No. 17-13376-K

IN THE UNITED STATES COURT OF APPEALS
FOR THE ELEVENTH CIRCUIT

HI-TECH PHARMACEUTICALS, INC., *ET AL.*,
***Appellants*,**
v.
UNITED STATES OF AMERICA,
***Appellee*.**

On appeal from the United States District Court for the Northern District of Georgia, No. 1:13-cv-03675-WBH

BRIEF FOR APPELLANTS HI-TECH PHARMACEUTICALS, INC. & JARED WHEAT

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CERTIFICATE OF INTERESTED PERSONS

The following is a list of all known judges, attorneys, persons, associations of persons, firms, partnerships, corporations, and other legal entities that have an interest in the outcome of this case, including subsidiaries, conglomerates, affiliates and parent corporations, any publicly held company that owns 10 percent or more of a party's stock, and other identifiable legal entities related to a party:

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41. Wheat, Jared (Appellant)

STATEMENT REGARDING ORAL ARGUMENT

This case arises from an extreme act of overreach by the Food and Drug Administration. In the Dietary Supplement Health and Education Act of 1994, known as DSHEA, Congress rolled back what had been the FDA's practice of removing safe and natural dietary supplements from the marketplace. Among other things, Congress instructed the FDA that as a general matter, if it wished to stop a business from marketing a dietary ingredient that is part of a plant—or, to use DSHEA's terms, a "constituent" of a "botanical"—the agency first must establish that the ingredient is unsafe.

In this case, the FDA tried to circumvent DSHEA by seizing dietary supplements containing an ingredient, known as DMAA, that is safe and, as numerous studies have shown, present in geranium plants. Yet DMAA came under attack in an ill-founded and even fraudulent public-relations campaign, and the FDA sought an end-run around DSHEA. After seizing millions of dollars' worth of DMAA-containing supplements from Hi-Tech, the FDA sought the supplements' forfeiture—not on the theory that DMAA is unsafe, but on the theory that it

is not present in geraniums. After considering the evidence, the District Court found that the FDA was wrong. Yet the Court upheld the seizure on a theory the Government never advanced, reasoning that DMAA is not a "constituent" of a "botanical" because historically, instead of extracting the DMAA from geraniums in usable amounts, businesses have used chemical processes to synthesize it.

That ruling was erroneous on a number of fronts. The Court misread DSHEA, which makes "constituent[s]" of "botanical[s]" presumptively marketable regardless of whether businesses historically have extracted them directly from plants. To make matters worse, the Court applied its newly minted interpretation in a way that was fundamentally unfair to Hi-Tech, refusing to give it an opportunity to show that businesses *can* extract usable quantities of DMAA from geraniums. Just as critically, the Court let stand the FDA's abuse of the civil-forfeiture process, which allowed it to take a dietary supplement off the market that it could not show to be unsafe. Oral argument will help show why these concerns should lead this Court to reverse.

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STATEMENT OF JURISDICTION

The District Court had subject-matter jurisdiction over the two consolidated cases from which this appeal arises. The first of these cases was an action Hi-Tech Pharmaceuticals, Inc., filed against the FDA and various federal officials under the Administrative Procedure Act and 42 U.S.C. § 1983. The District Court had federal-question jurisdiction over that case under 28 U.S.C. § 1331. The second case was an *in rem* forfeiture action the United States filed against the DMAA-containing products themselves, where Hi-Tech and its CEO, Jared Wheat, intervened as claimants. The District Court had jurisdiction under 28 U.S.C. § 1345, which gives "the district courts . . . original jurisdiction of all civil actions, suits or proceedings commenced by the United States," and 21 U.S.C. § 334(a)(1), which provides that the Government may proceed with Food, Drug, and Cosmetic Act condemnation actions "in any district court of the United States or United States court of a Territory within the jurisdiction of which the article is found."

This Court has jurisdiction over Hi-Tech and Wheat's appeal. The District Court entered a summary-judgment order finding the DMAA subject to forfeiture and rejecting Hi-Tech's APA and § 1983 claims. *See*

Docs. 140 & 141. The resulting judgment disposed of all claims and therefore was appealable under 28 U.S.C. § 1291.

Hi-Tech and Wheat's appeal was timely. The District Court issued its final judgment on April 3, 2017. *See* Doc. 141. On April 17, within the 28-day period allowed by the rules, Hi-Tech and Wheat filed a motion to reconsider and vacate the judgment under Rule 59(e) of the Rules of Civil Procedure. *See* Doc. 142. Rule 4 of the Rules of Appellate Procedure tolled the period for Hi-Tech and Wheat to file any appeal of the District Court's judgment until "the entry of the order disposing of [that] motion," FED. R. APP. P. 4(a)(4), which the District Court denied on June 2, 2017, *see* Doc. 148. Because the parties include the "United States," one of its "agenc[ies]," and several of its "officer[s] . . . sued in an official capacity," Hi-Tech and Wheat had "60 days" to appeal. FED. R. APP. P. 4(a)(1)(B)(i)-(iii). Hi-Tech and Wheat satisfied that deadline by filing a notice of appeal 54 days later, on July 26, 2017. *See* Doc. 149.

STATEMENT OF THE ISSUES

I. DMAA as a "constituent" of a "botanical." DSHEA provides that the FDA generally cannot ban a substance added to food if it is a "constituent" of a "botanical" unless the FDA can prove that it is unsafe. 21 U.S.C. § 321(ff)(1)(C) & (F). In the forfeiture proceeding below, the Government did not purport to prove that DMAA is unsafe, and the District Court found that the Government had not met its "burden of establishing that DMAA has not been found in geraniums." Did the District Court err in nonetheless adopting a reading of DSHEA the Government had not advanced and holding, on summary judgment, that DMAA is not a "constituent" of a "botanical" because there is no "history of [it] having been extracted" from geraniums in "usable quantities"?

II. DMAA as Generally Recognized as Safe. Even if DMAA were not a "constituent" of a "botanical," DSHEA would allow manufacturers to market it if it is "generally recognized" as safe. In the proceedings below, Hi-Tech and Wheat offered, among other things, testimony from two physicians who concluded that DMAA is generally recognized as safe. Did the District Court err in nonetheless finding, as a matter of law, that DMAA is not generally recognized as safe?

STATEMENT OF THE CASE

I. Nature of the case

These cases arose when the FDA detained, and ultimately seized, Hi-Tech's dietary supplements containing an ingredient called DMAA. This ingredient has an energy-boosting effect akin to caffeine's. Hi-Tech challenged the seizure under the APA and § 1983, and the Government filed its own action seeking forfeiture of the supplements under the Federal Food, Drug, and Cosmetic Act, which is known as the FDCA, as amended by DSHEA. After the District Court consolidated the cases and the parties conducted discovery, the District Court entered summary judgment for the Government. In so doing, the District Court rejected the Government's theory of why DMAA violated the law but nonetheless found that the DMAA was subject to forfeiture under an interpretation of DSHEA no party had advanced or contemplated. The Court held that its ruling precluded Hi-Tech's claims under the APA and § 1983, and rejected Hi-Tech and Wheat's request that they be afforded an opportunity to develop the record and show that they could satisfy the new standard the District Court had announced.

II. Statement of the facts

Three considerations supply the crucial context here. The first is the legal and regulatory backdrop against which dietary-supplement manufacturers market their products. The second is the relationship between geranium plants and DMAA. The third is the sequence of events that led the FDA to make efforts to take DMAA-containing products off the market.

A. The statutory and regulatory backdrop

The FDA is responsible for monitoring the quality and safety of food and drugs in the United States. The FDA's authority stems from the FDCA, which Congress passed in 1938. *See* 21 U.S.C. § 301 *et seq*. Half a century later, Congress amended the FDCA through DSHEA, an acronym many FDA practitioners pronounce "Duh-SHAY-uh." The amendments substantially deregulated the companies that make and sell products commonly known as dietary supplements, which enhance the nutritional value of food.

One of DSHEA's most critical innovations was to classify dietary supplements as food. *See* 21 U.S.C. § 321(ff). Congress needed to take this step because the FDA had been treating dietary supplements as if

they were drugs, to the detriment of manufacturers and consumers alike. Pre-DSHEA regulations required manufacturers, before selling any dietary supplements, to obtain the agency's approval and to persuade it that they were safe and effective. *See* 21 U.S.C. § 355 (premarket approval process for drugs); 21 C.F.R. §§ 101.13-14; 101.70. Getting approval often proved difficult and costly, so the FDA's approach shut many popular dietary supplements out of the market.

Congress responded with DSHEA. In reclassifying dietary supplements as a type of food, DSHEA flipped the relevant presumptions. Congress found that "although the Federal Government should take swift action against products that are unsafe or adulterated, the Federal Government should not take any actions to impose unreasonable regulatory barriers limiting or slowing the flow of safe products." Dietary Supplement Health and Education Act of 1994, Pub. L. No. 103-417, § 2(13), 108 Stat. 4325 (1994); *codified at* 21 U.S.C.A. § 321 note. The Senate Committee Report explained that the amendments thus reversed the agency's practice of requiring federal preclearance before manufacturers and producers could sell their dietary supplements. Instead, DSHEA shifted the "burden of proof" to "the [FDA] to prove that

a product is unsafe before it can be removed from the marketplace." S. Comm. on Labor and Human Res., Dietary Supplement Health and Education Act of 1994, S. Rep. 103-410, at 2 (1994).

In accordance with this framework, DSHEA puts dietary-supplement ingredients into three categories that determine whether a manufacturer may produce and distribute them:

(1) "dietary ingredients";
(2) substances that, while not "dietary ingredients," are "generally recognized as safe" (or "GRAS" for short); and
(3) "food additives."

The full text of the provisions establishing this framework appears in the statutory addendum to this brief. The question in this case concerns which of these three boxes is the right fit for DMAA.

1. Category 1: "Dietary ingredients" deemed safe and marketable

Hi-Tech contends that DMAA falls within the first of the three boxes, as a "dietary ingredient," and thus that DSHEA allows Hi-Tech to market it without FDA preapproval. This category generally encompasses naturally occurring substances used in food. The statute includes the following items within the "dietary ingredient" definition:

> (A) a vitamin;
> (B) a mineral;
> (C) an herb or *other botanical*;
> (D) an amino acid;
> (E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or
> (F) a concentrate, metabolite, *constituent*, *extract*, or combination *of any ingredient described in clause (A), (B), (C), (D), or (E)*.

21 U.S.C. § 321(ff)(1) (emphases added).

Hi-Tech claims that DMAA is a freely marketable "dietary ingredient" through the interaction of subsections (C) and (F): it is a "constituent" of a geranium plant and thus a "constituent" of a "botanical."

DMAA's status as a "dietary ingredient" is important because DSHEA presumes, as a general matter, that dietary ingredients are safe. DSHEA therefore allows manufacturers to freely market and sell dietary supplements containing those ingredients without FDA preapproval. If the FDA wants to take a dietary ingredient off the market, the agency must first establish that the dietary ingredient or supplement containing it is "adulterated." 21 U.S.C. § 342(f). To make that showing, the FDA must prove that the supplement or ingredient "presents a significant or unreasonable risk of illness or injury under condi-

tions of use recommended or suggested in labeling, or if no conditions of use are suggested or recommended in the labeling, under ordinary conditions of use." 21 U.S.C. § 342(f)(1)(A)(i)-(ii). Before taking enforcement action against a dietary supplement for being adulterated in this way, the FDA must give the affected party "appropriate notice and the opportunity to present views, orally and in writing." 21 U.S.C. § 342(f)(2). The FDA has not taken any such step against Hi-Tech, so if Hi-Tech is correct that DMAA is a dietary ingredient, the FDA had no statutory justification for seizing Hi-Tech's products under DSHEA.

2. Category 2: Non-dietary ingredients "Generally Recognized as Safe" and thus marketable

Hi-Tech also claims, in the alternative, that even if DMAA is not a "constituent" of a "botanical" and thus not a "dietary ingredient" under DSHEA, it still is marketable because at the very least it falls within the FDCA's provisions granting safe harbor to substances considered not to be dangerous. The FDCA defines the products that generally are subject to preapproval in a manner that excludes substances "*generally recognized*, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown . . . *to be*

safe under the conditions of its intended use." 21 U.S.C. § 321(s) (emphasis added). This clause, which FDCA practitioners sometimes refer to as the "GRAS" provision, allows manufacturers to market substances that do not qualify as "dietary ingredients." But unlike "dietary ingredients"—for which, as noted above, the Government has the burden of showing that the product is *un*safe, *see supra* at pp. 7-9—the GRAS provision places the burden on manufacturers to show that the opposite is true of non-dietary ingredients.

FDA regulations specify that manufacturers satisfy this burden when they point to "common knowledge throughout the scientific community knowledgeable about the safety of substances directly or indirectly added to food." 21 C.F.R. § 170.30(a). Manufacturers who want to market products under the GRAS standard thus endeavor to show that in light of the scientific community's common knowledge, "there is reasonable certainty that the substance is not harmful under the conditions of its intended use." *Id.* Relevant considerations include how much of the substance is expected to be consumed and the warnings manufacturers provide on their product labels. *See infra* at pp. 58-60.

When manufacturers show that a non-dietary ingredient is generally recognized as safe, then they can market supplements containing it in the same way they might sell supplements containing dietary ingredients. As explained in more detail below, in addition to providing evidence that DMAA is a "constituent" of a "botanical" and therefore a "dietary ingredient," Hi-Tech and Wheat supported their claims to the DMAA-containing products in the District Court with testimony from various witnesses showing that the DMAA Hi-Tech includes in its products is generally recognized as safe when used for its intended purposes. *See infra* at pp. 16, 30-31.

3. Category 3: "Food additives" that are presumptively not marketable

The third relevant category for present purposes consists of "food additives": items used for food that are neither "dietary ingredients" nor "generally recognized as safe." *See* 21 U.S.C. § 321(s). If a dietary supplement contains an unsafe "food additive," the FDCA deems it "adulterated." *See* 21 U.S.C. § 342(a)(2)(C)(i); 21 U.S.C. § 348(a). Adulterated dietary supplements containing "food additives" are subject to seizure, condemnation, and forfeiture. *See* 21 U.S.C. § 334. The District Court

below held that Hi-Tech's DMAA-containing products fall within this category.

B. DMAA's presence in geranium plants

Hi-Tech's argument that DMAA is a "constituent" of a "botanical" and thus a freely marketable "dietary ingredient" stems from studies showing that DMAA naturally occurs in certain kinds of geranium plants. Geraniums are known as a staple of flower beds, but the word "geranium" is used, confusingly enough, to refer both to flowers of the geranium and the pelargonium genus:

The pertinent "geraniums" for present purposes are those within the pelargonium genus. In addition to beautifying landscapes, they

have been "routinely consumed," in various forms, "for over 100 years." Doc. 108-6 at p. 352, ¶53. People grow *pelargonium graveolens* for these purposes in various locations throughout the world. *See* Doc. 108-7 at p. 407 (reproducing Zang Ping *et al.*, *A Study On the Chemical Constituents of Geranium Oil,* 25 J. GUIZHOU INST. TECH. 82 (1996)). Sometimes people eat the flower; other times they add the plant's oil to part of their meal, like salad or dessert. *See* Doc. 108-6 at p. 352, ¶53; Doc. 108-6 at p. 211, ¶40.

These geraniums contain hundreds of organic compounds. *See* Doc. 108-7 at p. 436, tr. 86:13-87:14; Doc. 108-4 at p. 482, tr. 74-20-75:2. Scientists have not identified all of them, but one they have found is DMAA—also known as 4-methylhexan-2-amine, 1,3-dimethylpentylamine, and methylhexaneamine. *See, e.g.*, Doc. 108-7 at pp. 274-75, ¶73; Doc. 108-6 at p. 351, ¶¶51-52. The first study detecting DMAA in geraniums, known as the Ping Study, was published by Chinese researchers in 1996. *See* Doc. 108-7 at p. 407. Two more recent studies, the Li Study and Fleming Study, reported similar results. *See* Doc. 108-5 at p. 34 (reproducing J.S. Li *et al.*, *Identification and Quantification of Dimethylamylamine in Geranium by Liquid Gas Chromatography Tandem*

Mass Spectrometry, 7 ANALYTICAL CHEMISTRY INSIGHTS 47 (2012)); Doc. 103-3 at p. 91 (reproducing HL Fleming *et al.*, *Analysis and Confirmation of 1,3-DMAA and 1,4-DMAA in Geranium Plants Using High Performance Liquid Chromatography with Tandem Mass Spectrometry at ng/g Concentrations*, 7 ANALYTICAL CHEMISTRY INSIGHTS 59 (2012)). The District Court also favorably cited a survey paper from 2013 concluding that "[o]verall" these studies "show that 1,3-DMAA is found naturally in some, but not all, geranium plants and extracted geranium oils." Doc. 140 at p. 5 (quoting Thomas D. Gauthier, *Evidence for the Presence of 1,3-Dimethylamylamine (1,3-DMAA) in Geranium Plant Materials*, 8 ANALYTICAL CHEMISTRY INSIGHTS 29-40 (2013), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3682735/).

The District Court thus found "substantial evidence" that DMAA is present in geraniums, and in so doing relied on additional evidence. Doc. 140 at p.5. For example, New Zealand's government issued a report in 2015 finding it "likely that DMAA does occur naturally in geraniums." Doc. 108-8 at p. 78. And one of the Government's experts in this case testified that he had detected DMAA in geranium samples. *See* Doc. 108-7 at p. 429, tr. 58:17-59:17.

C. DMAA's uses

American manufacturers have used DMAA in two kinds of products. For both, they have chemically synthesized the DMAA, rather than taking it directly out of the plant.

The first known DMAA synthesis occurred in the 1940s, when Eli Lilly developed and patented a version of DMAA and used it as an ingredient in a nasal decongestant. *See* Doc. 107-4 at pp. 2-5 (U.S. Patent No. 2,350,318 (issued May 30, 1944)). The company marketed and sold the decongestant until the 1980s. *See* Withdrawal of Approval of New Drug Applications, 48 FED. REG. 51,536 (1983). Those events happened before the Ping Study and thus before it became known that DMAA is in geraniums.

The more relevant use to which American manufacturers have put DMAA happened after the Ping Study. DMAA is understood to have energy-boosting qualities that help people exercise harder and thus lose weight. So in 2006, a dietary-supplement manufacturer began adding DMAA to its products. *See* Doc. 108-5 at p. 114. Other manufacturers followed suit. *See* Doc. 108-8 at pp. 331-32, tr. 42:18-43:8, 48:12-18, 49:14-19. One of those manufacturers is Hi-Tech, a Georgia company

whose products are on shelves at stores like GNC, CVS, Walgreen's, Wal-Mart, K-Mart, and Kroger. *See* Doc. 108-8 at p. 353, tr. 132:9-133:6; Doc. 41-1 at p. 4, ¶5; *see generally* https://hitechpharma.com/. Hi-Tech sold more than 3 million units of DMAA-containing supplements in the five years after it started marketing them. *See* Doc. 108-6 at p. 366, ¶75.

Various witnesses testified below that DMAA is safe when consumed as Hi-Tech's product labels instruct. Four experts all agreed that there is no evidence DMAA is unsafe when consumed at recommended doses: Marvin Heuer, a family-medical practitioner who has 30 years of consulting experience in the dietary-supplement industry; Matthew Lee, a physician, pharmacologist, and toxicologist; Mitchell Elkind, a board-certified neurologist; and Michael Lumpkin, a Ph.D. toxicologist. *See* Doc. 108-6 at p. 359, ¶63 (Heuer Decl.); Doc. 108-8 at pp. 166-67, tr. 69:14-70:17 (Lee Depo.); Doc. 108-8 at pp. 113-14 & 116, ¶¶55 & 59 (Lee Decl.); Doc. 108-6 at pp. 215-16, ¶53 (Elkind Decl.); Doc. 108-4 at pp. 66-67 & 75-76, ¶¶83 & 94.2 (Lumpkin Decl.).

D. USADA's campaign to have the FDA take DMAA off the market

The FDA did not initially take the position that DMAA was anything other than a freely marketable "constituent" of a "botanical." The enforcement action the FDA took that gave rise to this case, and its push to take DMAA off the market more generally, arose only after a non-governmental organization called the United States Anti-Doping Agency, commonly known as USADA, began efforts to persuade the FDA that DMAA is not present in geraniums. The discovery process in this case revealed that, in waging that campaign, USADA had not disclosed the results of studies showing that DMAA does, in fact, occur in these plants.

USADA's campaign against DMAA appears to have had its genesis in 2010. Around that time, the World Anti-Doping Agency, known as WADA, placed DMAA on its prohibited-substance list. *See* Doc. 108-4 at pp. 132-33, tr. 25:13-26:19 (Eichner Depo.). WADA is the international organization that decides what substances athletes can consume if they want to compete in international competitions like the Olympics; it reportedly now is considering whether to put caffeine on the prohibited-substance list. *See* Marissa Payne, *Caffeine Could be Headed to World*

Anti-Doping Agency's Prohibited Substance List, WASHINGTON POST, March 8, 2017, *available at* http://wapo.st/2mBVWce?tid=ss_mail-&utm_term=.127d5aaeca3c. In response to WADA's decision to put DMAA on that same list, USADA—the domestic analog to WADA—began communicating with officials at the FDA.

USADA's initial inquiries appeared to be innocent enough. The representative who first contacted the FDA, Amy Eichner, stated that she was looking to help American athletes avoid getting disqualified for accidentally consuming DMAA. To that end, Eichner asked how DMAA was getting into the food supply. *See* Doc. 108-4 at p. 135, tr. 36:16-37:13.

In contrast to the position the FDA eventually would take in this litigation, the agency official who responded to Eichner explained that "[DMAA] is found in the oil of many geraniums – princip[al]ly Pelargonium graveolens, the oil of which has a fairly long history of food use as an essential oil." Doc. 108-4 at p. 290. The same official advised Eichner that, as a result, DMAA "appears to be a dietary ingredient under [DSHEA] because it is a constituent of another dietary ingredient, (i.e.,

a plant)." *Id.* at p. 292. The FDA official pointed Eichner to the Ping Study. *See id* at p. 289.

Eichner was not satisfied with that response and soon began lobbying the FDA to change its views. Eichner told the FDA that the Ping Study was "obscure." Doc. 108-4 at p. 297. She disparaged its authors for working at a "third rate university in China." *Id.* And shifting from her initial approach—in which she had purported to be merely seeking the FDA's advice about how DMAA entered the food supply—she claimed that "we have reason to argue that [DMAA] in fact is NOT in geranium oil, and that [DMAA] should be regulated as a drug." *Id.*

Other events may have influenced Eichner's advocacy. Four servicemen had died after reportedly using DMAA-containing products. A study commissioned by the Department of Defense ultimately concluded that it was "unlikely that DMAA played a role in these four deaths." Doc. 108-7 at p. 28; Doc. 108-6 at pp. 234-36, ¶¶88 & 90-91; Doc. 108-4 at pp. 55-59, ¶¶57-67. But the Department of Defense eventually barred companies from selling DMAA-containing products on military bases. *See* Doc. 130 at p. 54, tr. 210:17-20; Doc. 133 at p. 36, tr. 139:22-140:13; *see also* Doc. 108-4 at p. 276 (New York Times article titled "Is the Sell-

er to Blame?"). Eichner was in touch with one of the servicemen's families. *See* Doc. 108-4 at p. 136, tr. 39:15-40:17. The family eventually filed a wrongful-death suit over the incident, but the court concluded that the evidence offered to show that DMAA caused the death was "unreliable" and excluded the expert testimony on that point. Doc. 108-6 at pp. 167-68, 179-80, 187-88 (reproducing *Sparling v. Doyle*, No. EP-13-CV-323-DCG, 2015 WL 4528759 (W.D. Tex. July 27, 2015)).

Whether Eichner was motivated by that incident or something else, USADA continued to lobby the FDA to change its position. It even went so far as to fund a study where researchers, after consultation with USADA, made misleading and incomplete representations about DMAA's presence in geraniums. USADA paid a research center at the University of Mississippi—the National Center for Natural Product Research, which receives millions in funding each year from the FDA—to conduct tests Eichner hoped would rebut the Ping Study. *See* Doc. 108-4 at p. 143, tr. 66:17-67:23; Doc. 108-4 at p. 548. Even though Eichner had virtually no training or expertise in chemistry, she helped form the study's hypothesis that DMAA could *not* be found in geraniums. *See* Doc. 108-4 at p. 129, tr. 12:6-11; *id.* at pp. 480-81, tr. 69:14-72:13. But

the initial results showed that Eichner's hypothesis was wrong: researchers informed her that they had detected DMAA in low amounts. *See id.* at pp. 559-60. One of Eichner's USADA colleagues then suggested that a "low level" should not be enough. Doc. 108-4 at p. 565. The researchers responded that if the studies showed levels of "2 – 8" parts per billion, they could report the DMAA as "absent" under a higher "detection level of 10 ppb, or something like that." *Id.*; *see also id.* at pp. 559-63, 566-70 (further email correspondence). The final published study then used that higher level and reported that "[n]one of the analyzed oils or the plant material (young and mature, fresh and dried leaves and stems) showed any detectable level of" DMAA. Doc. 108-4 at pp. 572, 585 (reproducing Mahmoud L. ElSohly *et al.*, *Pelargonium Oil and Methyl Hexaneamine (MHA): Analytical Approaches Supporting the Absence of MHA in Authenticated Pelargonium Graveolens Plant Material and Oil*, J. ANALYTICAL TOXICOLOGY 1 (2012)).

That was not the last time these researchers fudged their results. Shortly after the University of Mississippi researchers published their paper, the Li study—commissioned by a supplement manufacturer—reported findings showing "conclusively that DMAA is naturally occur-

ring in geranium plants." Doc. 108-5 at p. 43. That prompted yet another University of Mississippi study, this time employing four different research centers to run the pertinent tests. *See* Doc. 108-5 at p. 47 (filed under seal). Once again, things did not go as planned: one of the four labs detected low levels of DMAA in geraniums from China. *See* Doc. 108-5 at pp. 62-67 (email correspondence from Min Yang of the Shanghai Institute of Materia Medica). The Mississippi researchers told that lab that "if you say that we did not find anything under" the higher detection limit, "we are Ok." *Id.* at p. 62. And once again, the researchers used the higher detection level to report that they had detected no DMAA in the plants. *See* Doc. 108-5 at p. 51 (reproducing Mahmoud A. ElSohly *et al.*, *Methylhexanamine is Not Detectable in Pelargonium or Geranium Species and Their Essential Oils: A Multicentre Investigation*, DRUG TESTING & ANALYSIS (2014)).

Another DMAA study conducted during the same approximate time period at the University of Texas suffered from similar flaws. The original unpublished version of the study concluded that DMAA did naturally occur in geraniums. *See* 108-5 at pp. 2-11. But as had happened with the published versions of the studies from the University of

Mississippi, the published version of the Texas study said, without any acknowledgement of the results in the draft version, that it had not found DMAA in the geraniums "with a limit of detection of 10 parts per billion." Doc. 108-5 at p. 20 (reproducing Ying Zhang et al., *1,3 Dimethylamylamine (DMAA) in Supplements and Geranium Products: Natural or Synthetic?*, DRUG TESTING ANALYSIS (2012)).

E. The FDA's actions against DMAA

The same year the University of Mississippi researchers published their first DMAA study and the University of Texas researchers published theirs, the FDA began taking enforcement action against DMAA. The FDA sent warning letters to 11 supplement companies setting forth the agency's new view that the DMAA at issue did not qualify as a "dietary ingredient" and demanding that these companies stop distributing their DMAA-containing products. *See* Doc. 108-5 at p. 26; Doc. 108-7 at p. 112. Hi-Tech was not among those companies, and the position the FDA put forward in those letters was not the same one it eventually took in the forfeiture proceedings against Hi-Tech. Rather than asserting that DMAA does not naturally occur in geraniums, the FDA's letters to those manufacturers maintained that their DMAA could not be a "di-

etary ingredient" because they had synthesized it. *See id.* at p. 113. The letters also contended that, at the very least, the companies had failed to comply with statutory provisions requiring notice relating to "new dietary ingredients." *See id.* at p. 112 (citing 21 U.S.C. §350b(a)(2); 21 C.F.R. § 190.6). Although one of the companies forcefully objected, all 11 ultimately gave in and removed their products from the market. *See* Doc. 108-6 at p. 377; Doc. 108-5 at p. 32.

Despite not sending a warning letter to Hi-Tech, the FDA inspected Hi-Tech's facilities more than a year later, without giving Hi-Tech prior notice, and seized, via an administrative-detention order, approximately $2.2 million in DMAA-containing products and raw materials. *See* Doc. 41-7 at p. 20 (detention order); Doc. 45 at p. 11.

III. Course of proceedings below

While the Government appears committed to the result of having DMAA declared unlawful, the proceedings below reveal that it has not settled on a coherent theory as to why. The arguments the Government pursued in the District Court were different from the ones it set forth in its warning letters to the other manufacturers in 2012. Moreover,

whereas the Government initially suggested that it intended to rely on the University of Mississippi and Texas studies to establish that DMAA is not in geraniums—and identified one of the University of Mississippi researchers as an expert—it found itself not relying on those studies, or on that expert or his report, when it moved for summary judgment. And when the District Court eventually held that Hi-Tech's products were due to be forfeited, it did so based on a theory the Government never had proposed, and on which the parties had not conducted discovery.

A. The initial filings and discovery

Before the Government commenced any forfeiture proceeding relating to the seizure, Hi-Tech filed its own action against the FDA and various agency officials in the District Court for the District of Columbia, claiming that their actions in detaining Hi-Tech's products violated the APA and § 1983. *See* Doc. 41-1. Hi-Tech's complaint alleged that the FDA and its officers had acted arbitrarily and capriciously and bypassed the various procedural steps DSHEA required them to take before the agency could seize and effectively ban DMAA. *See generally id.* at pp. 8-11, ¶¶19-27.

The United States then filed the forfeiture action in the Northern District of Georgia. *See* Doc. 1. The complaint did not allege, as the FDA had claimed in the warning letters, that DMAA was a "new dietary ingredient" for which manufacturers had failed to provide proper notice. *See supra* at pp. 23-24. Instead, as pertinent here, the complaint alleged that Hi-Tech's supplements were "adulterated" on the theory that DMAA is an unsafe "food additive" under 21 U.S.C. § 348. *See* Doc. 1 at p. 3, ¶5.

After the D.C. District Court transferred Hi-Tech's APA and § 1983 action to the Northern District of Georgia, the District Court consolidated the two cases. *See* Doc. 29. Substantial discovery then ensued. It revealed the problems with the two University of Mississippi-based studies and the University of Texas-based study. *See* Doc. 108-1 at pp. 8-16 (Hi-Tech Memorandum in Support of Motion for Summary Judgment). It also revealed that the Government had abandoned its position, staked out in the warning letters, that a substance that otherwise is a "constituent" of a "botanical" will not have that status when a manufacturer synthesizes it in a lab rather than drawing it directly from a plant. *See* Doc. 108-6 at p. 85, tr. 27:4-23 (deposition of Govern-

ment expert Cara Welch). Following those developments, the parties filed cross-motions for summary judgment. *See* Docs. 107 & 108.

B. The District Court's ruling on summary judgment

On the question of DMAA's marketability under DSHEA, the parties' summary judgment submissions put two principal questions before the District Court. The first was whether the Government had established that DMAA is not a "constituent" of a "botanical" and thus not a freely marketable "dietary ingredient." *See generally supra* at pp. 7-9 (citing 21 U.S.C. § 321(ff)(1)). The second was whether, even if DMAA does not amount to a "constituent" of a "botanical," Hi-Tech had established that DMAA is generally regarded as safe. *See generally supra* at pp. 9-11 (citing 21 U.S.C. § 321(s)).

1. DMAA's status as a "dietary ingredient"

On the question whether DMAA is a "constituent" of a "botanical," the revelations about the Mississippi and Texas studies had left the Government in a precarious position. The Government previously had identified one of the University of Mississippi researchers, Ikhlas Khan, as a testifying expert and had disclosed his report. *See* Doc. 108-4 at pp.

303-04. But the brief the Government submitted in support of its motion for summary judgment excluded all mention of him or the studies with which he was associated, as well as the Texas study on which he had also relied. *See id.* at pp. 17-18, ¶34 (Khan report); Doc. 107-1 at pp. 15-22 (section of Government's brief addressing "dietary ingredient" question); *but see* Doc. 120 at pp. 15-24 (Government's opposition to arguments from Hi-Tech's motion for summary judgment concerning those studies).

The sole evidence the Government used instead came from another purported expert, Paula Brown, who opined that "DMAA is not naturally produced by the geranium plant." Doc. 107-6 at p. 3, ¶4 (Third Brown Decl.). In reaching that opinion, Brown did not cite the Mississippi or Texas studies or any other study affirmatively asserting that DMAA is not present in geraniums. She instead asserted that the various studies Hi-Tech and Wheat had introduced evidencing DMAA's presence in geraniums—the Ping Study, the Li Study, and the Fleming Study—were faulty because they had not identified any "biological process" or "biosynthetic pathway" by which "a geranium plant could make DMAA." Doc. 107-6 at pp. 5-6, ¶¶13-15; *see also* Doc. 107-1 at pp. 15-17

(Government brief). As a result, the Government and Brown opined that these studies could "not preclude the possibility that [DMAA] is a contaminant," introduced into geraniums by fertilizer or other means, that is "not naturally produced by the plant." Doc. 107-1 at p. 18; Doc. 107-6 at pp. 4-5, ¶¶9-11.

The District Court had little trouble finding that this testimony did not satisfy the Government's burden. The Court explained that Hi-Tech had presented "substantial evidence," through the various studies discussed above, that DMAA does "naturally occur[] in geraniums." Doc. 140 at p. 5. In contrast, the Court reasoned, Brown's testimony did not exclude the possibility that DMAA naturally occurs in geraniums, and did not explain why certain studies found DMAA present in the plant. *See id.* at p. 6. As a result, the Court found that "the Government has failed to meet its burden of establishing that DMAA has not been found in geraniums." *Id.* at p. 7.

Even though it had rejected the only argument the Government offered on the point, the Court nonetheless concluded that DMAA is not a "dietary ingredient" as a matter of law based on the Court's own interpretation of DSHEA. The Court reasoned that "to be a botanical, the

substance must have been extracted from a plant or plant-like organism and used, for example, in or as a medicine." *Id.* at p. 8. While acknowledging that a synthetically manufactured botanical could qualify as a "dietary ingredient," the Court ruled that there still must necessarily be "at least some history of the substance in question having been extracted in usable quantities" from a plant. *Id.* Under that standard, the Court concluded, "DMAA is not a botanical and thus not a dietary ingredient" because "[w]hile very small amounts of DMAA might be present in geraniums," the "DMAA in the marketplace has *never* been extracted from geraniums or any other plant." *Id.* at pp. 8, 9.

2. DMAA's status as Generally Recognized as Safe.

The District Court's ruling on the "dietary ingredient" issue did not dispose of all the DSHEA questions, for Hi-Tech and Wheat also had argued that DMAA is generally recognized as safe and thus marketable under the GRAS provision. *See generally supra* at pp. 9-11 (citing 21 U.S.C. § 321(s)). To this end, Hi-Tech and Wheat had cited the testimony of the four experts mentioned above. *See supra* at p. 16. Two of the physicians—Heuer, a family-medicine practitioner with 30 years of experience consulting in the industry, and Lee, who is trained in both

pharmacology and toxicology—directly opined that DMAA is generally recognized as safe. *See* Doc. 108-1 at p. 43 (Hi-Tech brief); Doc. 108-6 at p. 359, ¶63 (Heuer Decl.); Doc. 108-8 at pp. 166-67, tr. 69:14-70:17 (Lee Depo.). The other two experts, a toxicologist and a neurologist, otherwise testified that there is no evidence DMAA is unsafe when used at recommended doses. *See* Doc. 108-6 at pp. 215-16, ¶53 (Elkind Decl.); Doc. 108-4 at pp. 66-67 & 75-76, ¶¶83 & 94.2 (Lumpkin Decl.).

The Government had responded with the testimony of one witness, Dennis Keefe, the Director of FDA's Office of Food Additive Safety. *See* Doc. 107-1 at pp. 23-32; Doc. 107-8 at pp. 1-2, ¶1 (Keefe Decl.). Keefe is not an expert in toxicology, pharmacology, physiology, or other topics related to the safety of particular substances. *See* Doc. 108-6 at p. 26, tr. 70:8-71:9 (Keefe Depo.). Instead, Keefe relied on his experience helping the FDA make GRAS determinations and his review of the literature, opining that there was insufficient information that DMAA is generally recognized as safe. He argued that there were not enough studies analyzing the long-term effects of consuming DMAA. *See* Doc. 107-8 at p. 8, ¶¶16-17. The Government argued that his testimony showed that there was too much "uncertainty" about DMAA, based on

articles "describ[ing] … adverse outcomes that occurred when DMAA-containing products were consumed," even though the Government acknowledged that those articles "did not purport to establish cause-and-effect." Doc. 107-1 at p. 29 (citing Doc. 107-8 at pp. 9 & 11, ¶¶18 & 20).

The District Court held that this evidence required summary judgment for the Government on the GRAS issue. The Court reasoned that the expert opinions Hi-Tech and Wheat offered to show that Hi-Tech is generally regarded as safe, and its other testimony showing that any "concerns about [the safety of] DMAA may be unfounded," did "not matter." Doc. 140 at p. 12. This was so, the Court stated, because "the question" was "whether there is a consensus among experts regarding DMAA's safety." *Id.* On that point, the Court held, Hi-Tech "failed to present sufficient evidence." *Id.* On that theory the Court ruled that Hi-Tech could not establish that DMAA falls within the GRAS provision.

3. Hi-Tech's APA and § 1983 claims

Having ruled on summary judgment that the DMAA was subject to forfeiture, the Court turned only briefly to Hi-Tech's APA and § 1983 claims. Those claims had three components. First, Hi-Tech had argued

that the FDA, by labeling DMAA a "food additive" in a forfeiture proceeding, had improperly avoided its burden under DSHEA to first prove that dietary supplements are "adulterated" before removing them from the marketplace. *See* Doc. 108-1 at pp. 41-42. Second, Hi-Tech argued that the APA and § 1983 required the FDA to give Hi-Tech "notice and the opportunity to present views" before seizing the products. *See id.*; Doc. 119 at pp. 24-26 (Hi-Tech Opp'n to MSJ); 21 U.S.C. § 342(f)(2). Third, Hi-Tech claimed that the FDA, through warning letters, detention orders, and seizures, had effectively taken final agency action arbitrarily and capriciously banning DMAA-containing products from the marketplace. *See* Doc. 119 at p. 29. Hi-Tech argued that this final agency action could have been achieved only via a rulemaking process allowing for notice and comment.

The Court's summary-judgment order did not address these claims in any detail. It instead held that its forfeiture ruling precluded them. *See* Doc. 140 at pp. 12-13.

C. The District Court's ruling on reconsideration

Hi-Tech and Wheat asked the Court to reconsider various aspects of its summary-judgment order, and focused on the new standard the

Court had developed for determining whether a substance is a "constituent" of a "botanical." *See* Doc. 142.

In addition to arguing that the Court had misread the statute, Hi-Tech and Wheat took issue with the way the Court had applied its new standard to the record in the case. Hi-Tech and Wheat observed that the record does contain evidence that DMAA historically has been extracted from geraniums in usable quantities: one of Hi-Tech's experts had testified that two patent applications had been filed for processes that would achieve that result. *See id.* at p. 21 (citing Doc. 108-6 at p. 355, ¶58 (Heuer Decl.)); Doc. 130 at pp. 57-58, tr. 225:21-232:12 (Heuer Depo.); Doc. 146 at pp. 10-11. Second, Hi-Tech and Wheat observed that, because the Government had not sought forfeiture under the standard the Court had adopted, the Court at least needed to reopen discovery to allow Hi-Tech and Wheat to assemble evidence about the extent to which DMAA can be extracted from geraniums in usable quantities. *See* Doc. 142 at pp. 22-23; Doc. 146 at pp. 8-10.

The District Court declined to reconsider its order. *See* Doc. 148. In addition to reaffirming its new interpretation of DSHEA, the Court held that Hi-Tech and Wheat were not entitled to further discovery. The

Court reasoned that it was "obvious from the record that no one" had "extracted DMAA from geraniums or some other plant and placed that DMAA in a product." *Id.* at pp. 2-3. The Court did not address the evidence in the record of patent applications for DMAA-extraction processes.

This appeal followed. *See* Doc. 149.

IV. Standard of Review

On both questions presented, this Court reviews the District Court's decision *de novo*. In forfeiture actions the Government brings against dietary supplements under the FDCA, "courts shall decide any issue … on a *de novo* basis." 21 U.S.C. § 342(f)(1)(D). The District Court's novel interpretation of DSHEA is likewise a pure question of law reviewed *de novo*. *See S.E.C. v. Vittor*, 323 F.3d 930, 933 (11th Cir. 2003). And this Court reviews the District Court's grant of summary judgment to the Government *de novo*, applying the same legal standards used by the District Court. *See, e.g.*, *Wooden v. Bd. of Regents of Univ. Sys. of Ga.*, 247 F.3d 1262, 1271 (11th Cir. 2001).

SUMMARY OF THE ARGUMENT

I. The District Court erred when it ruled as a matter of law that DMAA is not a "constituent" of a "botanical" and thus not a freely marketable "dietary ingredient" under DSHEA.

A. As an initial matter, the District Court correctly held that the Government did not satisfy its burden of establishing that DMAA does not naturally occur in geraniums. Hi-Tech and Wheat offered substantial evidence that scientists have found DMAA in the plants. Discovery revealed serious flaws in the studies on which the Government had intended to rely, and it had no choice but to abandon them. The District Court rightly found that the sole expert the Government offered did not establish that geraniums do not produce DMAA.

B. That finding should have ended the case, and the District Court erred when it ruled for the Government based on a novel interpretation of the statute that the Government had not proposed. Contrary to that interpretation, DSHEA's text makes a component part of a plant a "constituent" of a "botanical" even when it does not have a history of being extracted in usable quantities. The District Court's interpretation runs contrary to DSHEA's purposes and will cast doubt upon

beneficial dietary supplements whose marketability no one previously has questioned. By adopting this interpretation *sua sponte*, the District Court exacerbated the APA and due-process problems this case already presented. Once the Government had forsaken the evidence on which it had justified the seizure, summary judgment for Hi-Tech and Wheat should have followed. At the very least the District Court should have allowed discovery on the issues its novel interpretation raised.

II. The District Court also erred when it held, as a matter of law, that DMAA is not marketable because it is not "Generally Recognized as Safe." Hi-Tech and Wheat provided testimony from multiple qualified experts, trained in disciplines including toxicology, pharmacology, and neurology, that the scientific community recognizes DMAA as safe when consumed in recommended doses. The sole expert who testified for the Government was an FDA official who is not trained in the relevant disciplines. He focused on irrelevant evidence about DMAA's safety when consumed in excessive amounts and not, as the statute requires, safety when consumed as recommended. At the very least Hi-Tech and Wheat's evidence created a factual dispute that required a trial.

ARGUMENT

The maneuvers the FDA employed in this case, if left unchecked, would work an end-run around the principles that led Congress to enact DSHEA. The statute starts with the presumption that businesses may market dietary supplements containing natural substances without governmental interference. When the FDA wishes to take these supplements off the market, the burden is on the agency—not the businesses—to make an affirmative showing that the supplements are unsafe. The Government's required showing on that front, as the former Fifth Circuit explained in a similar context, is of the type that is best made in "a formal, legislative rulemaking proceeding, complete with notice, comment, and, if needed, judicial review." *Se. Minerals Inc. v. Harris*, 622 F.2d 758, 767 (5th Cir. 1980). The FDA previously has taken that approach with respect to other supplements. *See* Rule Declaring Dietary Supplements Containing Ephedrine Alkaloids Adulterated, 69 FED. REG. 6787 (2004). Yet the FDA did not institute any such rulemaking here because it cannot show that DMAA is unsafe when used for its intended purposes. For this reason, Hi-Tech and other manufacturers should be marketing their DMAA products to this day.

But the FDA contravened DSHEA on this issue, sending warning letters to the other manufacturers and initiating these forfeiture proceedings against Hi-Tech. The litigation that ensued proves the wisdom of the former Fifth Circuit's criticism of the FDA's use of similar individualized, non-rulemaking procedures in another context: the case marks a "needless waste of the time, wealth, and energies of the agency, the industry, the judiciary, and society as a whole." *Id.* The Government's forfeiture push focused not on any argument that DMAA is unsafe, but on an argument that DMAA is not in geraniums at all. During discovery, Hi-Tech and Wheat showed that the studies from which the FDA sought to establish that proposition were deeply and disturbingly flawed. The Government then abandoned any reliance on that evidence in its motion for summary judgment.

Once that happened, the Department of Justice should have dropped this case. Any seizure based on that evidence was arbitrary and capricious, in violation of Hi-Tech and Wheat's due-process rights. If the FDA still wished to take DMAA off the market at that point, it should have initiated formal rulemaking and sought to prove, following notice and public comment, that this substance is unsafe. Yet the Gov-

ernment continued with this litigation, and the District Court rightly concluded that the slender evidentiary reed on which the FDA was proceeding "failed to meet its burden of establishing that DMAA has not been found in geraniums." Doc. 140 at p. 7.

That finding, in turn, should have led the Court to enter summary judgment in Hi-Tech and Wheat's favor—or, at the very least, to order a trial. In entering summary judgment for the Government, the District Court erred in important respects. It adopted a novel, erroneous reading of DSHEA under which it could deem DMAA to not be a "constituent" of a "botanical" even while conceding that Hi-Tech and Wheat had provided substantial evidence that DMAA is part of a plant. The Court compounded that error by denying Hi-Tech and Wheat an opportunity to conduct discovery showing that DMAA could satisfy the new test the Court had created. And particularly because the FDA had elected to use this individualized enforcement proceeding rather than notice-and-comment rulemaking, the Court erred further in holding that Hi-Tech and Wheat had not provided substantial evidence warranting a trial on whether DMAA is generally recognized as safe. Each of these considerations, discussed in more detail below, should lead the Court to reverse.

I. The District Court erred in holding that DMAA is not a freely marketable "dietary ingredient"

Once the Government decided that it could not rely on the Mississippi and Texas studies concerning DMAA's status as a "constituent" of a "botanical," it committed itself to a path that should not have led to the result below. Based on the record before it, the District Court was right to say that the Government had "failed to meet its burden of establishing that DMAA has not been found in geraniums." Doc. 140 at p. 7. The District Court also was right to say that Hi-Tech had presented "substantial evidence" that DMAA naturally occurs in geraniums. *Id.* at p. 5. These rulings required summary judgment for Hi-Tech and Wheat, not the Government. At the very least they required a trial.

A. The District Court correctly held that the Government had failed to satisfy its burden of establishing that DMAA does not naturally occur in geraniums

As a threshold matter, there can be no doubt that the Government failed to establish that DMAA is not a "dietary ingredient" on the premise that motivated it to seize Hi-Tech and Wheat's products. The Government's motion for summary judgment did not argue that DMAA is not a "constituent" of a "botanical" on the theory the Court employed;

the Government did not assert that the substance must historically have been "extracted" from the plant in "usable quantities." Both sides agreed below that a "constituent" of a "botanical" is, under the ordinary meanings of the terms, a "naturally occur[ring]" part of a plant. *See* Doc. 107-1 at p. 15 (U.S. Brief Supporting Motion for Summary Judgment); Doc. 108-1 at p. 39 (Hi-Tech Brief Supporting Motion for Summary Judgment). The Government's argument to the District Court was that geraniums "cannot make DMAA" at all. Doc. 107-1 at p. 17. As the District Court observed, the Government "failed to meet its burden of establishing" that proposition, and Hi-Tech and Wheat put forward "substantial evidence" to the contrary. Doc. 140 at pp. 5, 7.

Hi-Tech and Wheat offered that evidence on multiple fronts. Marvin Heuer, a physician and former Research and Development director with one of the world's largest dietary-supplement companies, opined, based on the Ping, Li, and Fleming studies, that "DMAA is of natural origin and the chemical is found in geranium." Doc. 108-6 at pp. 351-55, ¶¶52-57. Chemist Paul Simone, who had studied the presence of DMAA in geraniums before the Government commenced the forfeiture action, testified that he had found DMAA in multiple geranium sam-

ples. *See* Doc. 108-7 at pp. 274-75, ¶73; Doc. 108-8 at p. 326, tr. 114:15-116:22 (Simone Depo.); *see also* Doc. 108-7 at p. 407 (Ping Study); Doc. 108-5 at p. 34 (Li Study); Doc. 103-3 at p. 91 (Fleming Study). The District Court cited to yet another study whose author surveyed the available literature and data on DMAA's presence in geraniums and concluded that "[o]verall" these studies "show that 1,3-DMAA is found naturally in some, but not all, geranium plants and extracted geranium oils." Doc. 140 at p. 5.

The District Court accurately observed that the sole testimony the Government invoked in response, from Dr. Paula Brown, could not effectively rebut this evidence. While the Government had asserted that Brown's testimony made "clear" that "[g]eraniums cannot make DMAA," the District Court rightly perceived that Brown's testimony was "nowhere near as unequivocal." Doc. 140 at p. 6. Instead, Brown had stated that "there is no *known* biological process by which a geranium plant could make DMAA." Doc. 107-6, ¶13 (Brown Third Decl.) (emphasis added). But Brown did not conduct any studies or analyses of her own. She instead examined textbooks and literature about the biosynthetic pathways of plants generally, and claimed she did not find a pub-

lished pathway she believed would match one that should be in geraniums and produce DMAA. *See* Doc. 108-8 at p. 16, tr. 56:4-8; *id.* at pp. 34-35, tr. 128:21-129:20; 130:8-131:23. As Brown admitted—and multiple experts in this case explained—science has yet to discover all the biosynthetic pathways by which plants make substances. *See, e.g.*, *id.* at p. 17, tr. 59:24-60:11; Doc. 108-7 at p. 435, tr. 84:18-22 (Kababick Depo.). So Brown's testimony that "[t]hose suggesting [DMAA] is naturally occurring in [geraniums] have not proposed a biosynthetic pathway by which the compound could be produced," the District Court rightly observed, "is nothing close to uncontroverted evidence that geraniums cannot make DMAA." Doc. 140 at p. 6 (quoting Doc. 113-1 at pp. 29, 27). It was, instead, speculation that the DMAA's presence in the geraniums *might* have resulted from something besides its production by the plants themselves.

That reality should have ended the dietary-ingredient inquiry and led to summary judgment for Hi-Tech and Wheat. The Government acknowledged that it bore the burden to prove, in this forfeiture proceeding, that DMAA does *not* naturally appear in geraniums and thus is not a dietary ingredient. *See* Doc. 107-1 at p. 12. A party that bears the

burden of proof cannot create a genuine issue of fact with "inference[s]" and "speculation," particularly when the opposing party has pointed to evidence to the contrary. *First Nat'l Bank v. Cities Serv. Co.*, 391 U.S. 253, 278-84 (1968).

B. The District Court wrongly held that DMAA, though naturally occurring in geraniums, is not a "constituent" of a "botanical" because it has no history of being "extracted" in usable quantities

With Hi-Tech and Wheat having offered substantial evidence that DMAA was a "constituent" of a "botanical" as the Government understood those terms, the only thing that saved the Government from a ruling that the seizure had been unlawful was the intervention of the District Court. Unmooring itself from both the Government's theory of the case and critical components of DSHEA's text, the Court stated that it was "inconceivable" that Congress could have "intended" for DMAA to be a "dietary ingredient." Doc. 140 at p. 8. That was so, the Court explained, because DMAA appears only in "trace amounts" in geraniums. *Id.* at p. 7. The Court posited that to fall within this provision, the substance must have had "a history of having been extracted in usable quantities." *Id.* at p. 9. And the Court concluded that DMAA could not

be a dietary ingredient, as a matter of law, because it had no such history. *Id.* at p. 8. That conclusion should not have won the day for the Government for a number of reasons.

1. The District Court's interpretation of DSHEA was wrong

As an initial matter, the District Court's interpretation of DSHEA's dietary-ingredient provision was contrary to both its text and purposes. It was particularly contrary to the ordinary meaning of the statutory term that matters most. In reading statutes, courts turn first to the text and attribute to any undefined terms their "ordinary meanings." *United States v. Takhalov*, 827 F.3d 1307, 1312 (11th Cir. 2016). Yet when the Court outlined the limitations it was placing on the statute, it did not purport to discern the ordinary meaning of the term "constituent." The Court mentioned the term only once, in passing, in quoting the dietary-ingredient definition in its entirety. The Court purported to be interpreting the word "botanical" instead. But the term "botanical" does not appear in isolation in DSHEA. It appears adjacent to, and operates in conjunction with, the term "constituent." "[T]he words of a statute must be read in their context and with a view to their place in the overall statutory scheme." *King v. Burwell*, 135 S. Ct. 2480, 2483

(2015). And the ordinary meaning of the term "constituent," when it operates in conjunction with the term "botanical," is contrary to the District Court's instincts about the limitations Congress wanted to place on the statute. Both now and when Congress enacted DSHEA, the common meaning of "constituent" has been "[o]ne part of something that makes up a whole; an element." BLACK'S LAW DICTIONARY 306 (7th ed. 1999). It is a "component" of something else. THE AMERICAN HERITAGE DICTIONARY OF THE ENGLISH LANGUAGE 404 (3d ed. 1992). Nothing in that language suggests that a substance is not a "constituent" of a "botanical" merely because it has not previously been "extracted" from the plant, or because it is not present in some threshold "usable" amount.

DSHEA's other terms confirm that the statute does not impose requirements of that sort. "Constituent[s]" are not the only botanical substances DSHEA makes dietary ingredients: the statute also says, among other things, that "extract[s]" of botanicals are dietary ingredients too. 21 U.S.C. § 321(ff)(1)(F). Courts take care to avoid "interpretations of statutes that render language superfluous" or result in words being "'discarded as meaningless, redundant, or mere surplusage.'" *United States v. DBB, Inc.*, 180 F.3d 1277, 1281 (11th Cir. 1999) (quot-

ing *Conn. Nat'l Bank v. Germain*, 503 U.S. 249, 253 (1992)). If "constituents" must be extracted from a plant, then the word "extract" would add nothing to DSHEA's scope. The presence of both terms shows that the statute deems a plant's "constituent" a dietary ingredient even when manufacturers do not actually "extract" it from the botanical.

DSHEA's underlying purposes also belie the District Court's narrowing of the statute's list of marketable dietary ingredients. The Senate Report accompanying DSHEA explained that Congress's overarching intent was to make it *easier* for dietary-supplement manufacturers to "add[] safe and natural plants and their constituents" to supplements "to support and protect bodily functions and processes." S. Rep. 103-410, at 10. DSHEA therefore set out a list of dietary ingredients that was "expansive," to make "the broadest possible range of ingredients" marketable without the FDA's preapproval. Scott Bass & Emily Marden, *The New Dietary Ingredient Safety Provision of DSHEA: A Return to Congressional Intent*, 31 AM. J.L. & MED. 285, 294-95 (2005) (emphasis deleted). Through its various subsections, the definition "essentially opens the dietary supplement category to an almost limitless variety of ingredients." *Id.* at 296. To the extent that DSHEA envisioned the FDA

taking dietary supplements off the market, it was through rulemakings over whether those supplements were safe—not through judicially created limitations on the definition of "dietary ingredient" that do not appear in its text.

The District Court's limitation of dietary ingredients to constituents extracted in "usable quantities" could have dire consequences for the dietary-supplement industry—especially for two widely used ingredients that have substantial benefits for the public. Pterostilbene is an effective antioxidant that appears in blueberries, but only in "trace amounts" of approximately 10 parts per million. *See generally* Denise McCormack & David McFadden, *A Review of Pterostilbene Antioxidant Activity and Disease Modification*, OXIDATIVE MEDICINE AND CELLULAR LONGEVITY (2013), *available at* https://www.hindawi.com/journals/omcl/2013/575482/ . Resveratrol is a similar chemical that makes the grapes in red wine healthy, but there is only between 0.03-1.07 milligrams of it in each glass. *See* Doc. 142 at p. 20 (Hi-Tech Mot. to Reconsider); Oregon State Univ. Linus Pauling Inst., *Micronutrient Info. Ctr.: Resveratrol* (2015), *available at* http://lpi.oregonstate.edu/mic/dietary-factors/phytochemicals/resveratrol. Manufacturers therefore routinely

synthesize both these constituents, rather than trying to extract them from the botanicals of which they are a part, to incorporate them into supplements in more usable and beneficial quantities. *See, e.g.*, James McNulty, *A scalable process for the synthesis of (E)-pterostilbene involving aqueous Wittig olefination chemistry*, SCIENCE DIRECT J. (May 2013); Bob Yirka, *Chemists Figure Out How to Synthesize Compounds from Resveratrol*, PHYSORG.COM (June 23, 2011), *available at* https://phys.org/news/2011-06-chemists-figure-compounds-resveratrol.html . No one previously has suggested that dietary supplements containing these ingredients are not freely marketable, but someone might if the District Court's interpretation becomes the law.

The District Court's attempt to narrow DSHEA's list of dietary ingredients thus runs contrary to the statute's text and its overarching purposes, and it is unworkable in any event. The District Court did not say how long of a "history" of extraction the constituent must have, or what quantity counts as "usable." Nor did the Court make clear whether a substance may *become* a dietary ingredient, despite its previous lack of a history of extraction in usable quantities, if an enterprising manufacturer develops a new process to create that "history" in the fu-

ture.

The policy concerns the District Court cited cannot justify its re-writing of the statute. The Court said it needed to impose these limits because otherwise, a manufacturer could incorporate a new substance into its product and claim that it is a freely marketable "dietary ingredient" after fortuitously discovering the same substance in a "fungus found only in a remote Tibetan river valley." *See* Doc. 140 at p. 9. DSHEA already contains safeguards that ameliorate any such concern. The statute would categorize that fungus's constituent as a "new" dietary ingredient because it was not "marketed before October 15, 1994." 21 U.S.C. § 350b(a)(2). By making that classification, DSHEA would require the manufacturer, as a condition of marketing the ingredient, to first present a notification with information showing that the ingredient will "reasonably be expected to be safe." *Id.*

But there is a more fundamental point to be made here: even if the policy concerns the District Court cited would be legitimate considerations for policymakers who are charged with drafting legislation, "[c]ourts are not authorized to rewrite the statute because they might deem its effects susceptible of improvement." *Badaracco v. C.I.R.*, 464

U.S. 386, 398 (1984). DSHEA includes in its list of dietary ingredients any "constituent" of a "botanical"—not any "constituent" of a "botanical" that has a "history of extraction" in "usable quantities." To the extent that the supplement industry begins relying on Tibetan funguses and to the extent that doing so creates policy issues, Congress is free to write that new language into the statute. The District Court was not. The statute Congress wanted, and the statute Congress wrote, defined dietary supplements broadly, in a way that included all constituents of botanicals. Under that statute, Hi-Tech and Wheat were entitled to a finding that DMAA is a "dietary ingredient" as a matter of law—and at the very least were entitled to a trial on the issue.

2. The District Court's application of its new interpretation exacerbated the APA and § 1983 problems with the seizure

Additionally, although the District Court's new interpretation of DSHEA was wrong in any event, the APA and § 1983 claims Hi-Tech raised should have precluded the Court from applying that interpretation in this particular case. Hi-Tech's central APA and § 1983 claim was that the FDA's decision to take DMAA off the market—through the warning letters to the other manufacturers and the seizure at Hi-

Tech—had amounted to "arbitrary and capricious" action that did not satisfy due process or the agency's obligation to engage in "reasoned decisionmaking" under the APA. 5 U.S.C. § 706; *Michigan v. E.P.A.*, 135 S. Ct. 2699, 2706 (2015) (citation omitted).

The litigation below proved Hi-Tech's point. Discovery revealed the Mississippi and Texas studies' serious and disturbing flaws. *See supra* at pp. 17-23, 26. The Government had relied on those studies when seizing Hi-Tech's products and had even disclosed one of the authors as an expert. *See id.* at pp. 27-28. The Government then abandoned all reliance on those studies and that expert in the end. *See id.* at pp. 28-29. In trying to keep its case alive, the Government invoked the testimony of a single witness, apparently only after the fact, whom the District Court rightly held had not rebutted Hi-Tech and Wheat's evidence. *See id.* These developments confirmed that, in deciding to take DMAA off the market, the FDA had operated in contravention of the APA by "rel[ying] on factors which Congress has not intended it to consider," by "entirely fail[ing] to consider an important aspect of the problem," and by "offer[ing] an explanation for its decision that runs counter to the evidence" that was "before the agency." *Ala.-Tombigbee Rivers Coal. v.*

Kempthorne, 477 F.3d 1250, 1254 (11th Cir. 2007).

Far from ending the need to consider these issues as the District Court thought, *see* Doc. 140 at pp. 12-13, the Court's *sua sponte* salvaging of the Government's case made the APA and due-process problems worse. Although courts may "uphold a decision of less than ideal clarity if the agency's path may reasonably be discerned," courts "may not supply a reasoned basis for the agency's action that the agency itself has not given." *Black Warrior Riverkeeper, Inc. v. U.S. Army Corps of Eng'rs*, 781 F.3d 1271, 1288 (11th Cir. 2015) (quotations and citations omitted). With the Government having abandoned some of its rationales and the District Court having rightly discarded the others, the Government could not validly proceed. The only proper course of action for the Court was to enter summary judgment against the Government.

3. The District Court at least should have afforded Hi-Tech and Wheat an opportunity to develop the record on whether DMAA has been or can be extracted from geraniums

At the very least, the fact that the interpretation of DSHEA that ultimately controlled below was the Court's and not the Government's meant that the Court should not have entered summary judgment against Hi-Tech and Wheat. Throughout the 2½ years of this litigation,

neither the Government nor the claimants had suggested that the case turned on whether DMAA had a history of being extracted in usable quantities. All parties agreed that the dispositive issue was whether DMAA is "naturally produced by geranium plants." Doc. 107-1 at p. 1. So when the Court announced its own standard for assessing whether DMAA is a "constituent" of a "botanical," the record was undeveloped on the matters the Court thought critical. The parties had not explored or briefed whether DMAA historically had been, or could be, extracted from geraniums in what the Court deemed to be "usable quantities."

The limited record evidence on this issue pointed against the conclusion the Court had drawn. One of Hi-Tech and Wheat's experts had testified that in 2012 two applications had been filed for patents to commercially extract DMAA from geraniums. *See supra* at p. 34. He explained how the patent applications describe a complex scientific extraction method by which DMAA is culled from geranium oil to achieve a high concentration of DMAA. *See* Doc. 130 at pp. 57-58, tr. 225:21-232:12 (Heuer Depo.). That testimony should have stood as substantial evidence precluding the Court from granting summary judgment to the Government under its new standard and requiring the Court to enter

summary judgment for Hi-Tech and Wheat.

That evidence at the very least suggested that more discovery and record development were needed. The Eighth Circuit has held that a "district court commits reversible error by granting summary judgment on an issue not raised or discussed by the parties if the losing party did not have notice and an opportunity to respond." *Montgomery v. City of Ames*, 749 F.3d 689, 697 (8th Cir. 2014). As the former Fifth Circuit put the point, a court cannot enter summary judgment on a particular basis *sua sponte* without giving the affected parties a "chance to present" their arguments and to show "through discovery procedures or opposing affidavits" that "a material fact dispute exist[s]." *Sharlitt v. Gorinstein*, 535 F.2d 282, 284-85 (5th Cir. 1976). In other words, a court "must provide the parties with notice of its intention to consider granting summary judgment so that they have an opportunity to marshal evidence on the motion for submission to the court." *Acumed LLC v. Advanced Surgical Servs.*, 561 F.3d 199, 223-24 (3d Cir. 2009).

The District Court failed to give the parties that opportunity here. When the Court announced its new reading of DSHEA, Hi-Tech and Wheat—while disputing that the interpretation was correct at all—also

asked for a chance to show that DMAA is a "dietary ingredient" under that standard. The Court's denial of that request was particularly erroneous in light of the important regulatory issues the agency had put at stake. Issues of this magnitude should be decided on an industry-wide basis, through a broad-ranging "formal, legislative rulemaking proceeding, complete with notice, comment, and, if needed, judicial review." *Se. Minerals*, 622 F.2d at 767. Because the FDA was not willing to go that route—and because the District Court had adopted a dispositive interpretation with wide-ranging consequences for an important dietary supplement—due process required the Court to give the parties a full opportunity to build a record on the points the Court believed to be important.

II. The District Court erred in holding that DMAA is not "Generally Recognized as Safe"

Even if the Government had established that DMAA is not a freely marketable "dietary ingredient," the District Court still should not have ordered forfeiture of the products the FDA had seized. In the proceedings below, Hi-Tech and Wheat also invoked the FDCA's provision making non-dietary ingredients marketable when a manufacturer

shows them to be "generally recognized" as "safe." 21 U.S.C. § 321(s). They offered the opinions of numerous qualified experts who made that showing as to DMAA. *See supra* at pp. 30-32. In holding that the Government was entitled to summary judgment on this issue, the District Court misapplied the law.

The critical statutory text from the GRAS provision shows that manufacturers need not establish that the substance at issue is generally recognized as safe for *all* conceivable uses. The manufacturer instead must demonstrate that the substance is safe "under the conditions of its *intended* use." 21 U.S.C. § 321(s) (emphasis added). The Government's own expert, Keefe, thus conceded that the Court should consider how much of the substance is expected to be consumed and, if there are labels, what warnings the manufacturer provides. Doc. 108-6 at pp. 20-21, tr. 48:21-50:3. Too much of anything—coffee, sugar, even water—can be dangerous or even deadly. *See, e.g.,* D.J. Farrell and L. Bower, *Fatal Water Intoxication*, 56 J. CLINICAL PATHOLOGY 803, 803-04 (2003), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1770067/. So courts have focused not on whether a product might present dangers if taken irresponsibly, but rather on the "recommended dosages" from

the product's warning labels. *See United States v. 1,048,000 Capsules, More or Less, "Afrodex,"* 494 F.2d 1158, 1161 (5th Cir. 1974); *United States v. Articles of Drug Labeled "Quick-O-Ver*," 274 F. Supp. 443, 449 (D. Md. 1967).

Hi-Tech and Wheat's evidence thus honed in on the recommended dosage amounts for Hi-Tech's supplements, as set forth in one of its expert's declarations. *See* Doc. 108-8 at p. 115, ¶57 (Lee Decl.). Each of Hi-Tech and Wheat's four experts—trained in diverse areas including toxicology, pharmacology, neurology, and, in Heuer's case, having vast experience in the dietary-supplement industry—offered testimony that at those doses DMAA is safe. *See supra* at pp. 16, 30-31. Two of these experts specifically testified that the scientific community considers DMAA to be safe. *See id*. That testimony was substantial evidence that DMAA is generally recognized as safe "under the conditions of its intended use." 21 U.S.C. § 321(s).

The Government's sole witness on the issue—Keefe, an FDA regulator who is not trained in the same disciplines—did not have the same focus. In concluding that he, as an administrator, would not deem DMAA generally recognized as safe, Keefe relied on case reports involv-

ing DMAA consumption at doses that, by his own admission, were far greater than what the labels recommended or involved people who simultaneously had consumed drugs or alcohol. *See* Doc. 108-6 at pp. 35-36, tr. 109:20-113:10. Hi-Tech's experts confirmed that in those and other case reports it was "difficult or impossible to establish the dosage of DMAA consumed or the presence of additional potential agents that may have been consumed." Doc. 108-6 at pp. 242-43, ¶108. In any event, Hi-Tech's witnesses explained, "[c]ase reports, or single reports of subjective effects are insufficient and could not be used alone to conclude that a medication is or is not safe." Doc. 108-8 at p. 123, ¶79.

Hi-Tech and Wheat thus were the only parties to offer substantial evidence on this issue, and the criticisms the District Court offered of their showing were insufficient to warrant summary judgment in the Government's favor. The Court claimed, for example, that "the sample sizes of [the] studies" presented by both sides were "simply too small." Doc. 140 at pp. 10-12. But the Court did not say what sample size would be large enough, and even the Government's witness acknowledged that a finding that a substance is generally recognized as safe does not require a minimum number of studies or subjects. *See* Doc. 108-6 at p. 19,

tr. 45:4-15. Even in the Court's estimation, Hi-Tech and Wheat had provided "extensive documentation regarding DMAA and the studies that have been performed on the effects of DMAA on humans and animals." Doc. 140 at pp. 10-12. The Government might have raised questions about sample size at trial, but that consideration could not, by itself, compel summary judgment for the Government. *Cf. United States v. Article of Food Consisting of 345/50-Pound Bags*, 622 F.2d 768, 773 (5th Cir. 1980) (reversing district court and remanding for trial since material fact issues existed on GRAS issues).

Nor can the fact that the Government produced an FDA employee who disagreed with the opinions expressed by Hi-Tech and Wheat's witnesses mean that the Government was automatically entitled to win at the summary-judgment stage. The statute requires manufacturers to show that the product is "generally" regarded as safe, not that it is universally so. The former Fifth Circuit rightly looked with skepticism on a trial court's "broad[] statement of the rule" that "suggest[ed] that any conflict in the expert testimony is sufficient to prove the lack of a general reputation for safety." *United States v. Articles of Food & Drug Consisting of Coli-Trol 80, F4C-60 Feed Grade, Entrol-S Medicated, En-*

trol-P, 518 F.2d 743, 747 (5th Cir. 1975). As one district court has put the point in the context of drug seizures, "[t]he government should not be given license to seize non-new drugs simply because it can find a small contingent within the scientific community dissenting from the view that the drugs are safe and effective." *United States v. Articles of Drug*, 624 F. Supp. 776, 782-83 (N.D. Ill. 1985), *aff'd*, 826 F.2d 564 (7th Cir. 1987).

Just this month, the FDA issued draft industry guidance underscoring the problems with the way it handled the GRAS inquiry below. *See Best Practices for Convening a GRAS Panel* (Nov. 2017 Draft), *available at* https://www.fda.gov/downloads/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/UCM584930.pdf. The draft sets forth "best practices for" manufacturers to make a GRAS showing through "a panel of qualified experts who independently evaluate whether" a substance used as food qualifies as GRAS "under the conditions of its intended use." *Id.* at 4. The guidance states that "general recognition of safety does not require unanimous agreement." *Id.* at 21. And critically for present purposes, the guidance recommends including experts from a wide variety of disciplines reflecting "the scientific ques-

tions that arise in relation to the conditions of [a substance's] intended use." *Id.* at 19. Those disciplines include "[a]t a minimum" "chemistry or biochemistry, toxicology, and exposure assessment." *Id.* That guidance fits hand-in-glove with the multi-expert presentation Hi-Tech and Wheat made below, and looks nothing like the Government's proffer of a single FDA employee.

The Court's entry of summary judgment for the Government was particularly problematic because the FDA had elected to proceed with an individualized forfeiture proceeding rather than a rulemaking. GRAS was the issue when the former Fifth Circuit urged the FDA to "provide a definitive agency determination" in "a single administrative proceeding in which each manufacturer may be heard." *Se. Minerals*, 622 F.2d at 767 (quoting *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 625 (1973)). When the FDA declines to go that route, the Government should not be able to short-circuit the GRAS inquiry by having a single expert cast a heckler's veto. If an agency chooses individualized prosecution over notice-and-comment rulemaking, "[t]he purposes of accuracy and fairness require that the courts not slavishly defer to the agency." *United States v. Boston Farm Ctr., Inc.*, 590 F.2d

149, 151 (5th Cir. 1979). When manufacturers offer multiple experts' opinions that their products are generally recognized as safe and that isolated concerns presented by the Government are "unfounded," they are entitled to summary judgment. At the very least they are entitled to a trial where they can show that the Government's evidence does not accurately portray the scientific consensus on the question at hand.

* * *

At each step of the way, the Government's actions in this case foisted burdens on Hi-Tech and Wheat that Congress did not want manufacturers to bear. DSHEA presumes that dietary-supplement manufacturers will not need the FDA's preapproval to market their products and that the FDA can take those products off the market only by showing that they are unsafe. The FDA could make no such showing here. It proceeded with the seizure based on flawed studies it eventually abandoned. It succeeded with the forfeiture only because the District Court adopted an interpretation of "dietary ingredient" the Government never had advanced, and because the District Court placed a virtually insurmountable burden on Hi-Tech and Wheat to show that no one has even "unfounded" concerns about DMAA's safety. The statute does not

give the FDA power to take a dietary supplement off the market in these circumstances, and both the United States Code and due process call for a different result from the one reached below.

CONCLUSION

This Court should reverse the District Court's judgment and remand with instructions for the District Court to enter summary judgment for Hi-Tech and Wheat or to hold other proceedings consistent with the Court's opinion.

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

This brief complies with the applicable type-volume limitation under Rule 32(a)(7) of the Federal Rules of Appellate Procedure and 11th Circuit Rule 32-4. According to the word count in Microsoft Word 2010, the relevant parts of this brief contain 12,244 words. This brief complies with the applicable type-style requirements limitation under Rule 32 of the Federal Rules of Appellate Procedure. I prepared this brief in a proportionally spaced Century Schoolbook font sized 14 point or, for headings, with a larger point size.

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CERTIFICATE OF SERVICE

On November 22, 2017, I efiled this brief with the Court via CM-ECF, which will serve the following attorneys for the United States:

Daniel Aguilar
James Harlow

On the same day, I mailed seven copies to the Court via First Class United States Mail, postage prepaid.

s/ John C. Neiman, Jr.
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STATUTORY ADDENDUM

21 U.S.C. § 321. Definitions; generally

For the purposes of this chapter—

(s) The term "food additive" means any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use), if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use; except that such term does not include—

(1) a pesticide chemical residue in or on a raw agricultural commodity or processed food; or

(2) a pesticide chemical; or

(3) a color additive; or

(4) any substance used in accordance with a sanction or approval granted prior to September 6, 1958, pursuant to this chapter, the Poultry Products Inspection Act [21 U.S.C.A. § 451 et seq.] or the Meat Inspection Act of March 4, 1907, as amended and extended [21 U.S.C.A. § 601 et seq.];

(5) a new animal drug; or

(6) an ingredient described in paragraph (ff) in, or intended for use in, a dietary supplement.

…

(ff) The term "dietary supplement"—

(1) means a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients:

(A) a vitamin;

(B) a mineral;

(C) an herb or other botanical;

(D) an amino acid;

(E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or

(F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E);

(2) means a product that—

(A)(i) is intended for ingestion in a form described in section 350(c)(1)(B)(i) of this title; or

(ii) complies with section 350(c)(1)(B)(ii) of this title;

(B) is not represented for use as a conventional food or as a sole item of a meal or the diet; and

(C) is labeled as a dietary supplement; and

(3) does—

(A) include an article that is approved as a new drug under section 355 of this title or licensed as a biologic under section 262 of Title 42 and was, prior to such approval, certification, or license, marketed as a dietary supplement or as a food unless the Secretary has issued a regulation, after notice and comment, finding that the article, when used as or in a dietary supplement under the conditions of use and dosages set forth in the labeling for such dietary supplement, is unlawful under section 342(f) of this title; and

(B) not include—

(i) an article that is approved as a new drug under section 355 of this title, certified as an antibiotic under section 357 of this title, or licensed as a biologic under section 262 of Title 42, or

(ii) an article authorized for investigation as a new drug, antibiotic, or biological for which substantial clinical investigations have been instituted and for

which the existence of such investigations has been made public,

which was not before such approval, certification, licensing, or authorization marketed as a dietary supplement or as a food unless the Secretary, in the Secretary's discretion, has issued a regulation, after notice and comment, finding that the article would be lawful under this chapter.

Except for purposes of paragraph (g) and section 350f of this title, a dietary supplement shall be deemed to be a food within the meaning of this chapter.

21 U.S.C. § 342. Adulterated food

A food shall be deemed to be adulterated—

(a) Poisonous, insanitary, etc., ingredients

…

(2)(A) if it bears or contains any added poisonous or added deleterious substance (other than a substance that is a pesticide chemical residue in or on a raw agricultural commodity or processed food, a food additive, a color additive, or a new animal drug) that is unsafe within the meaning of section 346 of this title; or

…

(C) if it is or if it bears or contains (i) any food additive that is unsafe within the meaning of section 348 of this title; …

(f) Dietary supplement or ingredient: safety

(1) If it is a dietary supplement or contains a dietary ingredient that—

(A) presents a significant or unreasonable risk of illness or injury under—

(i) conditions of use recommended or suggested in labeling, or

(ii) if no conditions of use are suggested or recommended in the labeling, under ordinary conditions of use;

(B) is a new dietary ingredient for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury;

…

(D) is or contains a dietary ingredient that renders it adulterated under paragraph (a)(1) under the conditions of use recommended or suggested in the labeling of such dietary supplement.

In any proceeding under this subparagraph, the United States shall bear the burden of proof on each element to show that a dietary supplement is adulterated. The court

shall decide any issue under this paragraph on a de novo basis.

(2) Before the Secretary may report to a United States attorney a violation of paragraph (1)(A) for a civil proceeding, the person against whom such proceeding would be initiated shall be given appropriate notice and the opportunity to present views, orally and in writing, at least 10 days before such notice, with regard to such proceeding.

21 U.S.C. § 348. Food additives

(a) Unsafe Food Additives; Exception For Conformity With Exemption or Regulation A food additive shall, with respect to any particular use or intended use of such additives, be deemed to be unsafe for the purposes of the application of clause (2)(C) of section 342(a) of this title, unless—

(1) it and its use or intended use conform to the terms of an exemption which is in effect pursuant to subsection (j) of this section;

(2) there is in effect, and it and its use or intended use are in conformity with, a regulation issued under this section prescribing the conditions under which such additive may be safely used; or

(3) in the case of a food additive as defined in this chapter that is a food contact substance, there is—

(A) in effect, and such substance and the use of such substance are in conformity with, a regulation issued under this section prescribing the conditions under which such additive may be safely used; or

(B) a notification submitted under subsection (h) that is effective.

While such a regulation relating to a food additive, or such a notification under subsection (h)(1) relating to a food additive that is a food contact substance, is in effect, and has not been revoked pursuant to subsection (i), a food shall not, by reason of bearing or containing such a food additive in accordance with the regulation or notification, be considered adulterated under section 342(a)(1) of this title.