

Before the
DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
Center for Food Safety and Applied Nutrition
Rockville, MD

In re:)
Draft Guidance for Industry)
(Substantiation for Dietary)
Supplement Claims Made) Docket No. 2004D-0466
Under Section 403(r)(6) of the)
Federal Food, Drug, and)
Cosmetic Act))

To: Division of Dockets Management (HFA-305),
Food and Drug Administration,
5630 Fisher Lane, Rm. 1061,
Rockville, MD 20852

COMMENTS OF BASIC RESEARCH, L.L.C.

Jonathan W. Emord
Andrea G. Ferrenz
Michelle C. Gayeski
Emord & Associates, P.C.
1800 Alexander Bell Dr.
Suite 200
Reston, VA 20191
Phone: 202-466-6937
Fax: 202-466-6938
jemord@emord.com

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COMMENTS OF BASIC RESEARCH, L.L.C.

Basic Research, L.L.C. (“Basic Research”), by counsel and pursuant to 21 C.F.R. §§ 10.40, 10.20, hereby responds to the agency’s request for comments in the Federal Register, 69 Fed. Reg. 64962 (Nov. 9, 2004) (hereinafter “Draft Guidance” or “proposed standard”). In the Draft Guidance, the FDA proposes to define the statutory term “substantiation” contained in the misbranding section of the Act, 21 U.S.C. § 343(r)(6). Section 343(r)(6) pertains to so-called “structure/function” claims for dietary supplements.¹

The Federal Food, Drug, and Cosmetic Act requires manufacturers of dietary supplements to “[have] substantiation that [structure/function claims are] truthful and not misleading.” 21 U.S.C. § 343(r)(6)(B). The Draft Guidance would define

¹ In 2000, the FDA declared claims made in accordance with the provisions of 21 U.S.C. § 343(r)(6) to be “structure/function” claims and defined the difference between those claims and claims associating a nutrient with a disease or disease condition. See 65 Fed. Reg. 1000 (Jan. 6, 2000) (Ex. A). While the former may be made without premarket approval upon filing notice no later than thirty days after first marketing a product with the claim, the latter may not be made without advance FDA approval or allowance. Compare 21 C.F.R. § 101.93(a)(1), with 21 C.F.R. § 101.14(d), (e).

“substantiation” in 21 U.S.C. § 343(r)(6)(B) as “competent and reliable scientific evidence,” borrowing that phrase and its definition from the Federal Trade Commission (FTC). At the FTC, “competent and reliable scientific evidence” is used as an evidentiary standard to test whether health benefit representations in advertising are deceptive. FDA proposes to use the phrase to define structure/function claim substantiation but neither commits to giving it a meaning identical to that given the phrase by the FTC nor supplies the phrase with any other clear meaning.

As explained in detail herein, (1) the proposed standard violates the First Amendment because it would restrict use of speech not based on proof by FDA that the statements in question are inherently misleading but based on a finding by FDA that evidence held by the manufacturer in support of the statements does not prove the statement’s scientific validity. (2) The proposed standard also violates the First Amendment because it impermissibly shifts the burden of proof from the FDA to the regulated class. Under the First Amendment, the government must prove inherent misleadingness to justify speech suppression; the regulated class cannot be required to possess substantiation backed by “competent and reliable scientific evidence” as a condition precedent to its right to communicate protected speech, including structure/function claims that are not inherently misleading. (3) The proposed standard further violates the First Amendment by requiring compliance with a *de facto*, albeit exceedingly ambiguous, scientific proof standard before speech may be uttered without fear of prosecution, thereby threatening the regulated class with adverse government action if the regulated class errs in its estimation of whether a structure/function claim is backed by “competent and reliable scientific evidence.” The vagueness of the standard,

its absence of requisite definitional certainty in the regulation of speech, causes it to violate the First and Fifth Amendments. It lacks requisite procedural safeguards to avoid suppression of protected speech. Moreover, as explained herein, (4) the proposed standard violates 21 U.S.C. § 343(r)(6)(B) by changing the compliance standard from one that protects all structure/function claims that are “truthful and not misleading” to one that threatens adverse government action against all structure/function claims except those backed by “competent and reliable scientific evidence.” Further, as explained herein, (5) the proposed standard violates the Administrative Procedure Act (APA) prohibition against arbitrary and capricious agency action (5 U.S.C. § 706(2)(A)) because it fails to define “competent and reliable scientific evidence” with sufficient specificity to guide the regulated class in discerning whether any particular structure/function claim would, in context, be reliably accepted by FDA as “adequately substantiated.” For these reasons explained below, Basic Research respectfully requests that FDA withdraw the Draft Guidance.

A. BACKGROUND AND INTEREST OF BASIC RESEARCH

Basic Research, LLC is a Utah-based company that develops and manufactures dietary supplements. More than 17,000 individual retail outlets worldwide carry formulations developed by Basic Research. The company holds and/or licenses patents related to more than 20 formulations. Basic Research uses structure/function claims on its dietary supplements in the regular course of business to inform its consumers of the uses of its products. The recommended reforms directly and materially affect the business, sale, and marketing practices of Basic Research.

B. SUMMARY OF THE DRAFT GUIDANCE

1. Statutory Predicate

Structure/function claims governed by 21 U.S.C. § 343(r)(6) may be made without advance notice to the FDA provided that certain conditions are met. In particular, each structure/function claim must fall within a definitional category prescribed in 21 U.S.C. § 343(r)(6)(A) (*i.e.*, the statement must (a) “claim a benefit related to a classical nutrient deficiency disease and disclose[] the prevalence of the disease in the United States;” (b) “describe[] the role of a nutrient or dietary ingredient intended to affect the structure or function in humans;” (c) “characterize[] the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function;” or (d) “describe[] general well-being from consumption of a nutrient or dietary ingredient”). Section 343(r)(6)(B) requires that the “manufacturer of the dietary supplement [have] substantiation that such statement is truthful and not misleading.” Section 343(r)(6)(C) requires that each structure/function claim be associated with a mandatory disclaimer, reading: “This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.” By regulation, FDA has explained how disclaimers are to be used, has prescribed the content required for structure/function claim submissions, and has required the filing of a certification confirming that the manufacturer has requisite substantiation that each structure/function claim is truthful and not misleading. See 21 C.F.R. § 101.93.

2. The Draft Guidance

In the Draft Guidance, the FDA informs the regulated class that it intends to require more than the certification of truthfulness prescribed in 21 C.F.R. § 101.93(a)(3) as proof of adequate “substantiation” under 21 U.S.C. § 343(r)(6)(B). It announces the agency’s intent to discern whether structure/function claims are backed by “competent and reliable scientific evidence,” a standard not proscribed by statute but borrowed from the FTC and said not to be identical to the FTC’s deceptive advertising review standard (described in FTC, “Dietary Supplements: An Advertising Guide for Industry” (Ex. B)) but “modeled on” and a “complement” to that standard. See Draft Guidance at 3. Under the Draft Guidance, if backed by “competent and reliable scientific evidence,” a structure/function claim would be deemed adequately substantiated. Id. at 4, 15. If not so backed, a structure/function claim would be deemed inadequately substantiated, and the product would be misbranded under 21 U.S.C. § 343(r)(b)(6). See Id.

Even were the FDA to adopt the very same “competent and reliable scientific evidence” standard now used by the FTC, that standard would not survive constitutional and Administrative Procedure Act review. It is too vague to be applied in a way that reliably and consistently avoids suppression of protected speech. It is too vague to afford the regulated class that degree of assurance it must have against adverse government action to communicate protected speech without a chilling effect. It comes with no procedural safeguards to segregate inherently misleading speech (suppressible outright, see Peel v. Atty. Registration & Disciplinary Comm’n, 496 U.S. 91, 111 (1990) (citing In re R. M. J., 455 U.S. 191, 203 (1982)); Thompson v. Western States Medical Center, 535 U.S. 357, 367 (2002)) from potentially misleading speech (protected against suppression,

see Peel, 496 U.S. at 111; Washington Legal Foundation v. Henney, 56 F. Supp. 2d 81, 85 (D.D.C. 1999)). It does not impose, as it must, a condition precedent on state action that compels reliance on disclaimers as less speech restrictive alternatives to outright suppression whenever disclaimers suffice to avoid misleadingness. It lacks sufficient definitional certitude to apprise regulatees of precisely what level, degree, quality, and quantity of scientific evidence must be possessed to afford the regulatee assurance that the speech in question will be protected against adverse state action. It creates a perpetual threat of adverse action, yet affords regulatees no reliable assurance that the scientific evidence they possess will satisfy regulators who, themselves, must necessarily differ person to person as to the applied meaning of such a vague and subjective standard. Regulatees have no way of knowing with reasonable certainty whether the science they do possess in support of a structure/function claim will be subjectively deemed “adequate” by regulators when they second-guess the evidence under the vague “competent and reliable scientific evidence” standard. In short, our First and Fifth Amendments impose on government speech and due process standards that prohibit reliance on this vague standard for speech regulation. The standard fails to pass constitutional muster. See, e.g., Smith v. Goguen, 415 U.S. 566, 572 (1974) (The due process doctrine of vagueness demands a greater degree of specificity when a statute’s literal scope is capable of reaching expression sheltered by the First Amendment); First Nat’l Bank of Boston v. Bellotti, 435 U.S. 765, 780 (1978) (First Amendment freedoms, including freedom of speech, always have been viewed as fundamental components of the liberty safeguarded by the Due Process Clause).²

² Basic Research directs FDA to the petition for rulemaking, “In Re: Petition for a Rule Authorizing Issuance of Advisory Opinions Concerning Dietary Supplement Structure/Function Claim Advertising or,

In the Draft Guidance, FDA states without elaboration that its version of “competent and reliable scientific evidence” is not identical to the FTC’s deceptive advertising review standard. Rather, the FDA states that it “intends to apply a standard for the substantiation of dietary supplement claims that is *consistent with the FTC approach.*” *Id.* at 3 (emphasis added). FDA does not reveal to the regulated class the precise similarities and differences it perceives between its proposed substantiation standard for structure/function claims under 21 U.S.C. § 343(r)(6) and the FTC’s deceptive advertising review standard under its 2001 Guidance Document, “Dietary Supplements: An Advertising Guide for Industry.” Without that explanation, the Draft Guidance nevertheless quotes the FTC’s definition for its deceptive advertising review standard³ and then states that it will expect that a manufacturer have “competent and reliable scientific evidence” for its structure/function claim to be “substantiated” under 21 U.S.C. § 343(r)(6). FDA states: “In determining whether the substantiation standard has been met with competent and reliable scientific evidence, we recommend the firms consider the following issues in their assessment: (1) the meaning of the claim(s) being made; (2) the relationship of the evidence to the claim; (3) the quality of the evidence; and (4) the totality of the evidence.” Draft Guidance at 4. The FDA explains that it expects a manufacturer to have “substantiation” for all meanings conveyed by a structure/function claim, whether express or implied, intended or unintended. *Id.* Among

in the Alternative, Defining the Criteria FTC Uses to Evaluate Scientific Evidence Required in Support of Dietary Supplement Structure/Function Claim Advertising” filed with the Federal Trade Commission for additional explanation of the constitutional and statutory defects of the FTC’s “competent and reliable scientific evidence” standard. See <http://www.ftc.gov/os/2000/12/petform.pdf> (Docket No. P004501) (Ex. C).

³ FTC defines the standard as: “tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that has been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results.” In Re Schering Corp., 118 F.T.C. 1030, 1123 (1994); Vital Basics, Inc., C-4107 (Consent Apr. 26, 2004) (Ex. D).

the examples given by FDA of claims that are deemed inadequately substantiated (and, thus, a violation of 21 U.S.C. § 343(r)(6)(B)) are the following:

Example 3: The labeling for a dietary supplement contains a statement saying, “Recommended by Scientists,” in connection with the product’s claim. The statement gives consumers the impression that there is a body of scientists, qualified experts, who believe that the claim being made is supported by evidence. Consumers might also reasonably interpret the statement as meaning that there is general scientific agreement or consensus regarding the claim. If the manufacturer does not possess evidence to demonstrate such a consensus, the claim may not be substantiated. The opinion of a single scientist or small group of scientists is probably not adequate substantiation for such a claim.

* * * *

Example 5: To illustrate this issue, assume that a firm has high quality studies that are also consistent with the totality of the scientific evidence. The firm would like to use these studies to substantiate a claim that its dietary supplement has a particular effect on the human body, but the studies involved the impact of a specific ingredient in foods on the human body, and did not involve the dietary supplement product itself. In this instance, although the studies might be of high quality, it is not clear whether the results are applicable to the specific dietary supplement product.

* * * *

Example 13: A dietary supplement claim states, “Data suggest that including Substance X in the diet may promote brain neuron health in healthy individuals.” The firm cites a study in which rats were fed diets containing Substance X and the brains of all rats were examined for ischemia-induced brain damage. The study does not provide a basis that Substance X would have the same effect on brain health in otherwise healthy humans. This study alone likely would not provide adequate substantiation of the claim being made because it relies solely on animal data.

Example 14: A dietary supplement claim states, “Grain Y has been used effectively for centuries to promote gastrointestinal health.” The firm has no clinical studies in humans, but has an industry monograph that relies only on historical descriptions of grain Y use by pre-modern civilizations. Although the monograph may be an accurate review of the historical use of grain Y, it would likely not constitute competent and reliable evidence to support the claim because it is not based on objective scientific evidence. Rather, it is largely anecdotal evidence that cannot be objectively evaluated to determine if it applies to the consumers who would use the product.

As explained in greater detail below, to avoid constitutional and statutory violations that arise from the proposed standard, the FDA should withdraw the Draft Guidance in its entirety.

C. COMMENT

1. The Draft Guidance Violates the First Amendment

a. The Proposed Standard Restricts Constitutionally-Protected Speech

The Draft Guidance violates the First Amendment. (1) It would restrict the use of speech *not based on FDA's proof that the statements in question are inherently misleading* but instead *based on FDA's view that evidence held by the manufacturer in support of the statements is inadequate* proof of the statement's scientific validity. (2) It impermissibly shifts the burden of proof from the FDA to the regulated class when, under the First Amendment, Government must prove inherent misleadingness to justify speech suppression; government has no power under the First Amendment to require regulatees in advance of speech to prove that their structure/function claims are backed by "competent and reliable scientific evidence." (3) It impermissibly requires compliance with a *de facto*, albeit exceedingly ambiguous, scientific proof standard before speech may be uttered without fear of prosecution, thereby threatening the regulated class with adverse government action if the regulated class errs in its estimation of the extent to which a structure/function claim is backed by "competent and reliable scientific evidence."

Few principles arise with greater clarity from our First Amendment precedent than these: (1) Government is to favor disclosure of information over its suppression (see,

e.g., Thompson v. Western States Medical Center, 535 U.S. 357, 371 (2002); Ibanez v. Fla. Dep't of Bus. & Prof'l Reg., 512 U.S. 136, 144-46 (1994); Peel v. Attorney Registration and Disciplinary Comm'n, 496 U.S. 91, 99-111 (1990)); (2) Government has the burden of proof to justify any act of speech restriction (see, e.g., Edenfield v. Fane, 507 U.S. 761, 770 (1993) (citing Bolger v. Youngs Drug Prods. Corp., 463 U.S. 60, 71, n. 20, (1983)); In re R.M.J., 455 U.S. 191, 203-04 (1982)); (3) Government may not suppress commercial speech unless it has proof that the speech is inherently misleading (see, e.g., Ibanez, 512 U.S. at 145 (citing Peel, 496 U.S. at 111); Wash. Legal Found. v. Henney, 56 F. Supp. 2d 81, 85 (D.D.C. 1999)); and (4) commercial speech that has a potential to mislead may not be suppressed if the provision of more information can suffice to eliminate misleadingness (see, e.g., Peel, 496 U.S. at 111 (citing In re R.M.J., 455 U.S. at 203)). Unfortunately, the Draft Guidance, flouts each of these principles.

The Draft Guidance threatens imposition of an unconstitutional condition on use of structure/function claims. At present, the statutory requirement that structure/function claims not be false or misleading, 21 U.S.C. § 343(r)(6)(B), dovetails the First Amendment requirement applicable to commercial speech (namely, that communications are not protected if they are inherently misleading). See Central Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n, 447 U.S. 557, 563 (1980). Under the First Amendment, the government, not the regulatee, bears the burden of proof whenever government elects to suppress commercial speech. See Edenfield, 507 U.S. at 770 (“It is well established that ‘the party seeking to uphold a restriction on commercial speech carries the burden of justifying it’”) (citing Bolger v. Youngs Drug Prods. Corp., 463 U.S. 60, 71, n. 20 (1983)); Greater New Orleans Broad. Ass'n., Inc. v. United States, 527 U.S. 173, 183

(1999) (“The Government bears the burden of identifying a substantial interest and justifying the challenged restriction”); Bd. of Trs. v. Fox, 492 U.S. 469, 480 (1989) (“The State bears the burden of justifying its restrictions . . .”).

The First Amendment starts with a presumption in favor of the truthfulness of the speech; the government can only rebut that presumption upon presentation of proof. See Pearson v. Shalala, 164 F.3d 650 (D.C. Cir. 1999), reh’g denied, 172 F.3d 72 (D.C. Cir. 1999) (hereinafter “Pearson I”); Whitaker v. Thompson, 248 F. Supp. 2d 1, 22, 36 (D.D.C. 2002). Thus, while under 21 U.S.C. § 343(r)(6)(B), the manufacturer of a dietary supplement is to have “substantiation that such statement is truthful and not misleading,” the FDA may not act against a manufacturer that lacks substantiation until FDA has satisfied its First Amendment burden of proving the statement made inherently misleading. Without an adduction of proof by FDA that a structure/function claim is false and misleading and cannot be cured through use of a disclaimer, the agency has no constitutional power to suppress the speech. See Peel, 496 U.S. at 111 (citing In re R.M.J., 455 U.S. at 203) (“[States] may not, however, ban potentially misleading commercial speech if narrower limitations could be crafted to ensure that the information is presented in a nonmisleading manner.”); Pearson I, 164 F.3d at 657 (“[T]he [Supreme] Court has . . . repeatedly point[ed] to disclaimers as constitutionally preferable to outright suppression.”); Whitaker v. Thompson, 248 F. Supp. 2d 1, 14 (D.D.C. 2002) (“Disclaimers are constitutionally preferable to outright suppression of commercial speech. In other words, more disclosure rather than less is the preferred approach, so long as commercial speech is not inherently misleading.”).

In other words, it is not enough that FDA prove a technical violation of 21 U.S.C. § 343(r)(6)(B) (*i.e.*, that a manufacturer lacks substantiation in support of a structure/function claim). To avoid a First Amendment violation, FDA must do more. It must carry its burden by adducing proof that the statement in question is inherently misleading and incapable of being rendered nonmisleading through the less restrictive means of a mandatory disclaimer. That requirement arose in First Amendment commercial speech precedent⁴, has been applied to the FDA in the health claim context⁵, and has equal force and validity when applied to any FDA restriction or suppression of commercial speech (including threats, express or implied, of adverse FDA action against structure/function claims).

If a dietary supplement company fails to have substantiation for a statement, FDA cannot proceed to suppress it without taking the additional step of proving the statement in context false and incapable of being rendered truthful through disclaimer. If the statement can be rendered nonmisleading through disclaimer, then FDA's only constitutional resort is to compel the party in question to use a disclaimer, not to punish the speaker or suppress the claim outright. In short, under the First Amendment, the absence of proof does not equal the presence of proof that a statement is false and misleading⁶, and only the presence of proof of inherent misleadingness can justify speech suppression. See Ibanez, 512 U.S. at 145 ("State may not . . . completely ban statements

⁴ See Central Hudson, 447 U.S. at 563-64; 44 Liquormart v. Rhode Island, 507 U.S. 484, 509 (1996); In re R.M.J., 455 U.S. at 203; Ibanez, 512 U.S. at 144; Peel, 496 U.S. at 111.

⁵ See Pearson I, 164 F.3d 650; Pearson v. Shalala, 130 F. Supp. 2d 105 (D.D.C. 2001) (hereinafter "Pearson II"); Pearson v. Thompson, 141 F. Supp. 2d 105 (D.D.C. 2001) (hereinafter "Pearson III"); Western States, 535 U.S. 357.

⁶ See Pearson III, 141 F. Supp. 2d at 110, n9; Ibanez, 512 U.S. at 143 (citing Edenfield, 507 U.S. at 770, 771) ("Mere speculation or conjecture" will not suffice; rather the State "must demonstrate that the harms it recites are real . . .").

that are not actually or inherently misleading”) (citing Peel, 496 U.S. at 111); Wash. Legal Found., 56 F. Supp. 2d at 85 (“[P]otentially misleading’ speech is not proscribable under the First Amendment”).

The Draft Guidance exceeds the limits of the First Amendment by holding unsubstantiated any claim that is not backed by scientific evidence this agency deems “competent and reliable.” If, in any instance, that standard of proof exceeds the level required to avoid falsity and misleadingness, it will violate the First Amendment. See Western States, 535 U.S. at 371, 373; see also Peel, 496 U.S. 91. If, in any instance, that elevated standard shifts the burden of proof from the FDA to a manufacturer of a dietary supplement, it will violate the First Amendment. If at any point the FDA suppresses a truthful and nonmisleading statement for want of scientific evidence deemed “competent and reliable,” then a First Amendment violation will occur. That is because, as this agency has been told many times, FDA has no constitutional power to suppress any statement that is truthful and nonmisleading or even one that is potentially misleading if the suppression is based on the agency’s conception of a lack of requisite scientific proof⁷. See Pearson I, 164 F.3d 650; Pearson II, 141 F. Supp. 2d 105; Pearson III, 141 F. Supp. 2d at 110, n9.

Moreover, FDA has no constitutional power to declare a structure/function claim unsubstantiated and false and misleading if in one of its potential interpretations the claim is believed to convey a misleading connotation. Commercial speech that has a potential

⁷ The articulation of First Amendment principles in the health claim cases is apposite to FDA’s proposed standard because those general principles apply whenever government restricts or suppresses commercial speech, as is apparent from the unbroken chain of Supreme Court decisions from the 1970s to the present cited in Pearson I, 164 F. 3d 650. See generally Central Hudson, 447 U.S. 557; In re R.M.J., 455 U.S. 191; Bolger, 463 U.S. 60; Shapero v. Kentucky Bar Ass’n, 486 U.S. 466 (1988); Peel, 496 U.S. 91; Edenfield, 507 U.S. 761; Ibanez, 512 U.S. 136; Rubin v. Coors Brewing Co., 514 U.S. 476 (1995); 44 Liquormart, 517 U.S. 484; see also Zauderer, 471 U.S. 626; Western States, 535 U.S. 357.

to mislead is still protected under the First Amendment. See In re R.M.J., 455 U.S. at 203 (1982); Ibanez, 512 U.S. at 144 (1994); Peel, 496 U.S. at 99-111; see also Wash. Legal Found., 56 F. Supp. 2d at 85 (“Speech that is merely ‘potentially misleading’ does not render it able to be proscribed under the commercial speech test without further analysis”); Pearson I, 164 F.3d at 655; Central Hudson, 447 U.S. at 562 (“Even when advertising only an incomplete version of the relevant facts, the First Amendment presumes that some accurate information is better than no information at all”). The proper constitutional resort for this agency when such a potential is found is not to suppress the speech but to require use of a reasonable disclaimer to avoid misleadingness. See Peel, 496 U.S. at 111 (citing In re R.M.J., 455 U.S. at 203); Pearson I, 164 F.3d at 657; Whitaker v. Thompson, 248 F. Supp. 2d at 14.

b. The Proposed Standard Impermissibly Shifts the First Amendment Burden of Proof

Under 21 U.S.C. § 343(r)(6)(B), manufacturers are required to have substantiation that their structure/function claims are “truthful and not misleading.” The First Amendment does not protect commercial speech that is inherently misleading (indeed, inherently misleading commercial speech may be suppressed outright). See Western States, 535 U.S. at 367. Read to be consonant with the First Amendment, section 343(r)(6)(B) may not impose a burden on the regulated class to prove speech not inherently misleading as a condition precedent to its lawful utterance. No, our First Amendment presumes speech protected and places upon the Government an incontrovertible burden of proof that Government must meet before it may restrict or suppress commercial speech. E.g., Edenfield, 507 U.S. at 770 (citing Bolger v. Youngs

Drug Prods. Corp., 463 U.S. 60, 71, n. 20, (1983)); In re R.M.J., 455 U.S. at 203-04.

Government may not threaten adverse action (as it does in the Draft Guidance) unless it possesses specific proof that the speech in question is inherently misleading. See Ibanez, 512 U.S. at 145 (citing Peel, 496 U.S. at 111).

It is axiomatic that a speaker may communicate a truthful or, at worst, only a potentially misleading structure/function claim and yet personally lack documentary evidence of the validity of that communication. Under the First Amendment, FDA has no constitutional power to require possession of the documentary evidence as a condition precedent to speech, and FDA has no constitutional power to threaten, or to take, adverse action against that speaker, regardless of the documentation it keeps unless FDA has first adduced evidence that the statement is inherently misleading. See Id.

By establishing a scientific proof substantiation requirement under threat of adverse FDA action, the Draft Guidance impermissibly shifts the First Amendment burden from the FDA to the regulated class. In so doing, FDA violates the First Amendment.

c. The Proposed Standard Impermissibly Chills Protected Speech

The Draft Guidance violates the First Amendment by requiring compliance with a *de facto*, albeit exceedingly ambiguous, scientific proof test before speech may be uttered without fear of prosecution. It thereby threatens the regulated class with adverse action if that class errs in its estimation of what truthful speech or, at worst, what potentially misleading speech FDA deems backed by “competent and reliable scientific evidence.”

Investing in speech police virtually unbridled discretion to define what is and is not a permissible utterance is the bane of the First Amendment. See, e.g., Lakewood v. Plain Dealer Pub. Co., 486 U.S. 750 (1988); FW/PBS, Inc. v. City of Dallas, 493 U.S. 215, 224-25 (1990) (the First Amendment abhors placement of “unbridled discretion in the hands of a government official or agency”) (citations omitted). By failing to make clear to the regulated class precisely what level, degree, quality, and quantity of scientific evidence FDA expects to be possessed as a condition precedent to lawful utterance of a structure/function claim, FDA necessarily grants to itself a breadth of censorship capable of enveloping all speech subjectively deemed “inadequately substantiated,” whether protected by the First Amendment or not⁸.

The threat of prosecution inherent in the Draft Guidance combined with its exceedingly ambiguous and subjective speech “standard” will cause the regulated class to refrain from communicating truthful structure/function claims for fear of agency second-guessing.⁹ See Reno v. ACLU, 521 U.S. 844, 872 (1997) (“The vagueness of such a

⁸ The problem is incapable of being rectified. FDA cannot predict every statement and every context. Its insistence on compliance with an ambiguous standard is just a transparent cover for the exercise of unbridled discretion by its speech police. The First Amendment requirement for exacting standards in government review of speech combined with the APA prohibition on arbitrary and capricious agency action make the Draft Guidance unlawful and warrant its withdrawal by the agency.

⁹ Of course, the chilling effect occurs in instances where parties are predisposed to be law-abiding. In other words, the perverse and ironic effect of the proposed standard (due to its vagueness) is that those who seek to follow the law will avoid the risk of transgressing a vague speech standard by engaging in self-censorship. By contrast, the chilling effect will not occur in instances where parties are predisposed to violate the law. Those parties—precisely the ones whose communication we should fear most for its fraud potential—will continue to transgress the law and flout the standard. The result will be an environment harmful to the law-abiding regulatee (by dint of the ultimate distrust engendered by others’ acts of fraud) and to the consumer (by leaving the market barren of much truthful information yet continuing to witness fraud from those predisposed to violate the law). Our First Amendment starts from the premise that a free and open exchange of information and ideas in the market offers the best hope for ferreting out falsehood; that suppression of truth ordinarily redounds to the detriment of consumers who cannot discern falsity but by exposure to truth. See, e.g., Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc., 425 U.S. 748, 772 (1976) (holding that a state may not completely suppress the dissemination of truthful information about entirely lawful activity because of concern over the effect that the speech will have upon its disseminators and its recipients); Wash. Legal Found. v. Friedman, 13 F. Supp. 2d at 58 (“To endeavor to support a restriction upon speech by alleging that the recipient needs to be shielded from that speech for

regulation raises special First Amendment concerns because of its obvious chilling effect on free speech”); Nike, Inc. v. Kasky, 539 U.S. 654, 668, 683 (2003) (citing N.Y. Times v. Sullivan, 376 U.S. 254, 278 (1964)). That chilling effect is evidence of inadequate tailoring of the regulatory means. Reno, 521 U.S. at 848 (“The CDA’s vagueness undermines the likelihood that it has been carefully tailored”). FDA may not constitutionally adopt such a vague standard and invest its speech police with virtually unbridled speech review discretion.

d. The Draft Guidance Examples Fail to Reveal First Amendment Limits to the Exercise of FDA Power and, Thus, Mislead

Precisely what the agency will deem “competent and reliable” is left largely undefined and, thus, to the relative whim of its speech regulators. The examples given by the agency of speech lacking adequate substantiation do not come with any analysis of the First Amendment implications. The agency does not plainly state that it lacks a constitutional power to act against any statements unless it has adduced proof that they are false and misleading and incurable by disclaimer. The agency does not plainly state that it has no lawful power to act against a manufacturer (has no met its First Amendment burden) solely because of a lack of substantiation in the hands of that manufacturer. The guidance thus misleads the regulated class into believing FDA has legal authority to act against any structure/function claim it deems not backed by “competent and reliable scientific evidence.” That FDA does not have, because it may only act adversely in

his or her own protection, which is the gravamen of FDA’s claim here, is practically an engraved invitation to have the restriction struck”); 44 Liquormart, 517 U.S. at 503 (“The First Amendment directs us to be especially skeptical of regulations that seek to keep people in the dark for what the government perceives to be their own good”).

compliance with the First Amendment when it possesses proof that a structure/function claim is inherently misleading and incapable of being rendered nonmisleading through disclaimer. The Draft Guidance also misleads the regulated class into believing that it cannot lawfully utter a structure/function claim for which it lacks substantiation even if the statement is true. The power to prohibit the utterance of truth neither this Government nor FDA possess under our First Amendment, *regardless of whether the particular party who speaks the truth possesses documentary proof.*

Example 3 reveals that the claim, “Recommended by Scientists,” would not be “competent and reliable” in the absence of proof that “there is general scientific agreement or consensus regarding the claim.” Thus, under the Draft Guidance, the statement would be presumptively false and misleading. However, the claim could be quite literally true (*e.g.*, if a group of scientists recommend the product) and, provided that sufficient information were revealed, could avoid a potential to mislead (*i.e.*, could avoid the view that a consensus of scientists recommend the product). For example, if the claim were accompanied by an asterisk and by the true qualification, “8 Ph.D.s in biochemistry have signed statements recommending this product,” then it would appear not to mislead. Nevertheless, it would not be backed by “competent and reliable scientific evidence” confirming the existence of a general scientific agreement or consensus. The absence of competent and reliable scientific evidence is, however, insufficient to justify any action by FDA to disallow use of the claim. The use of a disclaimer in this circumstance is sufficient to avoid misleadingness and defines the extent of constitutional action this agency may take in this instance.

Example 5 suggests that a claim based on high quality studies of a dietary ingredient in foods might not apply to the ingredient when sold in isolation in a dietary supplement (indicating that studies must be performed on the dietary ingredient itself). This example suffers from a false dichotomy. Because humans cannot survive without ingestion of a wide variety of dietary ingredients, consumption of a dietary ingredient in a food would ordinarily be presumed to have the same or a substantially similar effect when consumed in a dietary supplement. The contrary proposition is highly speculative absent proof that the ingredient requires the presence of others (as found in the particular food) to yield the physiological result. Again, the burden of proof is on the government to prove the ingredient in the supplement ineffectual, not on the regulatee to prove the ingredient effectual. If the study has identified the ingredient in the food as the active constituent, the evidence is at least credible that this ingredient is the responsible agent whether in the food or in a supplement unless and until sound evidence to the contrary appears. The FDA could only move to suppress such a structure/function claim if it possessed proof that the ingredient *did not have the claimed effect when consumed in a dietary supplement* as opposed to when consumed in a particular food. Once again, a lack of evidence is not the same as proof of falsity and misleadingness. Consequently, under the First Amendment, FDA lacks a constitutional power to prohibit the speech in question. Depending on the context, FDA may require use of a disclaimer to avoid a misleading connotation.

Example 13 is defined as possibly not providing adequate substantiation for a claim because it is an animal study, not a human trial. FDA would exceed its constitutional limits if it were to proscribe the claim based on a potential to mislead. If,

indeed, the animal study is accurately represented in the claim, the speech would be truthful. The obvious implication is that the effects in the animal will be replicated in the human, a circumstance that may or may not in fact be true. Thus, the claim has a potential to mislead. It is true to the extent that it accurately describes the animal study, but it harbors a potential to lead purchasers to believe that the animal study results will necessarily occur in human users. The claim is one, however, that may be rendered nonmisleading through the addition of a reasonable disclaimer, e.g.: “Human trials have not been conducted and the results in rats may not occur in humans.” The proper constitutional resort for the agency is to rely on a disclaimer as a less speech restrictive alternative to outright suppression.

Assuming that the monograph described in Exhibit 14 does in fact include an accurate review of the historical use of grain Y (*i.e.*, that it has been used for centuries to promote gastrointestinal health), the First Amendment protects the speech. Once again, FDA may not suppress the truthful speech without adducing proof that the speech is in fact false and misleading. The absence of scientific evidence to corroborate the claim is, again, a basis for demanding a disclaimer, *e.g.*, “No scientific evidence exists to corroborate this anecdotal report.”

No health message, regardless of its content (including FDA-approved drug and health claims), is ever pristine in its substantiation. Every statement can be said to lack proof, if that proof is but the omission of information. There is a difference between falsity and inherent misleadingness, on the one hand, and potential misleadingness on the other. Our courts recognize that difference and require government agencies that would regulate speech to appreciate it and suppress only the former. See Ibanez, 512 U.S. at

144-46; Peel, 496 U.S. 91; Pearson I, 164 F.3d 650. FDA’s amorphous “competent and reliable scientific evidence” approach invites subjective weighing of the relative level of proof and, upon a CFSAN officer’s discretionary finding of an absence of “sufficient proof,” allows suppression of that speech. That exercise of largely unbridled discretion over speech is forbidden by the First Amendment. Procedural safeguards must clearly be in place to ensure that protected speech is not suppressed. See Forsyth County v. Nationalist Movement, 505 U.S. 123, 133 (1992) (“The First Amendment prohibits the vesting of such unbridled discretion in a government official”); Lakewood v. Plain Dealer Pub. Co., 486 U.S. 750, 757(1992) (invalidating regulation that “places unbridled discretion in the hands of a government official or agency”); Southeastern Promotions, Ltd. v. Conrad, 420 U.S. 546, 553 (1975) (“Invariably, the Court has felt obliged to condemn systems in which the exercise of such authority was not bounded by precise and clear standards. The reasoning has been, simply, that the danger of censorship and of abridgment of our precious First Amendment freedoms is too great where officials have unbridled discretion . . .”).

If FDA adheres to the First Amendment limits on its power, it must rely, to the maximum extent possible, on disclaimers as a less speech restrictive alternative to suppression. Only then will it permit the free information exchange that is the intended by-product of our First Amendment. See Pearson I, 164 F.3d at 657. That exchange, so long as truthful, enables consumers to make informed choices. If FDA relies on its present guidance, it will at a minimum induce the regulated class to engage in self-censorship (not only of claims akin to those listed in the above examples, which will include protected speech, but also of claims subjectively deemed not backed by

“competent and reliable scientific evidence,” based on the regulatees’ best estimate of the FDA’s view of that amorphous phrase). It may well unleash a new round of agency censorship, where FDA will second guess company determinations about the adequacy of the proof for their structure/function claims, based not on FDA’s proof that the claims in question are inherently misleading but instead based on FDA’s supposition that evidence retained by the company in support of the claims is not enough. The First Amendment forbids that arrogant assumption of power. FDA should withdraw the Draft Guidance.

2. The Draft Guidance Violates 21 U.S.C. § 343(r)(6)(B) by Changing the Compliance Standard from “Truthful and Not Misleading” to “Competent and Reliable Scientific Evidence”

As explained above, the statute’s reliance on the “truthful and not misleading” standard dovetails with the First Amendment standard, whereas the “competent and reliable scientific evidence” standard departs from, and violates, the First Amendment limit on speech restrictive action by government. Under the canons of statutory construction, FDA is obliged to interpret the statute to avoid a serious constitutional issue. See DeBartolo Corp. v. Fla. Gulf Coast Bldg. & Constr. Trades Council, 485 U.S. 568, 575 (1988) (citing NLRB v. Catholic Bishop of Chi., 440 U.S. 490, 499-501, 504 (1979)); Hooper v. California, 155 U.S. 648, 657 (1895) (“The elementary rule is that every reasonable construction must be resorted to, in order to save a statute from unconstitutionality”). The statute plainly allows FDA to interpret its language constitutionally; indeed, Congress chose to prohibit false and misleading commercial speech as misbranded under the FDCA, and our First Amendment affords no protection to inherently misleading commercial speech. E.g., Zauderer, 471 U.S. at 638.

FDA's departure from the "truthful and not misleading" standard to one demanding scientific proof is a material deviation that reduces the scope of reliably-protected speech and, thus, violates the plain meaning of the statute and the statutory misbranding scheme. We must presume that Congress meant to protect structure/function claims consistent with the limits on government power in our First Amendment. See DeBartolo Corp., 485 U.S. at 575; Hooper, 155 U.S. at 657. FDA's "competent and reliable scientific evidence" standard constricts the universe of protection provided by Congress in 21 U.S.C. § 343(r)(6)(B) and thereby violates the statute as well as the First Amendment.

3. The Proposed "Standard" Fails to Provide Meaningful Guidance to the Regulated Class

The phrase "competent and reliable scientific evidence" requires sufficient definition to enable the regulated class to know with a high degree of certainty whether speech to be uttered may be uttered with confidence that FDA will not act against it. The FDA does not provide the phrase any definition sufficient to apprise the regulated class reliably of what may be said lawfully.

At the outset, what constitutes scientific evidence that is "competent" and "reliable" is a highly subjective determination. Informed opinions may vary, often greatly. Few but the most generally accepted propositions of science are universally regarded among scientists as competent and reliable (and even then, today's scientific orthodoxy often awaits tomorrow's heterodoxy over the very same point). In short, science, like all fields of intellectual endeavor, is subject to debate, depending on varying degrees of perceived validity. The best we can hope for is an accurate reflection of the

state of the science at any single time. The most we are likely to achieve in the commercial marketplace is a reasonable approximation of the state of the science at any single time given limited space for communication, limited consumer time, and varying consumer education levels, and yet that reasonable approximation is valuable, edifying, the very thing upon which the advance of our society depends, and it is speech our First Amendment protects. See Central Hudson, 447 U.S. at 562 (“Even when advertising only an incomplete version of the relevant facts, the First Amendment presumes that some accurate information is better than no information at all”); Bates v. State Bar of Arizona, 433 U.S. 350, 374-75 (1977). The FTC’s definition, necessarily construed without the benefit of inapplicable advertising precedent,¹⁰ is largely vacuous when taken out of a specific advertising context. FDA takes it out of context but does not supply it any new meaning and, so, it remains a largely meaningless set of words strung together.

Consider the language carefully bit by bit, “tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area.” That phrase conveys the impression that an enormous range of material would suffice to prove competence and reliability. Note well that there is no reference to peer-review, and yet FDA finds peer-review an important consideration. There is also no ranking of evidence, and yet, by the remaining terms of the Draft Guidance, we are led to believe that—depending on the circumstances—FDA will find intervention studies more persuasive than observational studies and, within those categories, varying levels of ranking. No

¹⁰ Advertising cases under sections 5 and 12 of the Federal Trade Commission Act (15 U.S.C. §§ 45(a), 52) construe evidentiary requirements to protect the consumer from economic injury due to deception (Has a deceptive message motivated a consumer to make a purchase?). See, e.g., FTC v. Trudeau, Civ. No. 03-C-3904 (N.D. Ill. Jun. 10, 2003); In the Matter of Natural Organics, Inc., Docket No. 9294 (F.T.C. Aug. 16, 2000) (Ex. E). By contrast, FDA’s mandate is to protect the public health by guarding against misbranding (is the statement of a regulated product’s content or usefulness on the label or in the labeling false or misleading?) that could cause a consumer to suffer illness or physical injury.

such point is conveyed by the plain language. What objectivity or concreteness is brought to bear in assessing whether a study is “based on the expertise” of “professionals in the relevant area”? How may we tell from any given study having multiple authors whether it is truly “based” on that one or one who is likely the lead expert, and what criteria will be used to assess whether the professionals involved in the study are in “the relevant area?” And, if not in the relevant area, if the study is highly touted as valid, does it really matter if the experts who performed it had one set of scientific credentials rather than another?

There can be no question but that scientists will debate (and do debate) endlessly whether a study (indeed, every study) has been “conducted and evaluated in an objective manner.” All science is questioned to a greater or lesser degree as to its conduct, as to its method of evaluation, and as to its objectivity. Indeed, it is a commonly-accepted principle that every study will to at least some degree be the subject of bias and confounding factors which, no matter how assiduously guarded against or compensated for, will invite debate over the reliability of the study. Thus, how is a manufacturer to know whether regulators within this agency will find any study to have been conducted and evaluated in an objective manner? In the end, the assessment will likely differ from regulator to regulator (with the political leadership of the agency making the final calls).

The definition of “persons qualified to do so” is as open to varying opinion as the definition of “professionals in the relevant area.” The phrases lack requisite concreteness to be of any utility to the regulated class. Note well that the definition focuses not on results that are generally accepted by scientists, but on use of “procedures generally accepted in the profession.” It is not at all difficult to imagine that a study could be based

on procedures that few in the scientific community would question but nevertheless be regarded as of poor quality based on the analysis of the data retrieved. The definition in the end is circular, asking for tests, etc. that “yield accurate and reliable results.” In that sense “competent and reliable scientific evidence” is circularly defined as that evidence which yields “accurate and reliable results.” There is no specification of the kind, nature, quality, quantity, or degree of scientific evidence needed. Moreover, even were those specifications given, they would define a scientific standard apart from the constitutional maximum “not false and misleading.” The deviation to a higher level of proof, to the extent that it would result in suppression of truthful or, at worst, potentially misleading speech, would violate the First Amendment.

“Competent and reliable scientific evidence” is keenly in need of more particular definition (when lifted from the post-market advertising context to the structure/function claim context) because under the Draft Guidance FDA intends it to be used to guide regulatees in constraining speech before they utter it in the marketplace.¹¹ The First Amendment requires that terms used in regulation of speech be defined with particularity, so that the regulated class can discern precisely what it is the speech police prohibit and what it is they do not. See Smith v. Goguen, 415 U.S. 566, 572 (1974) (The due process doctrine of vagueness demands a greater degree of specificity when a statute’s literal scope is capable of reaching expression sheltered by the First Amendment) (citations omitted); Freedman v. Maryland, 380 U.S. 51 (1965) (lack of adequate procedural safeguards creates an unconstitutional prior restraint); Nutritional Health Alliance v.

¹¹ The posture of structure/function claims is decidedly pre-market under 21 U.S.C. § 343(r) and 21 C.F.R. § 101.93 because ascertaining what speech may be communicated lawfully under the section depends on a pre-market assessment of the speech by the manufacturer. The FDA’s substantiation standard thus works, effectively, as a prior restraint—producing a chilling effect in advance of communication in the market.

Shalala, 144 F.3d 220, 227-28 (2d Cir. 1998) (prior restraint analysis applies to commercial speech); First Nat'l Bank of Boston v. Bellotti, 435 U.S. 765, 780 (1978) (First Amendment freedoms, including freedom of speech, always have been viewed as fundamental components of the liberty safeguarded by the Due Process Clause) (citations omitted). If the regulated class must guess as to whether any particular speech will be allowed, it will more times than not result in self-censorship, a chilling effect. The First Amendment does not permit discretionary proscription of speech because the regulatee must be able to predict with high certainty what it may communicate without adverse sanction in order to enjoy the freedoms guaranteed by the amendment. E.g., Lakewood v. Plain Dealer Pub. Co., 486 U.S. 750, 757 (1988) (“The mere existence of the licensor’s unfettered discretion, coupled with the power of prior restraint, intimidates parties into censoring their own speech, even if the discretion and power are never actually abused”). There is no substitute for definite standards. Goguen, 415 U.S. at 574 (Due process requires that all “be informed as to what the State commands or forbids”) (citing Lanzetta v. New Jersey, 306 U.S. 451, 453 (1939)). Thus, it would be far worse to have a guidance to aid in the regulation of speech that is ambiguous than to have no guidance at all. Based on that, the FDA would do well to withdraw the Draft Guidance.

FDA does not state that its definition of “competent and reliable scientific evidence” is the same as the Federal Trade Commission’s. Rather, FDA says that its use of the phrase is “consistent with the FTC approach.” At a minimum, FDA must explain precisely how its use of the phrase differs from how FTC uses it. The phrase comes with

considerable precedential baggage¹²; what of that baggage does FDA accept and what does it reject? No edification or clarity is provided in the Draft Guidance. Moreover, the FDA's "competent and reliable scientific evidence" "standard" is, at root, just as ambiguous and undefined as FDA's "significant scientific agreement" "standard" that in Pearson v. Shalala our Court of Appeals struck as arbitrary and capricious. See Pearson I, 164 F. 3d 650.

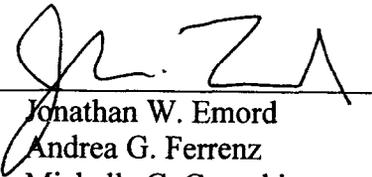
The APA is violated whenever the FDA fails to give the regulated class sufficient guidance to discern what action is lawful and what is not. See Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co., 463 U.S. 29, 43 (1983); see also Pearson I, 164 F.3d at 660-61. The Draft Guidance fails to provide adequate elucidation, yet carries with it the threat that regulators will punish regulatees who speak in ways deemed not backed by "competent and reliable scientific evidence." The regulated class does not know what is meant by the term "competent and reliable scientific evidence," and the agency never defines the terms with reasonable certitude, instead making it apparent that the terms' essential meaning will vary depending upon each context. Aside from knowing the relative ranking of scientific evidence, the regulated class cannot know whether any particular phrase, qualified or not, will be deemed by an FDA reviewer as lacking in some particular such that the structure/function claim is deemed not "adequately substantiated." The APA requires greater clarity. The First Amendment requires procedural safeguards to ensure that protected speech is not suppressed. See Pearson I, 164 F.3d at 661 ("[I]t must be possible for the regulated class to perceive the principles which are guiding agency action").

¹² See e.g., In Re Schering Corp., 118 F.T.C. 1030, 1123 (1994); In the Matter of KFC Corp., 2004 FTC LEXIS 90, *16; In the Matter of Telebrands Corp., 2003 FTC LEXIS 147, *23; Vital Basics, Inc., C-4107 (Consent Apr. 26, 2004) (Ex. F).

D. CONCLUSION

For the foregoing reasons, Basic Research respectfully requests that FDA withdraw the Draft Guidance in its entirety.

Respectfully submitted,
BASIC RESEARCH, LLC

By: 
Jonathan W. Emord
Andrea G. Ferrenz
Michelle C. Gayeski
Its Counsel

Emord & Associates, P.C.
1800 Alexander Bell Dr.
Suite 200
Reston, VA 20191
Tel: (202) 466-6937
Fax: (202) 466-6938
jemord@emord.com

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