UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

ALLIANCE FOR NATURAL HEALTH US, *et al.*, Plaintiffs, v. KATHLEEN SEBELIUS, *et al.*, Defendants.	Civil Action No. 09-1546 (BAH)

MEMORANDUM OPINION

Dietary supplement designers and industry groups brought this lawsuit challenging a decision of the Food and Drug Administration ("FDA") to deny a petition for authorization of certain qualified health claims regarding dietary supplements containing vitamin C and vitamin E. The plaintiffs assert the FDA's decision has violated their First Amendment rights. Invoking both circuit and district court opinions that have addressed similar claims, plaintiffs seek a declaratory judgment that the FDA's final order denying the petition is invalid and a permanent injunction enjoining the FDA from "taking any action that would preclude the Plaintiffs from placing [their proposed] health claims on the labels and in the labeling of their dietary supplements." Complaint ("Compl.") at 36. The plaintiffs' motion for summary judgment and the defendants' cross-motion for summary judgment are now before the Court. For the reasons explained below, the Court will grant in part and deny in part the parties' motions and remand certain claims to the FDA.

I. BACKGROUND

This case is the latest chapter in a lengthy saga of litigation concerning the FDA's regulation of the plaintiffs' marketing claims about the purported health benefits of various

dietary supplements. Plaintiffs Durk Pearson and Sandy Shaw are scientists who design dietary supplement formulations and license them to manufacturers and retailers. Compl. ¶ 9. The other plaintiffs – the Coalition to End FDA and FTC Censorship and the Alliance for Natural Health US – are dietary supplement industry organizations. *Id.* ¶¶ 8, 10. The defendants are Kathleen Sebelius, in her official capacity as Secretary of the United States Department of Health and Human Services, the United States Department of Health and Human Services, Margaret A. Hamburg, M.D., in her official capacity as Commissioner of the United States Food and Drug Administration, the Food and Drug Administration, and the United States of America (collectively, the "FDA" or the "defendants"). *Id.* ¶ 11.

In this case, the plaintiffs challenge an FDA decision declining to approve several health claims concerning the relationship between vitamins C and E and the risk for certain types of cancer. Before turning to the particular facts of this case, however, it is necessary to review the legal background underlying the parties' dispute and the previous court rulings that have addressed the issues involved here.[1]

A. Statutory and Regulatory Framework

A "dietary supplement" is a "product (other than tobacco) intended to supplement the diet that bears or contains" one or more of certain dietary ingredients, including vitamins, minerals, herbs or botanicals, and amino acids. 21 U.S.C. § 321(ff)(1). A dietary supplement is deemed to be "food," which is defined in part as "articles used for food or drink for man or other animals," *id.* § 321(f)(1), except when it meets the definition of a "drug," which is defined in part as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in

[1] In the following two sections, the Court largely reiterates the district court's effective summary of the relevant background in *Alliance for Natural Health US v. Sebelius*, 714 F. Supp. 2d 48 (D.D.C. 2010), a case which is substantially similar to this case, as discussed below, and which involved all of the same parties.

man or other animals." *Id.* § 321(g)(1)(B). A "health claim" is "any claim made on the label or in labeling of a food, including a dietary supplement, that expressly or by implication . . . characterizes the relationship of any substance to a disease or health-related condition." 21 C.F.R. § 101.14(a)(1); *see also* 21 U.S.C. § 343(r)(1)(A)-(B).

In 1990, Congress enacted the Nutrition Labeling and Education Act of 1990 ("NLEA"), Pub.L. No. 101-535, 104 Stat. 2353 (1990) (codified as amended at 21 U.S.C. §§ 301, 321, 337, 343, 343-1, 345, 371), which amended the Food, Drug, and Cosmetic Act ("FDCA") to provide the FDA with authority to regulate health claims on food, including dietary supplements. *Pearson v. Shalala*, 164 F.3d 650, 653 (D.C. Cir. 1999) ("*Pearson I*"). The NLEA created a "safe harbor" from the "drug" designation for foods and dietary supplements labeled with health claims. *Alliance for Natural Health US v. Sebelius*, 714 F. Supp. 2d 48, 51 (D.D.C. 2010) ("*Alliance I*"); *see also* 21 U.S.C. § 343(r)(1). Under the NLEA, a manufacturer may make a health claim on a *food* without FDA new drug approval if the FDA determines that "significant scientific agreement," based on the "totality of publicly available scientific evidence," supports the claim. 21 U.S.C. § 343(r)(3)(B)(i). For dietary supplement health claims, however, Congress declined to establish an authorization process and instead left the creation of an approval "procedure and standard" to the FDA. *Id.* § 343(r)(5)(D). The FDA subsequently promulgated a regulation adopting the NLEA's standard for food health claims (i.e., "significant scientific agreement") for dietary supplement health claims. 21 C.F.R. § 101.14(c) ("FDA will promulgate regulations authorizing a health claim only when it determines, based on the totality of publicly available scientific evidence . . . that there is significant scientific agreement . . . that the claim is supported by such evidence."). The FDA may consider a dietary supplement labeled with an unauthorized health claim to be a misbranded food, 21 U.S.C. § 343(r)(1)(B); a

misbranded drug, *id.* § 352(f); and/or an unapproved new drug. *Id.* § 355(a). A dietary supplement labeled with such a claim, or a claim that is false or misleading, is subject to seizure, and the FDA may enjoin the product's distribution or seek criminal penalties against its manufacturer. *Id.* §§ 331(a), 332, 334, 352(a).

B. *Pearson v. Shalala* and Its Progeny

The plaintiffs here and other individuals and groups affiliated with the production, sale, and use of dietary supplements have, for more than decade, sought judicial review of various FDA decisions denying a variety of proposed health claims. In the first of these lawsuits challenging the FDA's rejection of the plaintiffs' proposed claims on First Amendment grounds, the D.C. Circuit invalidated the FDA's then-existing approach to health claim review. *Pearson I*, 164 F.3d at 655-61. Since then, the FDA has struggled to balance its concerns for consumer protection and dietary supplement manufacturers' First Amendment commercial speech rights as defined by *Pearson I*. An abbreviated summary of these cases follows.

1. *Pearson I*

In 1995, a group of dietary supplement designers and others filed suit against the FDA and other defendants under the First Amendment, challenging the FDA's rejection of four health claims that the manufacturers sought to include on certain dietary supplements.[2] *Pearson v. Shalala*, 14 F. Supp. 2d 10, 14 (D.D.C. 1998) ("*First Pearson District Court Opinion*"). The claims characterized a relationship between dietary supplements and the risk of particular diseases.[3] *Id.* The FDA, applying the "significant scientific agreement" standard set forth in 21

[2] Two of these plaintiffs, Pearson and Shaw, are plaintiffs in the instant case. The predecessor organization to the Alliance for Natural Health US was also a plaintiff in *Pearson I*. *See* Compl. ¶ 8.

[3] *Pearson I* concerned the FDA's rejection of the following health claims: (1) "Consumption of antioxidant vitamins may reduce the risk of certain kinds of cancers"; (2) "Consumption of fiber may reduce the risk of colorectal cancer"; (3) "Consumption of omega-3 fatty acids may reduce the risk of coronary heart disease"; and (4) ". 8 mg of

C.F.R. § 101.14, determined that the evidence concerning the supplements "was inconclusive . . . and thus failed to give rise to 'significant scientific agreement.'" *Pearson I*, 164 F.3d at 653. The FDA therefore declined to authorize the claims, finding them to be "*inherently* misleading and thus entirely outside the protection of the First Amendment" as commercial speech. *Id.* at 655 (emphasis in original). The FDA also declined to consider the proposed alternative of "permitting the claim[s] while requiring . . . corrective disclaimer[s]," arguing that even if the proposed claims were only "potentially misleading," it had no obligation under the First Amendment to consider a "disclaimer approach," as opposed to suppression, where the claims at issue lacked significant scientific agreement. *Id.* at 654, 655, 657. The supplement designers sued, arguing that the FDA's "significant scientific agreement" standard was unconstitutionally vague and was tantamount to a blanket ban on commercial speech in violation of their First Amendment rights. *First Pearson District Court Opinion*, 14 F. Supp. 2d at 14.

After the district court denied the supplement designers' motion for summary judgment, the D.C. Circuit reversed. The Court of Appeals, applying the commercial speech test set forth in *Central Hudson Gas & Electric Corporation v. Public Service Commission of New York*, 447 U.S. 557 (1980), held that there was not a "'reasonable fit' between the government's goals" of protecting public health and preventing consumer fraud and "the means chosen to advance those goals," namely, the rejection of plaintiffs' proposed health claims without consideration of disclaimers. *Pearson I*, 164 F.3d at 656-58. Specifically, the Court held that under the First Amendment commercial speech doctrine, there is a "preference for disclosure over outright suppression" and for "less restrictive and more precise means" of regulating commercial speech. *Id.* at 657-58 (internal quotation marks omitted). The FDA's rejection of disclaimers without a

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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." *Pearson I*, 164 F.3d at 652.

showing that they were insufficient to meet the government's goal of avoiding consumer confusion demonstrated a disregard for a "less restrictive" means of speech regulation that violated the First Amendment. The Court remanded the case to the district court with instructions to remand it to the FDA to consider whether disclaimers could sufficiently prevent consumer confusion and, if so, to specify the content of those disclaimers. *Id.* at 659. The Court also held that the APA requires the FDA to "giv[e] some definitional content to the phrase 'significant scientific agreement,'" because to "declare-without explanation-that a proposed course of private action is not approved" is arbitrary and capricious. *Id.* at 660-61.

In requiring the FDA to consider the adequacy of possible disclaimers accompanying the supplement designers' proposed health claims, the Court recognized that "where evidence in support of a claim is outweighed by evidence against the claim, the FDA could deem it incurable by a disclaimer and ban it outright." *Id.* at 659. Similarly, the Court "s[aw] no problem with the FDA imposing an outright ban on a claim where evidence in support of the claim is *qualitatively* weaker than evidence against the claim." *Id.* at 659 n.10. However, the Court stated that the Agency "must still meet its burden of justifying a restriction on speech," and a "conclusory assertion" as to misleadingness is inadequate. *Id.* (citing *Ibanez v. Fla. Dep't of Bus. & Prof'l Regulation*, 512 U.S. 136, 146 (1994) ("If the protections afforded commercial speech are to retain their force, we cannot allow rote invocation of the words 'potentially misleading' to supplant the [government's] burden to demonstrate that the harms it recites are real and that its restriction will in fact alleviate them to a material degree.") (citations and internal quotation marks omitted)).

2. *Pearson II*

In late 2000, several of the plaintiffs from *Pearson I* and other dietary supplement

designers, sellers, and manufacturers filed a second lawsuit to challenge the FDA's decision prohibiting plaintiffs from including on their dietary supplements' labels a health claim concerning folic acid.[4] *Pearson v. Shalala*, 130 F. Supp. 2d 105, 107 (D.D.C. 2001) ("*Pearson II*"). After the decision in *Pearson I*, the FDA published a notice requesting submission of scientific data concerning the four health claims at issue in that case, including the folic acid claim. *Id.* at 110. The FDA also issued a guidance document, "Guidance for the Industry: Significant Scientific Agreement in the Review of Health Claims for Conventional Foods and Dietary Supplements." *Id.* at 111. After reviewing the newly submitted scientific data and applying the "significant scientific agreement standard" described in its guidance document and modified by an October 6, 2000 rule, the FDA issued a decision stating that it would not authorize the manufacturers' folic acid claim, even with clarifying disclaimers, because it found the claim to be inherently misleading. *Id.* The plaintiffs argued that the FDA's decision "fundamentally misread and misapplied the legal standard articulated" in *Pearson I* and violated the First Amendment, the FDCA, and the APA. *Id.* at 107, 112. They sought a preliminary injunction "enjoining the FDA from taking any action which would prevent Plaintiffs from using their desired folic acid health claim." *Id.* at 107.

The district court agreed with the plaintiffs, finding that the FDA "failed to comply with the constitutional guidelines outlined in *Pearson [I]*" when it concluded, without explanation,

[4] The folic acid health claim at issue in *Pearson II* was the same folic acid claim at issue in *Pearson I*, which stated 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." *Pearson I*, 164 F.3d at 652. With respect to this claim, the Court of Appeals in *Pearson I* "strongly suggested, without declaring so explicitly" that the claim "was only 'potentially misleading,' not 'inherently misleading,' and therefore the FDA's refusal to authorize [the claim] (or to propose a disclaimer to accompany the [c]laim) violated the First Amendment." *Pearson II*, 130 F. Supp. 2d at 110; *see also Pearson I*, 164 F.3d at 659 ("[I]t appears that credible evidence did support [the folic acid claim], and we suspect that a clarifying disclaimer could be added to the effect that 'The evidence in support of this claim is inconclusive.'" (citation omitted)).

that the "weight of the evidence is *against* . . . the proposed [folic acid] claim" and that the claim was therefore "inherently misleading" and not susceptible to correction by disclaimer. *Id.* at 112, 114. Although the court deferred to the FDA's "method of dissecting" and reading the folic acid claim per the APA, *id.* at 114 n. 24, it disagreed with the FDA's weighing of the scientific data and found "as a matter of law that [the folic acid claim] is not 'inherently misleading.'" *Id.* In coming to this conclusion, the court analyzed the scientific data regarding folic acid and concluded that "[t]he mere absence of significant affirmative evidence in support of a particular claim . . . does not translate into negative evidence 'against' it." *Id.* at 115. Moreover, the court held that the "question which must be answered under *Pearson [I]* is whether there is any 'credible evidence'" in support of the claim. *Id.* at 114, 118 (quoting *Pearson I*, 164 F.3d at 658). If so, unless that evidence is "outweighed by evidence against the claim" or is "qualitatively weaker" than evidence against the claim, the claim "may not be absolutely prohibited." *Id.* at 114-15.

Because the court found that there was credible evidence to support the folic acid claim, it held that the FDA's determination that the folic acid claim was "inherently misleading" and could not be cured by disclaimers was "arbitrary and capricious" under the APA and that the FDA had not "undertake[n] the necessary analysis required by *Pearson [I]*." *Id.* at 119. The court granted the plaintiffs' motion for a preliminary injunction and remanded the case to the FDA to "draft one or more appropriately short, succinct, and accurate disclaimers." *Id.* at 120.

3. *Pearson III*

After the preliminary injunction was entered in *Pearson II*, the FDA filed a motion for reconsideration, arguing that the district court had "assign[ed] undue weight to a particular clinical study and fail[ed] to consider the relevant scientific evidence in totality" and "creat[ed] a

legal standard which is inconsistent with [*Pearson I*]." *Pearson v. Thompson*, 141 F. Supp. 2d 105, 108 (D.D.C. 2001) ("*Pearson III*"). The district court denied the motion, pointing to the FDA's "fail[ure] to fully and accurately describe the record evidence" and "speculative" arguments. *Id.* at 109.

4. *Whitaker v. Thompson*

In June 2001, the plaintiffs filed another lawsuit to challenge the FDA's decision not to authorize an antioxidant claim that had been at issue in *Pearson I*.[5] *Whitaker*, 248 F. Supp. 2d at 2, 7. The FDA, after reviewing the antioxidant-cancer relationship studies submitted at its request subsequent to *Pearson I*, "found a lack of significant scientific agreement as to the relationship between antioxidant vitamin intake and reduction in the risk of developing cancer." *Id.* at 7. The FDA concluded "that the weight of the scientific evidence against the relationship [between cancer and antioxidant vitamins] was greater than the weight of evidence in favor of the relationship" and, similar to its analysis of the folic acid claim in *Pearson I* and *II*, it determined that the plaintiffs' antioxidant claim was therefore "inherently misleading and c[ould not] be made non-misleading with a disclaimer or other qualifying language." *Id.; see also Pearson II*, 130 F. Supp. 2d at 111-12. Plaintiffs argued that the FDA had again misapplied the standard articulated in *Pearson I* in violation of the First Amendment, and the district court agreed. *Id.* at 7-8.

Citing the Supreme Court's then-recent decision in *Thompson v. Western States Medical Center*, 535 U.S. 357 (2002), the court held that the FDA had not met its "burden . . . to prove

[5] The plaintiffs in *Whitaker* were Julian M. Whitaker, M.D., Durk Pearson, Sandy Shaw, American Association for Health Freedom, Wellness Lifestyles, Inc., and Pure Encapsulations, Inc. *Whitaker*, 248 F. Supp. 2d at 2 n.1. The claim at issue was that "Consumption of antioxidant vitamins may reduce the risk of certain kinds of cancers." *Id.* at 2; *see also Pearson I*, 164 F.3d at 652.

that its method of regulating speech [wa]s the least restrictive means of achieving its goals." *Whitaker*, 248 F. Supp. 2d at 9 (citing *Western States*, 535 U.S. at 371-73). Specifically, the court held that the FDA had failed to present evidence that the proposed antioxidant claim, "if accompanied by a disclaimer, would be deceptive or unlawful." *Id.* In coming to its conclusion, the court reviewed the FDA's analysis of the claim in light of *Pearson I*, noting that "[t]he deference due to an agency's expert evaluation of scientific data does not negate 'the duty of the court to ensure that an agency . . . conduct a process of *reasoned* decision-making." *Id.* at 11 (quoting *K N Energy, Inc. v. F.E.R.C.*, 968 F.2d 1295, 1303 (D.C. Cir. 1992)). As such, the court reviewed over 150 intervention and observational studies regarding the relationship between antioxidant vitamins and cancer relied upon by the FDA in reaching its conclusions and found that nearly one-third of the studies "supported" the antioxidant/cancer relationship. *Id.* The court determined that the FDA had "failed to follow its own [Guidance] Report and give appropriate weight" to these studies. *Id.* at 12. Furthermore, the court held that the FDA had improperly emphasized and de-emphasized the import of certain studies, directly contrary to the protocol it established in the Guidance Report. *Id.* In short, the court concluded that the "basic finding" on which the FDA rested its denial of the proposed claim was "unreasonable because it [wa]s not supported by an overall review of the available evidence or the FDA's own Guidance Report." *Id.* at 13. The court then found that the circumstances under which the FDA might ban a claim as misleading, described in *Pearson I*, were not present because (1) one-third of the evidence examined supported the claim; and (2) the FDA failed to provide "empirical evidence that an appropriate disclaimer would confuse customers and fail to correct for deceptiveness." *Id.* As a result, the court granted a preliminary injunction after concluding that the FDA's decision to suppress the claim did not "comport with the First Amendment's clear preference for

disclosure over suppression of commercial speech." *Id.* at 15, 17 (remanding case to FDA to draft "short, succinct, and accurate alternative disclaimers").

5. Alliance I

In *Alliance for Natural Health US v. Sebelius*, 714 F. Supp. 2d 48 (D.D.C. 2010) ("*Alliance I*"), the same plaintiffs present in this action filed suit against the FDA challenging the FDA's denial of approval for certain health claims regarding the relationship between cancer risk and selenium supplements. *Id.* at 57. The plaintiffs had proposed their selenium health claims as "qualified" claims, which are health claims that include one or more disclaimers designed to eliminate potentially misleading assertions.[6] *Id.* at 56 n.13. The FDA created the category of "qualified" claims in response to the D.C. Circuit's holding in *Pearson I*. *Id.* In the time between the decision in *Whitaker* and the filing of the lawsuit in *Alliance I*, the FDA had issued a new guidance document governing the evaluation of health claims, including "qualified claims." *See Guidance for Industry: Evidence-Based Review System for the Scientific Evaluation of Health Claims* (hereinafter "2009 Guidance Document") at Administrative Record ("A.R.") 2422-51. Applying its new "evidence-based review system" to the plaintiffs' selenium claims, the FDA banned certain of the plaintiffs' claims entirely, concluding that there was no credible scientific evidence supporting them, *Alliance I*, 714 F. Supp. 2d at 57-58, and the FDA exercised its "enforcement discretion" to permit modified versions of other claims that the FDA found to be supported by some credible evidence. *Id.*

[6] The plaintiffs' proposed qualified selenium health claims included: "Selenium may reduce the risk of certain cancers. Scientific evidence supporting this claim is convincing but not yet conclusive."; "Selenium may reduce the risk of lung and respiratory tract cancers. Scientific evidence supporting this claim is convincing but not yet conclusive."; and "Selenium may reduce the risk of colon and digestive tract cancers. Scientific evidence supporting this claim is convincing but not yet conclusive." *See Alliance I*, 714 F. Supp. 2d at 57.

The plaintiffs objected both to the FDA's decision to ban certain claims entirely as well as to the FDA's modified claims, contending that, in both instances, the FDA violated the plaintiffs' First Amendment rights. *Id.* The plaintiffs contended that the language of the modified claims infringed their First Amendment rights by constructively suppressing their claims "with the imposition of an onerous, value laden set of qualifications that only allow Plaintiffs to propound a false, negatively value-laden, and inaccurate claim to the public." *Id.*

The *Alliance I* court, in applying the relevant analysis dictated by the *Central Hudson* test as elaborated by the D.C. Circuit in *Pearson I*, "conduct[ed] an independent review of the record . . . without reliance on the [FDA's] determinations as to constitutional questions." *Id.* at 60. In accordance with binding precedent, however, the court gave "deference to the [FDA's] interpretation of scientific information, provided such interpretation [was] reasoned and not arbitrary or capricious." *Id.*

With respect to the claims that the FDA banned entirely, the *Alliance I* court began by noting that *Pearson I* suggested that when "'credible evidence' supports a claim, that claim may not be absolutely prohibited." *Id.* at 65 (citing *Whitaker*, 248 F. Supp. 2d at 10; *Pearson I*, 164 F.3d at 658-59 (where "credible evidence" supported a proposed claim, "a clarifying disclaimer could be added" to note that the evidence was inconclusive)). Since the FDA had justified its decision to ban the plaintiffs' claims on the grounds that the claims were not supported by any credible evidence, the court reviewed the record to evaluate whether the FDA's process of determining that the claims were not supported by credible evidence had been arbitrary and capricious. *Alliance I*, 714 F. Supp. 2d at 65. While the court found that many aspects of the FDA's determinations for each claim were not arbitrary and capricious, it also

found that certain aspects were arbitrary and capricious. *Id.* at 65-71. Accordingly, it remanded the claims to the FDA for reevaluation and drafting of disclaimers as appropriate.[7] *Id.* at 72.

With respect to the claims that the FDA permitted in modified form, the court agreed with the plaintiffs that the FDA's modified versions of the claims were "at odds with the Supreme Court's mandate that there be a 'reasonable fit' between the government's goal and the restrictions it imposes on commercial speech." *Id.* at 71. The court found that "[t]he [FDA] has not drafted a 'precise disclaimer' designed to qualify plaintiffs' claim while adhering to the 'First Amendment preference for disclosure over suppression,' as mandated . . . Rather, it has replaced plaintiffs' claim entirely. And the [FDA's] 'qualification' effectively negates any relationship between . . . cancer risk and selenium intake." *Id.* (citation omitted). Accordingly, the court remanded "for the purpose of reconsidering the scientific literature and drafting one or more short, succinct, and accurate disclaimers in light of that review." *Id.* at 72.

II. FACTUAL AND PROCEDURAL HISTORY

The instant case is quite similar to *Alliance I*, except that it concerns different proposed health claims. On April 9, 2008, the plaintiffs submitted a petition to the FDA seeking approval of 17 qualified health claims linking vitamins C and E with a reduction in the risk of certain types of cancer.[8] Pls.' Mem. in Supp. of Mot. for Summ. J. ("Pls.' Mem.") at 1; A.R. at 2473-74. In a decision dated June 19, 2009 (the "FDA Decision"), the FDA denied thirteen of the

[7] In addition to the claims it disallowed as unsupported by credible evidence, the FDA also disallowed certain other claims at issue in *Alliance I* because it deemed those claims "misleading on their face," "independent of the proffered scientific evidence" for failure to indicate the specific types of cancer allegedly affected by selenium. *Alliance I*, 714 F. Supp. 2d at 63-64. The court found this decision to be inconsistent with *Pearson I*, especially in light of the FDA's admission that the plaintiffs' proposed claims were "literally true . . . in that there is credible evidence that selenium may reduce the risk of at least three cancers." *Id.* Accordingly, the court remanded those claims to the FDA "for the purpose of drafting one or more disclaimers or, alternatively, setting forth empirical evidence that any disclaimer would fail to correct the claims' purported misleadingness." *Id.* at 65.

[8] The petition was submitted by Julian M. Whitaker, M.D., the Coalition to End FDA and FTC Censorship, Durk Pearson and Sandy Shaw, and Youngevity, Inc. A.R. at 2473.

proposed claims entirely and permitted four others to be made as qualified claims with modified language.[9] A.R. 2473-2526. The plaintiffs now challenge the FDA's ruling on six of these claims. Specifically, the proposed health claims at issue here are:

1. Vitamin C may reduce the risk of lung cancer. The scientific evidence supporting this claim is convincing, but not conclusive.

2. Vitamin C may reduce the risk of colon cancer. The scientific evidence supporting this claim is persuasive, but not conclusive.

3. Vitamin E may reduce the risk of lung cancer. The scientific evidence for this claim is convincing, but not conclusive.

4. Vitamin E may reduce the risk of gastric cancer. The scientific evidence for this claim is persuasive, but not conclusive.

5. Vitamin C may reduce the risk of gastric cancer. The scientific evidence supporting this claim is persuasive, but not conclusive.

6. Vitamin E may reduce the risk of bladder cancer. The scientific evidence for this claim is convincing, but not conclusive.

Compl. ¶ 26. The FDA Decision banned Claims 1, 2, 3, and 4 outright and permitted Claim 5 (Vitamin C-gastric cancer) and Claim 6 (Vitamin E-bladder cancer) to be made as qualified claims with the following modified language:

5. One small study suggests that Vitamin E supplements may reduce the risk of bladder cancer. However, two small studies showed no reduction of risk. Based on these studies, FDA concludes that it is highly unlikely that vitamin E supplements reduce the risk of bladder cancer.

[9] Technically, the FDA does not "authorize" or "permit" qualified claims, but rather "exercises enforcement discretion" to allow qualified claims that are supported by credible evidence and are not misleading. *See* Def.'s Mem. at 1 n.1 (citing 65 Fed. Reg. 59856). The reason for this technical distinction is that under the NLEA and the FDA's regulations, "the evidence supporting a health claim [must] be presented to FDA for review before the claim may appear in labeling," and the FDA is required to make a finding of "significant scientific agreement" before authorizing a health claim. 65 Fed. Reg. 59856. In other words, the FDA is not permitted by its statutory and regulatory authority to authorize claims that lack significant scientific agreement. Pursuant to *Pearson I*, however, the First Amendment precludes the FDA from prohibiting all claims that lack significant scientific agreement. Accordingly, the FDA exercises "enforcement discretion" to permit qualified claims – i.e., claims that the FDA cannot prohibit under the First Amendment, but that it also cannot technically authorize due to a of lack significant scientific agreement. For simplicity's sake, the Court will use the terms "allowed" or "permitted" in lieu of "exercise enforcement discretion." *See* Def.'s Mem. at 1 n.1.

6. One weak study and one study with inconsistent results suggest that vitamin C supplements may reduce the risk of gastric cancer. Based on these studies, FDA concludes that it is highly uncertain that vitamin C supplements reduce the risk of gastric cancer.

Compl. ¶ 30; *see also* FDA Decision at A.R. 2510-11.

The plaintiffs brought this action on August 14, 2009 seeking a declaration that the FDA Decision violates their First Amendment rights. Compl. ¶ 1. The plaintiffs contend that their "qualified health claims . . . [are] supported by credible scientific evidence," "[t]he scientific evidence for the claims is not outweighed by scientific evidence against them, and the claims are not inherently misleading." *Id.* ¶ 3. Accordingly, they contend that the FDA Decision violates their rights under the analysis set forth in *Pearson I*. *Id.*

The FDA filed the Administrative Record in this case on December 4, 2009. ECF No. 16. The plaintiffs filed a motion for summary judgment on December 30, 2009. ECF No. 17. The FDA then filed a cross-motion for summary judgment on February 22, 2010. ECF No. 19.

The parties' cross-motions for summary judgment are now before the Court.

III. ANALYSIS

A. Standard of Review

Pursuant to Federal Rule of Civil Procedure 56, the Court will grant a motion for summary judgment "if the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law" based upon the pleadings, depositions, and affidavits and other materials in the record. Fed. R. Civ. P. 56(a), (c); *Tao v. Freeh*, 27 F.3d 635, 638 (D.C. Cir. 1994). In this case, there are no disputed issues of fact and each party seeks judgment as a matter of law based on the facts reflected in the administrative record.

Plaintiffs bring their claims under the First Amendment to the United States

Constitution.[10] Compl. ¶¶ 58-63. "[A] Court's review of constitutional challenges to agency actions . . . is *de novo.*" *Alliance I*, 714 F. Supp. 2d at 59 (quoting *Poett v. United States*, 657 F. Supp. 2d 230, 241 (D.D.C. 2009) (internal quotation marks omitted). The Court shall make an independent assessment of constitutional claims when reviewing agency decision-making and need not accord deference to the agency's "pronouncement on a *constitutional* question." *Id.* (quoting *J.J. Cassone Bakery, Inc. v. NLRB*, 554 F.3d 1041, 1044 (D.C. Cir. 2009)).

While the Court "is obligated to conduct an independent review of the record and must do so without reliance on the [FDA's] determinations as to constitutional questions," it must also give deference to an agency's assessment of scientific or technical data within its area of expertise. *Id*. at 60; *see also Serono Labs., Inc. v. Shalala*, 158 F.3d 1313, 1320 (D.C. Cir. 1998) (agency "evaluations of scientific data within its area of expertise" are "entitled to a high level of deference") (internal quotations omitted).

"[D]eference to the [the FDA's] interpretation of scientific information, provided such interpretation is reasoned and not arbitrary or capricious, is consistent with the test set forth in *Pearson I*." *Alliance I*, 714 F. Supp. 2d at 60. "By instructing the FDA to employ less restrictive means of regulating speech and to provide greater empirical support for its regulatory decisions, the D.C. Circuit did not purport to tell the [FDA] how to assess scientific data. Rather, it provided the [FDA] with guidelines for developing regulations once it had evaluated the evidence before it."[11] *Id.*

[10] The Court "has the authority to examine and rule on any actions of a federal agency that allegedly violate the Constitution," apart from the power of review granted by the Administrative Procedure Act ("APA"). *Alliance I*, 714 F. Supp. 2d at 59 n.20 (quoting *Rydeen v. Quigg*, 748 F. Supp. 900, 905 (D.D.C. 1990), *aff'd mem.*, 937 F.2d 623 (Fed. Cir. 1991)). However, the APA "also provides for the Courts to make an independent assessment of constitutional issues," and the role of the Court is the same "whether the plaintiff sues directly under the Constitution or under [the APA]." *Id.* (citing *Rydeen* 748 F. Supp at 905 n.8); *see also* 5 U.S.C. § 706(2)(B).

[11] The parties' submissions, which were filed prior to the district court's decision in *Alliance I*, vigorously debate the appropriate standard of review. *Alliance I* resolved that debate in the manner adopted in this opinion: The Court

B. Legal Standard for Evaluating Commercial Speech Claims

Because the plaintiffs' qualified vitamin C and vitamin E health claims are commercial speech, the FDA's refusal to authorize them must be evaluated under the analytical framework established in *Central Hudson*, as elaborated upon by the D.C. Circuit in *Pearson I* and the Supreme Court in *Western States*. *Id*. at 60-61; *see also Pearson I*, 164 F.3d at 655.

Central Hudson established a multi-step analysis of speech regulation. "[A]s a threshold matter," the Court must determine "whether the commercial speech [being regulated] concerns unlawful activity or is misleading." *Western States*, 535 U.S. at 367. If so, the speech is not protected. *Id.* But if the speech is lawful and not misleading, or is only potentially misleading, the Court must ask "whether the asserted governmental interest in regulating the speech is substantial." *Id.* (quoting *Central Hudson*, 447 U.S. at 566). If it is, the Court then ascertains "whether the regulation [at issue] directly advances the governmental interest asserted" and, finally, "whether [the regulation] is not more extensive than is necessary to serve that interest." *Id.* (quoting *Central Hudson*, 447 U.S. at 566). This last step requires the Court to evaluate "whether the fit between the government's ends and the means chosen to accomplish those ends is . . . reasonable." *Pearson I*, 164 F.3d at 656 (citation omitted).

The government has the burden of showing that the regulations on speech that it seeks to impose are "not more extensive than is necessary to serve" the interests it attempts to advance. *Western States*, 535 U.S. at 371 (quoting *Central Hudson*, 447 U.S. at 566). "[I]f the Government c[an] achieve its interests in a manner that does not restrict [commercial] speech, or that restricts less speech, the Government must do so." *Id.* Therefore, the Court in *Pearson I* noted that disclaimers are "constitutionally preferable to outright suppression,"

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reviews an agency's decisions on constitutional questions *de novo*, but defers to an agency's interpretation of scientific information unless it is irrational or arbitrary and capricious. *Alliance I*, 714 F. Supp. 2d at 59-60.

Pearson I, 164 F.3d at 657, and that generally, "the preferred remedy is more disclosure, rather than less." *Id.* (quoting *Bates v. State Bar of Arizona*, 433 U.S. 350, 376 (1977)); *see also Pearson II*, 130 F. Supp. 2d at 113 ("[M]ore disclosure rather than less is the preferred approach, so long as advertising is not inherently misleading."). For this reason, the Court in *Pearson I* concluded that "when government chooses a policy of suppression over disclosure-at least where there is no showing that disclosure would not suffice to cure misleadingness-the government disregards a far less restrictive means." *Pearson I*, 164 F.3d at 658 (quotations omitted). However, the Court in *Pearson I* recognized that "where evidence in support of a claim is outweighed by evidence against the claim, the FDA could deem it incurable by a disclaimer and ban it outright." *Id.* at 659. Similarly, the Court "s[aw] no problem with the FDA imposing an outright ban on a claim where evidence in support of the claim is *qualitatively* weaker than evidence against the claim." *Id.* at 659 n.10.

The plaintiffs contend that even where there is no credible evidence in support of claim, or where the evidence in support of the claim is qualitatively inferior, the FDA still may not ban a claim outright without proving with empirical evidence that a disclaimer cannot cure any misleadingness. *See* Pls.' Mem. at 21 (citing *Whitaker*, 248 F. Supp. 2d at 5, 10). The FDA responds that there is no *per se* requirement to provide empirical evidence before disallowing a qualified health claim that is not supported by credible evidence, and that to the extent that *Whitaker* imposed such a requirement, it went beyond the standard articulated by the D.C. Circuit in *Pearson I*. Defs.' Cross-Mot. for Summ. J. and Opp'n to Pls.' Mot. for Summ. J. ("Defs.' Mem.") at 17-19, 18 n.13. Although the district court in *Alliance I* did not need to reach this issue, it strongly suggested in dicta that *Pearson I* did not require a showing of empirical evidence before the FDA could ban a claim that is unsupported by credible evidence. *See*

Alliance I, 714 F. Supp. 2d at 62 ("The court in *Whitaker* arguably went even further than *Pearson I*, holding that 'any complete ban of a claim would be approved only under narrow circumstances, *i.e.*, when there was almost no qualitative evidence in support of the claim *and* where the government provided empirical evidence proving that the public would still be deceived even if the claim was qualified by a disclaimer.'") (quoting *Whitaker*, 248 F. Supp. 2d at 11).

This Court agrees that *Pearson I* does not require the FDA to make an empirical showing of the inefficacy of a disclaimer before prohibiting a claim that is not supported by credible evidence. Regarding empirical evidence, the D.C. Circuit in *Pearson I* stated that "while we are skeptical that the government could demonstrate with empirical evidence that disclaimers similar to the ones we suggested above would bewilder consumers and fail to correct for deceptiveness, we do not rule out that possibility." 164 F.3d at 659-60. It is clear from the context of these remarks that the Court was referring to the disclaimers it had proposed to remedy the plaintiffs' potentially—although not inherently—misleading claims, which were based on credible, albeit inconclusive, evidence. In *Pearson I*, the FDA had argued that *any* allowance of health claims qualified by disclaimers would confuse consumers, *see id.* at 659, but the D.C. Circuit held that "the FDA's conclusory assertion" on this point failed to meet First Amendment burdens for justifying speech restrictions. *Id.* Nonetheless, the D.C. Circuit left open the possibility that "the government could demonstrate with empirical evidence that disclaimers similar to the ones [suggested by the Court] would bewilder consumers." *Id.* at 659-660. The D.C. Circuit did not hold, however, that a showing of empirical evidence was required in situations where the FDA could "reasonably determine" that a disclaimer would be insufficient because there was no credible evidence in support of the claim. *See id.* at 659 ("For example, if the weight of the

evidence were against the hypothetical claim that 'Consumption of Vitamin E reduces the risk of Alzheimer's disease,' the agency might reasonably determine that adding a disclaimer such as 'The FDA has determined that *no* evidence supports this claim' would not suffice to mitigate the claim's misleadingness.").

Contrary to the plaintiffs' arguments, this Court does not agree that the D.C. Circuit intended to suggest that, before banning an unsupported claim, the FDA would have to conduct an empirical study on the efficacy of a disclaimer such as "The FDA has determined that no evidence supports this claim." Rather, the clear implication of the language of *Pearson I* is that unsupported or very weakly supported claims may simply be banned outright. *See id.* at 659 n.10 ("[W]e see no problem with the FDA imposing an outright ban on a claim where evidence in support of the claim is *qualitatively* weaker than evidence against the claim . . ."). Presumably, such claims would qualify as unprotected commercial speech that can be prohibited under the threshold step of the *Central Hudson* analysis. *See Central Hudson*, 447 U.S. at 563 ("The government may ban forms of [commercial] communication more likely to deceive the public than to inform it."). In contrast to unsupported claims, health claims that are supported by some credible evidence, and which are therefore only potentially misleading, are protected commercial speech and are subject to a different test under the *Central Hudson* analysis. *Pearson I* teaches that empirical evidence of the inefficacy of using disclaimers is required for the FDA to ban a health claim that is only potentially misleading – i.e., a claim that is based on some credible evidence. *See Pearson I*, 164 F.3d 659 n.9 (explaining that the Court's citation of precedents related to the government's evidentiary burden to produce empirical evidence were directed at the direct advancement and reasonable fit prongs of the *Central Hudson* test). In the

absence of such empirical evidence, the FDA must rely on disclaimers to regulate a claim that is only potentially misleading.

C. FDA's Complete Ban on Certain of the Plaintiffs' Claims

The FDA Decision in response to the plaintiffs' petition banned plaintiffs from making four of the claims at issue here. *See* FDA Decision at A.R. 2475-76 (noting the FDA's determination that there is "no credible scientific evidence supporting" the vitamin C-lung cancer claim, the vitamin C-colon cancer claim, the vitamin E-lung cancer claim, and the vitamin E-gastric cancer claim). Under *Central Hudson* and *Pearson I*, the FDA may refuse to consider disclaimers for health claims (i.e., prohibit health claims completely) only if such claims are inherently misleading, or are potentially misleading but the FDA has determined the claim to be "incurable by a disclaimer." *Pearson I,* 164 F.3d at 659-60 (suggesting that government might completely ban health claim where "evidence in support of a claim is outweighed by evidence against the claim" or where it "demonstrate[d] with empirical evidence that disclaimers . . . would bewilder consumers and fail to correct for deceptiveness").

Here, the FDA justified its decision to ban these four claims based on the agency's determination that "there is no credible scientific evidence" supporting the claims. FDA Decision at A.R. 2475-76, 2503-2512. At a general level, such a decision appears consistent with *Pearson I,* which allowed for the possibility that "where evidence in support of a claim is outweighed by evidence against the claim, the FDA could deem it incurable by a disclaimer and ban it outright." 164 F. 3d at 659. However, the Court in *Pearson I* also suggested that when "credible evidence" supports a claim, that claim may not be absolutely prohibited. *Alliance I,* 714 F. Supp. 2d at 65; *see also Pearson I,* 164 F. 3d at 658-59 (where "credible evidence" supported a proposed claim, "a clarifying disclaimer could be added" to note that the evidence

was inconclusive). Therefore, as in *Alliance I*, this Court concludes that the proper inquiry here is whether the FDA properly determined that there was no "credible evidence" supporting the plaintiffs' claims. *See Alliance I*, 714 F. Supp. 2d at 65. The Court "is not in the position, nor is it the Court's role, to independently assess whether the" scientific evidence evaluated by the FDA constitutes "credible evidence" in support of plaintiffs' claims. *Id.* at 66 n.25. Rather, the Court must limit its consideration of this question to an assessment of whether the FDA's evaluation was inconsistent with its own standards, irrational, or arbitrary and capricious. *Id.*; *see also Whitaker*, 248 F. Supp. 2d at 11 (reviewing FDA's evaluation of scientific evidence to ensure the FDA conducted a "process of reasoned decision-making" and that decision was not arbitrary and capricious); *Serono Labs., Inc.*, 158 F.3d at 1320 (agency evaluations of scientific data within its area of expertise are entitled to a high level of deference).

1. The FDA's Evidence-Based Review System

In its 2009 Guidance Document, the FDA states that it uses an "evidence-based review system" to evaluate the strength of the evidence in support of a health claim. The process

> involves a series of steps to assess scientific studies and other data, eliminate those from which no conclusions about the substance/disease relationship can be drawn, rate the remaining studies for methodological quality and evaluate the strength of the totality of scientific evidence by considering study types, methodological quality, quantity of evidence for and against the claim (taking into account the numbers of various types of studies and study sample sizes), relevance to the U.S. population or target subgroup, replication of study results supporting the proposed claim, and overall consistency of the evidence. After assessing the totality of the scientific evidence, FDA determines whether there is [significant scientific agreement] to support an authorized health claim, or *credible evidence to support a qualified health claim.*

2009 Guidance Document at A.R. 2426 (emphasis added). While the document does not explicitly define "credible," it does set forth threshold questions and principles that the FDA uses to prioritize certain types of evidence over others and to identify evidence from which relevant scientific conclusions may be drawn. For example, it states that "[r]andomized, controlled trials offer the best assessment of a causal relationship between a substance and a disease." *Id.* at A.R.

2428. By contrast, "research synthesis studies," and "review articles" "do not provide sufficient information on the individual studies reviewed" to determine critical elements of the studies and whether those elements were flawed. *Id.* at A.R. 2432. Similarly, animal and *in vitro* studies, while useful for background, "do not provide information from which scientific conclusions can be drawn regarding a relationship between the substance and disease in humans." *Id.* at A.R. 2432-33. The FDA also explains the questions it considers in determining whether scientific conclusions can be drawn from an intervention or observational study, such as where the studies were conducted (i.e., on what type of population); what type of information was collected; and what type of biomarker of disease risk was measured.[12] *Id.* at A.R. 2428-32. If the FDA concludes that the elements of a study are flawed such that it is impossible to draw scientific conclusions from the study, it eliminates that study from further review. *Id.* at A.R. 2433.

The Guidance Document's framework for assessing the evidence in support of proposed supplement health claims appears generally consistent with the requirements of *Pearson I* and *Central Hudson.* It is designed to sort claims into three different tiers: (1) authorized health claims, which are supported by "significant scientific agreement"; (2) qualified health claims, which are supported by credible evidence short of significant scientific agreement; (3) and claims which are not supported by credible evidence. Claims which are not supported by credible evidence are misleading commercial speech and may be prohibited under the threshold step of the *Central Hudson* test. *See Central Hudson*, 447 U.S. at 563; *Pearson I*, 164 F.3d at 659-60. Claims which are supported by some credible, albeit inconclusive, evidence are not to be prohibited, but rather "qualified" by the use of disclaimers

[12] In an intervention study, subjects are provided with the substance being studied and the substance is typically controlled for quality and quantity. 2009 Guidance Document at A.R. 2428. Observational studies measure associations between the substance and the disease in a particular population living freely and lack the controlled setting of an intervention study. *Id.* at 2429.

because they are only potentially misleading. Thus, the FDA's Guidance Document gives effect to a "less restrictive means" of regulating such claims, providing a "'reasonable' fit between the government's goals and the means chosen to advance those goals."[13] *Pearson I*, 164 F.3d at 656-58.

The plaintiffs contend that the 2009 Guidance Document has actually reinstituted a "de facto pre-*Pearson I* standard where only conclusive scientific proof can survive the FDA's claim review." In the plaintiffs' view, the FDA has simply shifted the focus to the question of what constitutes "credible" evidence and has adopted an overly restrictive standard of credibility. Pls.' Mem. at 12. While this concern is plausible, it is dispelled by the FDA's actual application of the Guidance Document. For example, in this case, the FDA Decision found four of the plaintiffs' claims to be supported by inconclusive yet credible evidence.[14] FDA Decision at A.R. 2511. In the FDA Decision underlying *Alliance I*, the agency found the evidence supporting three of the plaintiffs' claims to be inconclusive yet credible. *See Alliance I*, 714 F. Supp. 2d at 58. Moreover, the factors that the FDA has applied in assessing credibility in this case appear reasonable to the Court, as discussed below.[15]

The Court also disagrees with the plaintiffs' argument that the FDA's approach is not

[13] In fact, the standard in the FDA's Guidance Document arguably tilts further in the direction of disclosure than required by *Pearson I*, insofar as *Pearson I* recognized that "where evidence in support of a claim is outweighed by evidence against the claim, the FDA could deem it incurable by a disclaimer and ban it outright." 164 F.3d at 659. As noted above, however, *Pearson I* also suggested that where "credible evidence" supported a claim, the claim could likely be cured by disclaimer. *Id.* at 658-59. Thus, since the precise standard required in *Pearson I* was not entirely clear, the FDA has appropriately endorsed an approach that would favor more disclosure.

[14] The validity of the modified language the FDA proposed for these claims is a separate issue, which is addressed independently below.

[15] The Court notes that, in reaching its decision here, it has not evaluated whether all of the FDA's criteria for assessing credibility in the Guidance Document are reasonable and not arbitrary and capricious. The Court has only evaluated those criteria necessary for the Court's decision. For example, the Complaint alleges that the "FDA refused to consider 5 intervention studies because they involved foreign subjects," Compl. ¶ 36, but the plaintiffs have not argued that these studies supported any of their claims in particular and the Court did not need to reach the issue of the viability of this alleged exclusion. *See infra* n.18 (explaining that the Court has only performed a detailed analysis of the FDA's treatment of studies that are directly and substantively addressed in the plaintiffs' memoranda and statement of facts in connection with each claim).

based on a review of the totality of the scientific evidence because the FDA categorically discounts certain types of studies based on their methodology or design. *See* Pls.' Mem. at 12. Rather, the FDA's Guidance Document has articulated certain factors the agency will use in evaluating the totality of the scientific evidence, including factors indicating certain types of studies that do not provide credible evidence of health claims for supplement use in humans. The application of predefined principles for identifying which studies can provide credible evidence for a health claim does not suggest a failure to consider the totality of the evidence.[16]

2. Plaintiffs' Vitamin C-Lung Cancer Claim

Using the procedure described in the Guidance Document, the FDA determined that there was no credible evidence to support the plaintiffs' vitamin C-lung cancer claim.[17] The plaintiffs contend that various studies that were discounted by the FDA do provide credible evidence supporting their claim and discuss, in particular, five studies: the Neuhoser *et al.* 2003 study; the Cho *et al.* 2006 study; the Feskanich *et al.* 2000 study; the Comstock *et al.* 1997 study; and the

[16] One particular point of contention regarding credibility is the relevance of peer review of scientific studies. Plaintiffs emphasize that "peer-reviewers considered the Plaintiffs' studies to be reasonable and justified by the evidence when each study was published in a peer-reviewed journal. . . . By definition, a peer-reviewed publication has survived the scrutiny of experts in the same field." Pls.' Mem. at 31. The FDA does not dispute that peer review provides some indicia of scientific validity, but rather logically points out that the plaintiffs cannot demonstrate that the "the articles' authors, the peer reviewers, or the publications believe that the studies support the health claims that plaintiffs seek to use to promote their products to consumers." Defs.' Reply in Supp. of Cross-Mot. for Summ. J. ("Defs.' Reply") at 16. The key question is whether a study provides *credible evidence for the plaintiffs' specific claim*, not whether it is scientifically sound in some more generic sense. Indeed, based on the review of the record in this case, there are examples of studies cited by plaintiffs that actually appear to undercut the plaintiffs' claims. *See, e.g.*, Cho *et al.* 2006, at A.R. at 752 (finding that "vitamin C intake combining food and supplemental sources and supplemental vitamin C alone were each not associated with lung cancer risk," but cited as evidence of plaintiffs' vitamin C-lung cancer claim, *see* Pls.' Mem. at 33). Further, as the FDA also points out, articles may be published for purely scientific purposes based on evidence that merely serves to generate hypotheses, debate, or to identify areas for further research. *See* Defs.' Reply at 16.

[17] As in *Alliance I*, the Court considers only the first sentence of each of plaintiffs' proposed claims, not the suggested disclaimer in the second sentence (i.e., that "Vitamin C may reduce the risk of lung cancer," not that the "scientific evidence supporting this claim is convincing, but not conclusive."). To the extent the FDA denied these claims outright based on a lack of credible evidence, it did so on the basis of the claimed relationship between the vitamins and the cancers, not because of the plaintiffs' proposed disclaimers. *See Alliance I*, 714 F. Supp. 2d at 62 n.22; FDA Decision at A.R. 2476 ("FDA considers the data and information provided in the petition . . . to determine whether the data and information could support a relationship between the substance and the disease or health-related condition.").

Gackowski *et al.* 2005 study.[18] *See* Pls.' Mem. at 32-33; Plaintiffs' Statement of Material Facts ("SMF") ¶¶ 39-42.

The FDA states that it discounted the Comstock and Gackowski studies because they used blood levels of vitamin C as a marker of vitamin C intake. FDA Decision at A.R. 2495-96, 2526. According to the FDA, "[s]ince circulating vitamin C or vitamin E levels and intake levels are poorly correlated, and many factors (e.g., [body mass index], serum lipid level, smoking) can alter the serum or plasma vitamin C or vitamin E concentration at a given point in time, scientific conclusions cannot be drawn from studies that used vitamin C or E levels as a biomarker of intake." *Id.* at A.R. 2496. In support of this conclusion, the FDA cited numerous different studies regarding the correlation between vitamin C and vitamin E intake and serum or plasma levels of the vitamins. *Id.* at A.R. 2495-96. The 2009 Guidance Document also states that "[t]here should be evidence to demonstrate a strong correlation between the intake level of the substance and the level of the substance . . . in the biological sample . . . If the correlation is weak . . ., then scientific conclusions cannot be drawn from studies that used that biological sample as a biomarker of intake." 2009 Guidance Document at A.R. 2437. Since the FDA has provided a reasoned explanation for the exclusion of these studies and the explanation is consistent with the FDA's Guidance Document, the FDA's decision that these studies do not constitute credible evidence of the claim must be upheld.

The FDA discounted the Cho study because it was a "meta-analysis" of studies reflected in a review article. FDA Decision at 2523. As explained in the 2009 Guidance Document,

[18] While the plaintiffs note that they submitted other studies as well, the Court assumes that the particular studies that are directly and substantively addressed in detail in the plaintiffs' memoranda and statement of facts in connection with each claim provide what the plaintiffs view as the strongest evidence in support of that claim. Given the voluminous scientific record before the Court and the limited nature of the Court's ability to review highly technical decisions grounded in an agency's scientific expertise, the Court will only perform a detailed analysis of the FDA's treatment of those studies that the plaintiffs' submissions have addressed detail in connection with each claim. *See Alliance I*, 714 F. Supp. 2d at 66 n.25 (adopting the same approach).

"research synthesis studies," and "review articles," including "most meta-analyses," "do not provide sufficient information on the individual studies reviewed" to determine critical elements of the studies and whether those elements were flawed. 2009 Guidance Document at A.R. 2432. The Guidance Document makes an exception for meta-analyses "that review[] all the publicly available studies on the substance/disease relationship." *Id.* Based on the Court's review of the Cho article, the FDA's decision to exclude this article as a meta-analysis was not arbitrary and capricious. *See Alliance I,* 714 F. Supp. 2d at 67. The article pooled information from only eight studies and actually concluded that "this pooled analysis of 8 prospective studies does not suggest that intakes of vitamins A, C, E, and folate reduce the risk of lung cancer." Cho at A.R. 752. Indeed, the study apparently found that "supplemental vitamin C alone [was] . . . not associated with lung cancer risk." *Id.* at 751.

Finally, the FDA discounted the Feskanich and Neuhoser studies because they are observational studies that estimated vitamin intake "from dietary sources intake" – i.e., from the foods eaten by the study's subjects. FDA Decision at A.R. 2525, 2493-95. The FDA Decision contains an extensive discussion of why the FDA will not rely on food intake studies as evidence of a particular nutrient's effect on a disease. *Id.* at 2493-95. The reasons include numerous potential weaknesses in the methods for accurately measuring an individual's food intake, which are usually based on self-reporting; variability in the nutrient content of foods based on different farming, production, cooking, and storage conditions; difficulty in isolating the effects of various nutrient components of foods; and evidence of previous cases in which dietary intake studies had indicated that a food nutrient may have a beneficial effect on a disease, while subsequent intervention studies showed that dietary supplements containing that nutrient do not confer any benefit or actually increase risk of the disease. *Id.* The 2009 Guidance Document also notes

these concerns and concludes that "scientific conclusions from observational studies cannot be drawn about a relationship between a food component and a disease." 2009 Guidance Document at A.R. 2438-39.

The plaintiffs object to the FDA's exclusion of observational studies based on food intake primarily because, according to the plaintiffs, the D.C. Circuit in *Pearson I* held that disclaimers were sufficient to cure vitamin supplement claims that were based upon food intake studies. *See* Pls.' Mem. at 28. In *Pearson I*, the FDA had determined that the plaintiffs' claims "lack significant scientific agreement because existing research had examined only the relationship between consumption of *foods* containing these components and the risk of these diseases." 164 F.3d at 658. The Court noted that "[t]he FDA logically determined that the specific effect of the *component* of the food constituting the dietary supplement could not be determined with certainty," yet concluded that "certainly this concern could be accommodated . . . for example, by adding a prominent disclaimer to the label along the following lines: 'The evidence is inconclusive because existing studies have been performed with *foods* containing antioxidant vitamins, and the effect of those foods on reducing the risk of cancer may result from other components in those foods.'" *Id.*

The FDA directly addressed the D.C. Circuit's comments on this issue in its decision. FDA Decision at A.R. 2494. In short, the FDA contends that observational studies based on food intake do not provide "inconclusive" evidence of single nutrient supplement claims; rather, they simply do not support valid scientific conclusions about single nutrient supplements. *Id.* The reason for the FDA's conclusion is not only because of the difficulties in disentangling the effects of various food components, which was the issue addressed by the D.C. Circuit in *Pearson I*, but also because of all the other factors discussed above, particularly the

understanding that nutrients in food do not necessarily have the same beneficial effect in supplement form, and that some studies have actually demonstrated increased disease risk from supplements predicted to be beneficial based on food studies. *Id.* As evidence of this understanding, which the FDA contends has emerged since the decision in *Pearson I*, the FDA points to a 2005 review article published in the Journal of the American Medical Association. *Id.*; *see also* Alice Lichtenstein and Robert Russell, *Essential Nutrients: Food or Supplements?*, 294 J. AM. MED. ASSOC. 351-58 (2005), at A.R. 3315-22.[19]

This Court is persuaded that the FDA has provided a reasonable basis for determining that observational studies based on food intake do not provide credible scientific evidence of the disease risk effects of single nutrient supplements. To the extent that the FDA's concern about food studies is premised on the difficulty in isolating the effects of specific nutrient components of food, the D.C. Circuit did conclude that "this concern could be accommodated" by disclaimer. *Pearson I*, 164 F.3d at 658. Accordingly, that concern alone would likely be insufficient to justify prohibiting a claim. As noted above, however, the FDA has identified several other compelling concerns about the validity of drawing scientific conclusions about single nutrient supplements from observational food studies. It is also significant that the D.C. Circuit's comments regarding food studies were made in the context of reviewing an FDA decision made

[19] The plaintiffs object to the FDA's citation of the Lichtenstein and Russell review article since the 2009 Guidance Document establishes that review articles *per se* provide insufficient evidence to support a health claim. *See* Pls.' Mem. in Reply and Opp'n to Defs.' Opp'n to Pls.' Mot. for Summ. J. and Cross-Mot. for Summ J. at 27. The 2009 Guidance Document states, however, the FDA may use review articles "as background" and to identify individual studies for consideration. 2009 Guidance Document at A.R. 2432. Here, in addition to citing the Lichtenstein and Russell review article, the FDA has also pointed to individual studies to support its concern about the discrepancies between food intake studies and intervention studies. For example, the Guidance Document states that "previous observational studies reported an association between fruits and vegetables high in beta-carotene and a reduced risk of lung cancer (Peto et al., 1981). However, subsequent intervention studies . . . demonstrated that beta-carotene supplements increase the risk of lung cancer in smokers and asbestos-exposed workers, respectively (The Alpha-Tocopherol and Beta Carotene Cancer Prevention Study Group, 1994; Omenn et al. 1996)." *Id.* at 2438-39; *see also* FDA Decision at A.R. 2494 (citing the same studies).

under a different standard that the FDA had not articulated well prior to its application. *See Pearson I*, 164 F.3d at 660-61. Here, the question is the validity of the FDA's criteria for considering evidence as "credible" scientific support for a claim. The FDA's criteria here were articulated in advance of their application, in the 2009 Guidance Document, and they appear to have a rational, scientific basis. Ultimately, this issue comes down to a judgment about the scientific validity of drawing certain conclusions from a particular methodology. In these circumstances, the Court will not attempt to replace the FDA's scientific judgment with its own.

Accordingly, the FDA's rejection of the studies cited by the plaintiffs as credible evidence of the claim that "Vitamin C may reduce the risk of lung cancer" was consistent with the FDA's established evaluation criteria and rationally justifiable based on the nature of the studies.

3. Plaintiffs' Vitamin C-Colon Cancer Claim

The FDA also determined the plaintiffs' vitamin C-colon cancer claim was not supported by credible evidence. Plaintiffs contend that the following five studies support their claim: Cahill *et al*. 1993, Bostick *et al*. 1993, Satia-Abouta *et al.* 2003, Chiu *et al.* 2003, and Olsen *et al*. 1994. Pls.' Mem. at 34-35; SMF ¶¶ 43-47.

The FDA did not credit the Cahill study as credible evidence because it measured effects that are not considered "validated surrogate endpoints of cancer risk" for colon cancer. FDA Decision at A.R. 2490, 2523. In other words, the study measured effects that are not proven indicators of the disease. According to the FDA, the only "validated endpoints" to use in evaluating risk reduction claims for colon cancer are (1) actual cases of colon cancer or (2) "recurrent adenomatous colorectal polyps," a medical condition involving colorectal polyps which are non-cancerous but which have proven to be correlated with colon cancer risk. FDA

Decision at A.R. 2484, 2490. Put another way, a study that measures effects other than the incidence of colon cancer or adenomatous colorectal polyps (or other proven indicators of colon cancer risk) in the study population would not generally provide credible evidence for colon cancer risk claims. The Cahill study measured the effect of vitamin C supplementation on colon "crypt cell proliferation" in a group of ten patients that had existing colorectal polyps. Defs.' Mem. at 29 (citing Cahill at A.R. 2734-38). The study found that vitamin C supplements reduced the rate of crypt cell proliferation. Cahill at A.R. 2738. While higher rates of crypt cell proliferation are observed in patients with colon cancer or polyps, the study did not show that these higher rates of cell proliferation are themselves a cause of cancer or that reducing them affects cancer risk. *Id.* at 2737-38. While the Cahill authors hypothesized that the observed effect on cell proliferation in patients with colon polyps "may reduce the risk of progression" to cancer or recurrent adenomatous colon polyps, this proposition does not itself appear to have been validated by the study. *See id.* Under these circumstances, the Court finds that the FDA's decision to exclude this study was not unreasonable. In addition, the FDA's exclusion of the Cahill study also appears consistent with its Guidance Document. *See* 2009 Guidance Document at A.R. 2436 ("Scientific conclusions cannot be drawn about the relationship between the substance and risk of disease if the risk biomarker is not a surrogate endpoint."); *see also id.* at A.R. 2433 (noting "adenomatous colon polyps" as a valid surrogate endpoint for colon cancer). Accordingly, the FDA's decision to exclude the Cahill study was not arbitrary and capricious.

The FDA also excluded the other four studies cited by the plaintiffs because those observational studies estimated vitamin intake from dietary sources or from a combination of dietary sources and multivitamin supplements, a factor which provides a valid basis for exclusion, as discussed above. *See* Defs.' Mem. at 30; FDA Decision at A.R. 2525 (excluding

Satia-Abouta *et al.* 2003, Bostick *et al.* 1993, Olsen *et al.* 1994, and Chiu *et al.* 2003).

Accordingly, the FDA's rejection of the studies cited by the plaintiffs' as credible evidence of the claim that "Vitamin C may reduce the risk of colon cancer" was consistent with the FDA's established evaluation criteria and rationally justifiable based on the nature of the studies.

4. Plaintiffs' Vitamin E-Lung Cancer Claim

The plaintiffs point to four studies in particular as evidence of their claim that vitamin E may reduce the risk for lung cancer: Woodson *et al.* 1999, Comstock *et al.* 1997, Knekt *et al.* 1991, and Lonn *et al.* 2005. Pls.' Mem. at 38-39; SMF ¶¶ 62-66.[20] The FDA discounted the Woodson *et al.* 1999 study and the Comstock *et al.* 1997 study because they relied on blood serum or plasma vitamin levels as a measure of vitamin E intake, which is a valid basis for exclusion, as discussed above. FDA Decision at A.R. 2526. The FDA excluded the Knekt *et al.* 1991 study because it estimated vitamin intake from dietary sources, which is also a valid basis for exclusion, as discussed above. *Id.* at 2526.

The Lonn *et al.* 2005 study was an intervention study designed to "[t]o evaluate whether long-term supplementation with vitamin E decreases the risk of cancer, cancer death, and major cardiovascular events." Lonn at A.R. 3346. The study was not specific to lung cancer and assessment of site-specific cancers was subsidiary. FDA Decision at A.R. 2487. The FDA discounted the study because it did not pre-screen subjects for specific cancers prior to the study, which the FDA contends may have resulted in biased incidences of lung cancer between the vitamin E group and the placebo group. *Id.* In any event, the main finding of the study, as stated

[20] Plaintiffs' memorandum and statement of facts asserts that they submitted 17 studies in support of this claim, but then lists, in summary form, more than 17 studies. *See* SMF ¶ 62. In any event, as noted above, the Court has only conducted a detailed review of the FDA's treatment of the studies that are specifically discussed in the plaintiffs' memorandum and statement of facts.

by the authors, was "the lack of benefit for vitamin E in preventing cancer or major cardiovascular events after a prolonged period of treatment and observation." Lonn at A.R. 3351. In addition, the authors also concluded that "our study raises concern about an increased risk of heart failure related to vitamin E." *Id.* While the study authors did observe a decreased incidence of lung cancer in the vitamin E group, when the authors applied the relevant "stringent statistical rules," the difference in lung cancer rates did not rise to the predefined level of statistical significance and the authors themselves concluded that "the differences [in lung cancer outcomes] observed in our study are likely a chance finding." *Id.* In short, the study found no statistically significant health benefits from vitamin E supplements. Thus, the study's results do not appear to support the plaintiffs' claim, while the FDA's concerns about potential for bias in the distribution of lung cancer cases in the study appear consistent with the authors' conclusions that any difference in lung cancer rates was likely due to chance. Accordingly, the FDA's decision that this study and the other cited studies do not constitute credible evidence for the plaintiffs' claim was not arbitrary and capricious.

5. Plaintiffs' Vitamin E-Gastric Cancer Claim

Plaintiffs point to five studies in particular to support their claim that vitamin E may reduce the risk of gastric cancer: Virtamo *et al*. 2000; You *et al*. 2000; Lopez-Carillo *et al*. 1999; Jenab *et al*. 2006b; and Buiatti *et al*. 1990. *See* Pls.' Mem. at 37; SMF ¶¶ 57-61.

The FDA validly discounted the Buatti and Lopez-Carillo studies because they estimated vitamin E intake based on food consumption. FDA Decision at A.R. 2525. The FDA also validly discounted the You and Jenab studies because they relied on serum or plasma levels of vitamin E as an indicator of intake. *Id.* at 2526. Finally, the FDA discounted the Virtamo article because, similar to the Lonn *et al.* 2005 study discussed above, the underlying trial was not designed to

study gastric cancer risk and no pre-screening for gastric cancer was performed. *Id.* at 2524. Indeed, as the FDA points out in its brief, the Virtamo article does not relate to the effect of vitamin E on gastric cancer. Defs.' Mem. at 41 n.32 (citing Virtamo at A.R. 3613-19). Rather, it relates to the effect of vitamin E on urinary tract cancer, and the authors concluded that vitamin E does not reduce the risk of urinary tract cancer.[21] *Id.* These exclusions were not arbitrary and capricious. Accordingly, the Court defers to the FDA's determination that the plaintiffs' claim lacks credible supporting evidence.

D. FDA's Qualification of Certain of the Plaintiffs' Claims

In its decision, the FDA found that four of the qualified claims proposed by the plaintiffs were supported by some credible scientific evidence under the procedures for evidentiary analysis spelled out in the Guidance Document. FDA Decision at A.R. 2511-12. However, the FDA found that it needed to revise the wording of the plaintiffs' qualified claims "so as to not mislead consumers." *Id.* Plaintiffs challenge the FDA's rewording of two of their qualified claims here – the vitamin C-gastric cancer claim and the vitamin E-bladder cancer claim. As noted above, the FDA reworded these claims to read as follows:

> **Vitamin E-Bladder Cancer Claim:**
>
> One small study suggests that Vitamin E supplements may reduce the risk of bladder cancer. However, two small studies showed no reduction of risk. Based on these studies, FDA concludes that it is highly unlikely that vitamin E supplements reduce the risk of bladder cancer.
>
> **Vitamin C-Gastric Cancer Claim:**
>
> One weak study and one study with inconsistent results suggest that vitamin C

[21] Plaintiffs appear to suggest that the study did pre-screen for cancers by citing a portion of the study explaining that "[p]articipants had three follow-up visits annually, during which information regarding illnesses, symptoms, and smoking were collected . . .," *see* Pls.' Mem. at 37-38 n.35 (citing Virtamo at A.R. 3614), but this citation regarding "follow-up visits" appears to refer to screening after the study was underway. In any event, as noted above, the study does not appear to have made findings with respect to gastric cancer.

> supplements may reduce the risk of gastric cancer. Based on these studies, FDA concludes that it is highly uncertain that vitamin C supplements reduce the risk of gastric cancer.

As in *Alliance I*, "[t]he Court agrees with plaintiffs' contention that the FDA's proposed claim is at odds with the Supreme Court's mandate that there be a 'reasonable fit' between the government's goal and the restrictions it imposes on commercial speech." *Alliance I*, 714 F. Supp. 2d at 71 (citing *Pearson I*, 164 F.3d at 656 n.5). Indeed, these disclaimers fail for the same reasons the disclaimers in *Alliance I* failed. The FDA has "not drafted [] 'precise disclaimer[s]' designed to qualify plaintiffs' claim[s] while adhering to the 'First Amendment preference for disclosure over suppression,' as mandated." *Id.* "Rather, it has replaced plaintiffs' claim[s] entirely." *Id.* Further, the FDA's "qualification" effectively negates any relationship between cancer risk and vitamin intake. *See id.* The FDA's rewording makes it difficult to tell what the original health claims are and appears to disavow the FDA's own conclusions that those claims are supported by credible evidence. "[T]he FDA has completely eviscerated plaintiffs' claim[s], with no explanation as to why a less restrictive approach would not be effective." *Id.* Where the evidence supporting a claim is inconclusive, the First Amendment permits the claim to be made; the FDA cannot require a disclaimer that simply swallows the claim.[22] "In short, the FDA's replacement of plaintiffs' claim[s] with different and contradictory language is inconsistent with the spirit, if not the letter, of *Pearson I*." *Id.* at 72. Accordingly, the Court will

[22] As noted above, in the plaintiffs' proposed claims, the first sentence characterized a possible substance-disease relationship, which is what the FDA evaluated for evidentiary support. The second sentence was a proposed disclaimer regarding the strength or nature of the evidentiary support for that substance-disease relationship. *See supra* n.17. In drafting disclaimers for a health claim regarding a substance-disease relationship supported by some credible evidence, the FDA's attention would ordinarily be directed primarily toward the latter characterization.

remand the vitamin C-gastric cancer and vitamin E-bladder cancer claims to the FDA for the purpose of drafting one or more precise disclaimers.[23] *Id.*

IV. CONCLUSION

For the reasons discussed above, the parties' motions for summary judgement are each granted in part and denied in part. The vitamin C-gastric cancer and vitamin E-bladder cancer claims are remanded to the FDA for further action consistent with this Memorandum Opinion and the other relief sought by the plaintiffs is denied.

DATED: April 13, 2011

/s/ *Beryl A. Howell*
BERYL A. HOWELL
United States District Judge

[23] It is not the Court's role to draft disclaimers in the first instance, *see Pearson I*, 164 F.3d at 659, but the Court refers the FDA to examples of disclaimers proposed by the D.C. Circuit in *Pearson I* to serve as relevant models of the type of disclaimers that may be appropriate. *See id*. at 658-60. In addition, since the Court remands this claim to the FDA on the basis of the FDA's complete substitution of plaintiffs' proposed claim, it did not need to review all of the studies excluded or relied on by the FDA in evaluating plaintiffs' claims. *See Alliance I*, 714 F. Supp. 2d at 72 n.30.