-record, but Defendants cannot achieve that objective under apposite precedent.

Moreover, Defendants opened the door to economic argument in the May 26 Ruling. In that letter FDA itself recognized (as Defendants' present argument attempts to obfuscate) that the cost of the drug approval process makes it an unlikely alternative for

[10] See Nez Perce Tribe v. Idaho Power Company, 847 F.Supp. 791, 808 (D. Idaho 1993) (stating that a law review article is persuasive, non-binding legal authority); United States v. Cree, 778 F.2d 474, 500 (8th Cir. 1985) (stating that a law review article is legal authority).

any product that can be characterized as a dietary supplement. In its May 26 Ruling FDA states:

Given the time and expense necessary to bring a new drug to market, it is unlikely that manufacturers would seek drug approval from FDA for any product containing a substance that could be characterized as a dietary supplement or conventional food component . . .

AR at 730. FDA was correct in that regard. DOJ's present argument is not. FDA's admission bolsters Plaintiffs' position that the prohibitive cost on Plaintiffs' speech effected by FDA's reclassification of the claim effectively deprives Plaintiffs of the right to communicate a truthful health message to the public. As explained in Pearson I and II, FDA cannot constitutionally suppress potentially misleading speech. It must allow it accompanied by such disclaimer as is, or such disclaimers as are, reasonably necessary to avoid a misleading connotation. It must favor disclosure over suppression under the higher authority of the First Amendment. See Pearson I 164 F.3d at 655 & 657; Pearson II No. 00-2724, 2001 U.S. Dist. LEXIS 1253 at *24-25 & *46.

Moreover, in Opp. at 11, having just argued to the Court that it should exclude all of Plaintiffs' cost evidence, the Defendants themselves present unsubstantiated argument that the cost of achieving Over-The-Counter (OTC) drug status for saw palmetto would be manageable to Plaintiffs (a false assertion), writing (contrary to the FDA's decision letter quoted above):

Plaintiffs further submit that, for a variety of reasons, they could not afford to seek approval for saw palmetto under the drug provisions of the Act. Plaintiffs ignore the statements in the final rule on OTC use of saw palmetto that specifically provide that the regulation could be reconsidered as a result of an NDA submission or by a citizen's petition to establish a monograph. . . . Accordingly, plaintiffs could proceed rather inexpensively by petitioning the agency to reconsider its ruling on OTC use of saw palmetto . . .[11]

[11] FDA's argument that OTC drug approval is available to Plaintiffs is disingenuous in light of FDA's prior ruling (and continuing argument) that saw palmetto cannot be approved as an OTC drug because no safety

FDA would have the Court consider its wholly speculative (and incorrect) argument on the cost issue but exclude Plaintiffs' argument backed by substantial affidavit support.

Because FDA did not solicit comments on comparative costs of its drug and dietary supplement health claim processes[12], yet included that analysis in its May 26 Ruling, FDA "failed to examine all relevant factors to adequately explain its grounds for decision" and thereby cannot deny Plaintiffs the opportunity to present evidence to this Court on comparative economic costs.[13] Even if Plaintiffs' cost data is excluded, there can be no doubt that Defendants' current position conflicts directly with the FDA

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warning will suffice to satisfy FDA's concerns of a delay in prostate cancer diagnosis. See Opp. at 7. In short, FDA cannot seriously describe its OTC process as a viable alternative when it relies on the very safety argument used to reject OTC status for saw palmetto as its continuing rationale in this case. Moreover, the safety and efficacy standards for grant of an OTC drug are identical to those for a prescription drug and, thus, can be expected to impose the same costs. Cf. 21 U.S.C. § 355 et seq., and 21 CFR § 314 (FDA drug approval regulations and requirements) with 21 CFR § 330.10 (FDA OTC drug classification process); see also FOOD AND DRUG ADMINISTRATION, FDA/ORA COMPLIANCE POLICY GUIDES SUB CHAPTER 450.100 CGMP ENFORCEMENT POLICY (1982) (the enforcement policy for CGMP regulations is the same for OTC drug products as it is for prescription drug products). Thus, the point that costs would be more reasonable is wholly unfounded. The unrebutted record evidence on the drug approval costs places the figure in the tens of millions of dollars ($58 million)—far beyond Plaintiffs' reach. SJ Exh. 7.

[12] In FDA's solicitation of comments, 65 Fed. Reg. 14219, 14222 (1999), FDA asked for comments in response to the following questions: "1. Does the language and structure of the act restrict the permissible types of substance-disease relationships that can be described in a health claim? 2. How should FDA interpret the health claim and drug provisions of the act and the medical food provision of the Orphan Drug Amendments in relationship to each other? 3. If FDA were to permit at least some claims about the effects on an existing disease as health claims, what criteria should be used to determine when a claim is a permissible health claim and when it is a drug claim under section 201 (g)(1)(B) of the act? 4. If FDA were to permit at least some disease treatment or mitigation claims as health claims, what about claims that are covered by an existing over-the-counter (OTC) drug monographs." FDA did not invite comments on the comparative cost of the drug approval process versus the dietary supplement health claim approval process.

[13] See Southwest Ctr. for Biological Diversity v. United States Forest Service, 100 F.3d 1443, 1450 (9th Cir. 1996) (A reviewing court may supplement the administrative record if "the agency failed to examine all relevant factors to adequately explain its grounds for decision . . ."); see also Esch v. Yeitter, 876 F.2d 976, 991 (D.C. Cir. 1989). The summary judgment rule in the Federal Rules of Evidence is designed to enable such matters as would ordinarily be admissible into evidence at trial to be filed with affidavit support. See Fed. R. Civ. P 56(e); Celotex v. Catrett, 477 U.S. 317, 324 (1986) (mere allegations are insufficient: motion must be supported by affidavits or other competent evidence). That approach has been followed by Plaintiffs in the affidavits on economics supporting their motion for summary judgment. Circuit Judge Clark, the principal draftsman of Rule 56, has stated: "The history of the development of this procedure shows that it is intended to permit 'a party to pierce the allegations of fact in the pleadings and to

admission in its May 26 Ruling quoted above (AR at 730) explaining that drug approval is not a viable option for dietary supplements. Moreover, we know that option is not viable for an additional reason: FDA continues in its Opp. at 7 to insist on the same drug safety argument upon which it relied to deny OTC status for saw palmetto initially, belying any suggestion that FDA would grant OTC status if a second OTC application were filed.

B. DEFENDANTS' NARROWING OF THE DEFINITION OF "HEALTH CLAIM" PREVENTS COMMUNICATION OF PROTECTED COMMERCIAL SPEECH

The Defendants do not argue, and have not adduced evidence to prove, that Plaintiffs' health claim is false. Indeed, they refused to review Plaintiffs' claim and, thus, have no substantive basis to challenge it. To the contrary, the record amply supports the truth of the claim that "Consumption of 320 mg daily of Saw Palmetto extract may improve urine flow, reduce nocturia and reduce voiding urgency associated with mild benign prostatic hyperplasia (BPH)." AR at 1-720. Nor have Defendants concluded that Saw Palmetto, sold as a dietary supplement in the U.S. since before 1994, is a substance that is intrinsically unsafe such that 21 U.S.C. § 342(f)(1) would preclude it from being sold as a dietary supplement. Nor have Defendants argued that Plaintiffs' saw palmetto extract is in any respect different from the same ingredient in foods or in dietary supplements lawfully sold.[14] FDA recognizes that the product is sold safely for prostate

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obtain relief by summary judgment where facts set forth in detail in affidavits, depositions, and admissions on file show that there are no genuine issues of fact to be tried.'" 3 Moore's Federal Practice 3175.

[14] See SJ Exh. 17 (U.S. Pharmacopeia: "No serious adverse events are known to be associated with saw palmetto;" "Saw palmetto was one of the most important foods for Florida's pre-Columbian, non-horticultural peoples and later Creek immigrants. Even today, among the older Seminole population the fruit is still consumed in moderate quantities and a sweetened traditional drink called 'shipe sofkee' is made from the juice.")

support, allows claims to that effect, and has taken no action to prevent the marketing and sale of saw palmetto as a dietary supplement with claims to that effect.[15]

It is a well-settled principle of First Amendment law that suppression of speech, effected through the imposition of extraordinary economic and regulatory costs, is the equivalent of direct speech suppression.[16] FDA cannot avoid its First Amendment burden of proof under Pearson I and II through recategorization of protected speech; nor can it shift that burden to Plaintiffs through recategorization. See Central Hudson Gas & Elec. Corp. v. Public Service Comm'n, 447 U.S. 557 (1980) (High First Amendment burden of proof is on the government when it presumes to regulate protected commercial speech); see also Pearson I, 164 F.3d at 659; Pearson II, No. 00-2724, 2001 U.S. Dist. LEXIS 1253 at *40-41. FDA's redefinition of health claim to exclude claims of a nutrient's "effect on an existing disease" is, thus, unconstitutional as applied to Plaintiffs' claim for saw palmetto, an unpatentable nutrient, because it causes suppression of protected speech.

In this instance, FDA's decision to exclude all claims of "an effect on an existing disease" from the dietary supplement health claim definition and to require that they only

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[15] FDA has received numerous notification letters alerting FDA of various prostate-support claims. See http://www.fda.gov/ohrms/dockets/dailys/01/Jan01/010401/c006253.pdf; see also http://www.fda.gov/ohrms/dockets/dailys/00/Dec00/120500/let6222.pdf. If FDA were truly concerned about delay in treatment of prostate cancer, one would fully expect that FDA would exercise its authority under 21 U.S.C. § 342(f) to prevent marketing of the product for that use or to require a warning statement. Instead, FDA permits "prostate health" structure/function claims to be made without reference to the agency's fear of delayed diagnosis of prostate cancer. See id.

[16] See Simon & Schuster, Inc. v. Members of the New York State Crime Victims Board, 502 U.S. 105, 115 (1991), citing Leathers v. Medlock, 499 U.S. 439, 447 (1991) ("A statute is presumptively inconsistent with the First Amendment if it imposes a financial burden on speakers because of the content of their speech"); see also Hoover v. Morales, 164 F.3d 221 (5th Cir. 1998); United States Satellite Board. Co. v. Lynch, 41 F.Supp.2d 1113, 1120 (E.D. Calif. 1999); Leathers v. Medlock, 499 U.S. 439, 447 (1991) ("For reasons that are obvious, a tax will trigger heightened scrutiny under the First Amendment if it discriminates on the basis of the content of taxpayer speech"); Arkansas Writers' Project v. Ragland, 481 U.S. 221, 232 (1987) (holding invalid a statutory scheme that exempted from a general sales tax only those journals with a

be allowed as part of an application to sell saw palmetto as a drug equates with a shift in the burden of proof on safety and efficacy from the government to the petitioner[17] and, concomitantly, with an imposition of extraordinary new costs that, in the case of an unpatentable substance like Saw Palmetto, effectively forbid the claim altogether.[18] The deprivation of that information imposes unnecessary hardships on all men because almost every male in America will experience mild, benign prostatic hyperplasia in his lifetime. AR at 11.

Thus, FDA's *post hoc* narrowing of the health claim definition—a definition left unrestricted in the statute ("characterizes the relationship of any nutrient . . . to a disease or a health-related condition," 21 U.S.C. § 343(r)(1)(B)), and in FDA's own NLEA implementing regulations ("characterizes the relationship of any substance to a disease or health related condition," 56 Fed. Reg. 60537, 60542 (1991); 21 C.F.R. § 101.14(a)(1))—has the very real effect of causing dietary supplement companies, including Plaintiffs, not to be able to communicate (and the public not to be able to receive) truthful and nonmisleading information on labels and in labeling concerning the accurate extent of the

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generally religious, sports, professional or trade oriented content); Cox v. New Hampshire, 312 U.S. 569, 577 (1941) (holding that a licensing fee is unconstitutional if it is unreasonable).

[17] A substance that meets the statutory definition of a dietary supplement, 21 U.S.C. § 321(ff), is entitled to a presumption in favor of its safety. It is incumbent upon the government to prove a lack of safety to justify restricting its labeling or removing the substance from the market. See, e.g., Dietary Supplements Containing Ephedrine Alkaloids, 62 Fed. Reg. 30678 (1997) (to be codified at 21 C.F.R. pt. 111) (proposed June 4, 1997); and 21 U.S.C. § 342(f)(1). A substance that is a drug is presumptively unsafe and inefficacious and may not be marketed until the FDA is satisfied that there is "substantial evidence" of its safety and efficacy pursuant to 21 U.S.C. § 355(b)(1)(A). That standard applies to all drugs, including those that are the subject of petitions for approval of over-the-counter status. Proof of safety and efficacy under the "substantial evidence" standard requires human clinical trials and several phases of experimentation that are very costly. See 21 C.F.R. § 310. Indeed, FDA review of drug approval applications, unlike dietary supplement health claim applications, is possible only upon payment of over $250,000 in an application fee, said to be necessary for FDA to evaluate the evidence of safety and efficacy. 21 U.S.C. §379(h)(b) (2000).

[18] FDA's reclassification of the claim is, in fact, a condemnation of it because FDA has already said in its OTC ruling, and again in its Opp. at 7, that no disclosure statement could suffice to eliminate its (in fact unfounded) safety concern that use of saw palmetto could delay diagnosis of prostate cancer. Thus, FDA will never approve saw palmetto as a drug.

nutrient-disease relationship. Because that shift in claim categorization entails suppression of protected speech, including Plaintiffs' truthful claim, FDA's statutory interpretation is untenable and is irrational; it violates the First Amendment.[19] Indeed, under the final prong of Central Hudson (see Pearson I, 164 F.3d at 656; Pearson II, No. 00-2724, 2001 U.S. Dist. LEXIS 1253 at *21-22) there are far less restrictive alternatives to suppression fully capable of addressing FDA's safety concerns but that still allow plaintiffs the freedom to communicate, and the public to receive, the protected speech. In Pearson, the D.C. Circuit explained that ". . . the government's interest in preventing the use of labels that are true but do not mention adverse effects would seem to be satisfied—at least ordinarily—by inclusion of a prominent disclaimer setting forth those adverse effects." Pearson I, 164 F.3d at 659. Here a disclosure statement would fully suffice to address FDA's ill-defined (and unsubstantiated) concern that somehow saw palmetto would delay diagnosis of prostate cancer.[20] The statement could read, "If you suffer from any prostate problem you should promptly see a physician and obtain a regular prostate cancer screening exam." Such a statement is fully acceptable to Plaintiffs and is

[19] See United States v. Rumely, 345 U.S. 41, 45 (1953) (When a statute is subject to a choice of fair alternatives one of which may raise serious constitutional questions, the Court must favor the alternative that is Constitutionally permissive); see also United States v. Thompson, 452 F.2d 1333, 1337 (D.C. Cir. 1971) (if interpretation of "Act would produce an unconstitutional result, there is at least a strong prima facie argument that the interpretation is erroneous").

[20] The agency's concern lacks any evidentiary basis in the record. It is instead based on illogic and speculation. FDA already allows prostate structure/function claims for saw palmetto products sold as dietary supplements. See generally, 65 Fed. Reg. 1000, 1008-1032 (2000). Thus, to the extent that men already rely on saw palmetto to support prostate health, one would suspect that this would be viewed by FDA as delaying diagnosis of prostate cancer among men, but FDA has taken no action against prostate structure/function claims on dietary supplements containing saw palmetto, has not required warning statements of any kind, even though by statute it must take action if a dietary supplement actually poses a threat to public health. See 21 U.S.C. § 342(f)(1). Moreover, prostate cancer screenings are routinely conducted annually on men beginning at age 50 by recommendation of the Centers for Disease Control and Prevention. See Prostate Cancer at a Glance 2000<http://www.cdc.gov/cancer/prostate/prostate.htm>. FDA has not argued, nor is there any evidence to support, that saw palmetto masks the normal indicia of prostate cancer during this cancer screening. Thus, its concerns lack an evidentiary basis. In any event,

one that would seem to suffice to allay the agency's ill-defined concerns that men with prostate cancer may mistakenly believe they have BPH and fail to obtain proper and prompt treatment.

C. FDA'S RECLASSIFICATION FAILS CHEVRON; PREVENTS ACHIEVEMENT OF NLEA'S PURPOSE; AND ERECTS AN IRRATIONAL REGULATORY SCHEME

Defendants would have the Court believe that it must ignore the legislative history contained in Senate Report 103-410, stating that the congressional sponsors of the DSHEA excluded the report from consideration as legislative history for that law (Opp. at 4). The argument misleads because Plaintiffs have not used the report to construe the DSHEA; rather, they use it as evidence of congressional intent for the meaning of the health claims provision codified in the NLEA, 21 U.S.C. §343(r)(1); SJ Exh. 2. Thus, Defendants' argument is wholly misplaced.[21] The Senate Report is insightful for understanding the NLEA health claims definition because it demonstrates that the congressional committee with FDA oversight understood nutrient-disease relationships embraced by the health claims definition to include those affecting existing diseases: e.g., garlic reducing serum blood cholesterol (S. Rep. 103-410 at 11; SJ Exh. 2 at 11); ginger relieving nausea and stomach distress (S. Rep. 103-410 at 11; SJ Exh. 2 at 11); quercitin reducing the allergy-inflammatory response (S. Rep. 103-410 at 14; SJ Exh. 2 at 14); and glucosamine sulfate repairing damaged joints (S. Rep. 103-410 at 14; SJ Exh. 2 at 14). Properly taken into account by this Court, the Senate Report provides proof devastating

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Plaintiffs have volunteered to accompany their saw palmetto claim with a statement urging men to have regular prostate cancer screening exams.

[21] The congressional agreement has not stopped the Tenth Circuit from using the Senate Report to interpret the DSHEA itself. See Pharmanex v. Shalala, 221 F.3d 1151, 1158 (10th Cir. 2000).

to the Defendants' argument that Congress did not understand "an effect on an existing disease" to be within the scope of the NLEA health claims definition. It quite plainly did.

1. The Inherent Irrationality of the Regulatory Scheme

The Defendants attempt to distinguish "treatment" from "prevention" (Opp. at 9-10) fails not only because the congressional goal of informing the public accurately of the extent of the nutrient-disease relationship is defeated by the agency's approach but also because there is no clear dividing line between the meaning of the two terms (and FDA has explained none to this Court). The meaning of the two terms overlap not slightly but substantially. Prevention is in fact a subset of treatment; prevention is a method of mitigating signs or symptoms of disease to stop or delay an on-going process leading to the ultimate manifestation of disease. Treatment involves the administration of articles designed to affect signs or symptoms of disease in such a way as to mitigate or cure the disease. Prevention involves the administration of articles designed to affect signs or symptoms of disease in such a way as to prevent the ultimate manifestation of the disease. The presence of disease processes before the latter adverse phases of the disease is frequently viewed as disease itself, as in the case of cholesterolemia (elevated cholesterol levels) and osteoporosis (bone density loss). Moreover, the lag time in the appearance of later adverse events is generally viewed not as delay in the onset of disease but as the progression of the disease (as, for example, when cancer cells develop in the body but are not diagnosable until tumor growth). By FDA's own admission, reference to lowering cholesterol is an implied claim that the product is a treatment for cholesterolemia, a disease. See 55 Fed. Reg. 5176, 5178 (1990) (a claim of "reducing serum cholesterol, and thus reducing the risk of coronary heart disease, would go beyond

the concept of health messages and enter the realm of drug claims.").[22] Yet, nonetheless, the following FDA-approved claim includes reference to cholesterol lowering:

> Development of heart disease depends on many factors. Eating a diet low in saturated fat and cholesterol and high in fruits, vegetables, and grain products that contain fiber *may lower blood cholesterol levels* and reduce your risk of heart disease.

21 C.F.R. § 101.77(e)(2) (emphasis added). It thus concerns an effect of nutrients on a present disease (cholesterolemia) as well as an effect on the incidence of a future disease, heart disease. By FDA's own admission, reference to normal bone density in post-menopausal women is an implied claim that the product is a treatment for osteoporosis, a disease. See 65 Fed. Reg. at 1013; 1017; 1018 (describing "prevents bone fragility in post-menopausal women" and "maintain normal bone density in post-menopausal women" as "disease claims"). Yet, nonetheless, FDA allows reference to reduction in bone density loss in its approved health claim for calcium and osteoporosis. See 21 C.F.R. § 101.72(c)(2)(C) ("When reference is made to . . . menopausal women, and elderly men and women, the claim may also state that adequate calcium intake is linked to reduced risk of osteoporosis through the mechanism of slowing the rate of bone loss").

Consider the irrationality inherent in the Defendants classification of Plaintiffs' claim, "Consumption of 320 mg daily of Saw Palmetto extract may improve urine flow, reduce nocturia and reduce voiding urgency associated with mild benign prostatic hyperplasia (BPH)." Recognize that improved urine flow, reduced nocturia, and reduced voiding urgency are in no way substantively different in kind from reduction in cholesterol or lessening of bone loss with the exception that urine flow, nocturia, and

[22] See also 65 Fed. Reg 1000, 1015 (Jan. 6, 2000) ("… a statement would be considered a disease claim if it explicitly or implicitly claimed an effect … on one or more signs or symptoms … of a specific disease … [S]uch disease claims [include]: 'lowers cholesterol'").

voiding urgency are not considered diseases themselves while FDA has concluded that cholesterol lowering and bone density loss are always implied claims of diseases (hypercholesterolemia and osteoporosis). One would think under FDA's present definition the foregoing would militate against including reference to cholesterol lowering and bone density loss in approved food or dietary supplement claims and in favor of making Plaintiffs' claim approved, but, in fact, we know the opposite has occurred. Recognize that improved urine flow, reduced nocturia, and reduced voiding urgency are not associated in Plaintiffs' claim with any actual disease. Benign prostatic hyperplasia is not a disease, it is a health-related condition, yet FDA has declared it to be a disease. Note well that Plaintiffs' claim does not state that reduction in the symptoms will *cure* BPH. The claim only states that the symptoms or signs will be reduced. FDA could have logically concluded that Plaintiffs' claim did not claim an effect on an existing disease. It chose instead to conclude that it did. The foregoing examples reveal the inherent irrationality of the Defendants' schema: it lacks reasonable definitional clarity and is arbitrary and capricious in its classification of some claims as "drug" claims approvable only through the extraordinarily costly drug approval process and others as "health claims" approvable through the dietary supplement health claim process. FDA's schema is not a reasonable interpretive choice under Chevron. It certainly cannot be viewed as a reliable way to fulfill the goal of ensuring that the public receives clear information on the nutrient-disease relationship.

2. The Irrationality of the Regulatory Scheme When Compared to the Congressional Goal

The Defendants argue that their interpretation of the term "health claim" is a

permissible NLEA construction because it is not expressly prohibited by the NLEA and by the legislative history underlying the Act. As explained in Plaintiffs' motion (at 26-31), the plain language used by Congress reveals that the health claims provision was meant to embrace every statement characterizing the relationship of a nutrient to a disease or a health-related condition, including disease treatment.[23] FDA has cited no, and there is no statement of, contrary intent in the pre-NLEA legislative history. Even if one assumes that the plain language of the health claims provision defining the term "health claim," 21 U.S.C. § 345(r)(1)(B), is ambiguous or that the legislative history and congressional purpose are unclear, FDA's chosen interpretation is irrational.

The Defendants' decision to exclude every claim of an unpatentable nutrient's "effect on an existing disease," deprives consumers of current, accurate, and complete information on the nutrient-disease relationship. That decision produces the wholly irrational result of permitting consumers to receive information on how a nutrient may *prevent* or *reduce* risk of disease while depriving them of information on how a nutrient affects an existing disease despite the substantial overlap between prevention and treatment.[24] It thereby disserves the admitted goal of ensuring that the public receives accurate information on the nutrient-disease relationship. See House of Rep. H.Rep. 101-

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[23] The NLEA House Floor Managers statement, Congressional Record, 101 Cong. 2nd Sess., 136 Cong. Rec. H 12951 at 12953 (October 26, 1990) reads:

> There is a great potential for defrauding consumers if food is sold that contains inaccurate or unsupportable health claims. The potential is just as great for vitamins as it is for other products. In our view, vitamins and the other substances covered by this provision should be subject to at least as strong a standard as is applicable to other foods that contains claims that the food will *treat a disease or health condition.*

SJ Exh. 6 at 20 (emphasis added). Although the House Floor Managers' statement was made after the Senate completed its consideration of the bill, it is "certainly significant" in determining the congressional intent of the phrase "health claim." See Nat'l Ass'n of Greeting Card Publ. v. U.S.P.S., 462 U.S. 810, 833 (1983) citing (Vaughn v. Rosen, 523 F.2d 1136, 1142 (D.C. Cir. 1975).

[24] Note that the prevention of a disease is often an intervention in an on-going disease process. Having a heart attack is not a random event (like winning the lottery). Lowering LDL cholesterol reduces heart

538; Nutrition Labeling & Education Act of 1990, June 13, 1990; see also 56 Fed. Reg. 60537, 60539, 60541, 60548, and 60552 (1991)

3. Irrationality of the Regulatory Scheme Violates the First Amendment

The Supreme Court has held irrationality of the regulatory scheme a factor that defeats satisfaction of the direct advancement prong of the Central Hudson test. See Rubin v. Coors, 514 U.S. 476, 488 (1995), ("§ 205(e)(2) cannot directly and materially advance its asserted interest because of the overall irrationality of the Government's regulatory scheme"). FDA's position on Plaintiffs' saw palmetto claim is patently irrational. The central purpose of the "NLEA was to assure that the public would be provided with clear information about the relationship of nutrition to disease, and to ascertain that that information would be accurate and not misleading" and "NLEA's goal [is to] assur[e] that consumers have access on food and dietary supplement labels to health claims that are scientifically supported, without having to wait until the degree of scientific certainty contemplated by the drug standard has been achieved." SJ Exh. 2 at 22, 23. Indeed, FDA understood those objectives because it reiterated them when it first implemented the NLEA provisions. See 56 Fed. Reg. 60537, 60539, 60541, 60548, and 60552 (1991) (in issuing "a regulation describ[ing] the relationship between the nutrient and the disease or health-related condition" FDA would ensure "an accurate representation" in a way "fully informative to consumers" that is "complete, truthful, and not misleading" without requiring "consensus" or "'unanimity' of scientific opinion").

Given those goals, the legislative scheme favors accurate disclosure and FDA's May 26 Ruling frustrates that scheme by suppressing Plaintiffs' claim. Rather than

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disease risk by interfering with an on-going disease process that would otherwise eventually cause the heart attack. In many cases, prevention is actually treatment.

ensure accurate communication, the agency's construct distorts the information provided to the marketplace by obscuring accurate information about the effect of saw palmetto on the symptoms of mild, benign prostatic hyperplasia. That irrationality violates the First Amendment.

II. PROCESSING PLAINTIFFS' HEALTH CLAIM WILL NOT CAUSE PLANT-BASED DRUGS TO BECOME SUPPLEMENTS AND WILL NOT POSE SAFETY RISKS

Defendants' most preposterous argument is a classic slippery slope fallacy. Defendants argue that all plant-based drugs would become dietary supplements if Plaintiffs' claim were processed as a health claim. The argument distorts the facts and the law. None of the plant-based drugs cited in FDA's Opp. could ever qualify for sale as dietary supplements under the Act because none was first lawfully sold as a dietary supplement (21 U.S.C. § 321(ff)(3)(A)) and each carries with it significant adverse effects making each unsafe for sale as a dietary supplement or food and, thus, ineligible for dietary supplement status (21 U.S.C. § 342(f)(1)(B)).[25]

The Act includes substantial restrictions that preclude the drug to supplement parade of horribles alleged by Defendants. In the definition of a dietary supplement, 21

[25] The drugs cited by FDA carry the following severe side effects as listed in the PHYSICIANS DESK REFERENCE (52d ed. 1998). Quinidine – a plant based drug: arrthythmia, abnormal electrocardiogram, asthenia, cerebral ischemia, cinchonism, hepatoxicity, and uticaria. Id. at 678. Plainly it is not safe for use as a food or a supplement. Atropine – a plant based drug: rash, urticaria, leopenia, agranulocytosis, thrombocytopenia, delrium, coma and respiratory failure. Id. at 1559. Unsafe. Tamoxifen Citrate (Nolvadex) – a non-plant based drug: hot flashes and nausea and/or vomiting; vaginal bleeding, vaginal discharge, menstrual irregularities and skin rash. Id. at 3175. Unsafe. Oncovin – a plant based drug: Leukopenia, neuritic pain, constipation, hair loss, sensory loss, paresthesia, difficulty in walking, and muscle waisting. Id. at 1493. Unsafe. Taxol – a plant based drug: Neutropenia, leukopenia, thrombocytopenia, anemia, and alopecia. Id. at 764-65. Unsafe. Heparin – a non-plant based drug: Hemorrhage, thrombocytopenia, asthma, rhinitus, and lacrimation. Id. at 3043. Unsafe. Cyclosporine (Neoral) – a non-plant based drug: Renal dysfunction, tremor, hirsutism, hypertension, gum hyperplasia, glomerular capillary thrombosis and hypomagnesemia. Id. at 1886. Unsafe. Velban – a plant-based drug: Epilation, leukopenia, alopecia, constipation, and hypertension. Id. at 1511. Unsafe. In short, none could qualify for sale as a dietary supplement under the Act (and FDA well knows this (see Pharmanex v. Shalala, No. 2:97CV262K (D.Utah Mar. 30, 2001) (attached as Exhibit 1)).

U.S.C. § 321(ff)(3)(A), a dietary supplement can only be an approved drug if the substance was "prior to such approval . . . marketed as a dietary supplement . . ." but even then it cannot continue to be marketed as a supplement if FDA finds it unlawful under section 402(f), i.e., FDA finds that when marketed as a dietary supplement the substance "present[s] a significant or unreasonable risk of illness or injury." 21 U.S.C. § 342(f)(1)(B). See generally Pharmanex v. Shalala, No. 2:97CV262K (D.Utah Mar. 30, 2001) (attached as Exhibit 1). If the drug substance (including all plant-based substances) was not previously marketed as a dietary supplement, 21 U.S.C. § 321(ff)(3)(B)(i-ii) precludes it from being classified as a dietary supplement. Under 21 U.S.C. § 331(v), it is illegal to "introduc[e] or deliver[] for introduction into interstate commerce . . . a dietary supplement that is unsafe under Section 413." Under Section 413 (21 U.S.C. § 350b), no substance not marketed as a dietary ingredient prior to October 15, 1994, may be marketed thereafter as one absent proof of safety to the FDA's satisfaction. See 21 U.S.C. § 350b; 21 U.S.C. § 342(f)(1)(B) (prohibiting new dietary ingredients "for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury"). Under 21 U.S.C. § 342, if a dietary supplement were ever found "poisonous or deleterious" it would be adulterated under the Act and thus not lawfully saleable. In particular, under 21 U.S.C. § 342(f), if the substance was sold as a dietary supplement or dietary ingredient and it presented "a significant or unreasonable risk of illness or injury" it would be proscribable by the FDA. Under 21 U.S.C. § 321(ff)(2)(A)(i), a supplement must be ingested; thus all injectable substances are excluded.

Thus, the Act prevents unsafe substances, injectable substances, and substances not previously marketed as dietary supplements from being lawfully marketed as dietary supplements (see, e.g., Pharmanex v. Shalala, No. 2:97CV262K (D.Utah Mar. 30, 2001) (Exhibit 1)). It is therefore not the case that plant-based drugs could be transformed into dietary supplements bearing health claims.

III. CONCLUSION

FDA's attempt to reclassify Plaintiffs' dietary supplement health claim into the drug category is yet another transparent effort to circumvent the First Amendment requirements of Pearson I and Pearson II, by imposing a cost prohibitive economic burden on Plaintiffs' truthful and nonmisleading speech concerning the effect of saw palmetto, an unpatentable nutrient, on the symptoms of mild, benign BPH, a health-related condition. This Court should not allow FDA to achieve that unconstitutional end. Instead, it should grant Plaintiffs the relief they seek.

Respectfully submitted,

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