IN THE UNITED STATES COURT FOR THE DISTRICT OF UTAH

CENTRAL DIVISION

NUTRACEUTICAL CORPORATION and SOLARAY, INC., Plaintiffs, vs. ANDREW VON ESCHENBACH, M.D., Commissioner, U.S. Food and Drug Administration, UNITED STATES FOOD AND DRUG ADMINISTRATION, TOMMY G. THOMPSON, Secretary, Department of Health and Human Services, DEPARTMENT OF HEALTH AND HUMAN SERVICES, and UNITED STATES OF AMERICA, Defendants.	**MEMORANDUM DECISION GRANTING DEFENDANTS' MOTION FOR SUMMARY JUDGMENT** Case No. 2:04-CV-00409 PGC

In 2004, the Food and Drug Administration promulgated a rule that banned ephedrine-alkaloid dietary supplements ("EDS") at any dosage level from the United States market. Before the effective date of this rule, the plaintiffs, Nutraceutical Corporation and Solaray, Inc. (collectively, "Nutraceutical"), marketed EDS in the United States. In this suit against the FDA, Andrew Von Eschenbach, Tommy Thompson, the Department of Health and Human Services, and the United States, Nutraceutical seeks to enjoin the FDA from enforcing this rule. The Tenth

Circuit already addressed a different portion of this case on appeal,[1] upholding the validity of the FDA's final rule on EDS pursuant to the Food, Drug, and Cosmetic Act[2] (FDCA), as amended by the Dietary Supplement Health and Education Act[3] (DSHEA).

Nutraceutical now claims the final rule on EDS is invalid because the FDA gave insufficient statutory notice and opportunity to comment on its use of a risk-benefit analysis to determine that EDS are adulterated. Nutraceutical also alleges the FDA acted in an arbitrary and capricious manner when it prohibited the marketing of EDS but failed to ban other products containing ephedrine alkaloids, such as conventional foods and traditional Asian medicines. While Nutraceutical's counsel has ably presented Nutraceutical's case, the case is simply unpersuasive. The defendants have successfully shown the FDA's process and its final rule comply with the notice-and-comment requirements of the Administrative Procedures Act.[4] The defendants have also shown the FDA acted consistently with the statutory scheme by excluding non-dietary supplement products containing ephedrine alkaloids from the reach of the final rule. It did not act in an arbitrary or capricious manner or abuse its discretion. Accordingly, the court finds Nutraceutical has failed to meet its burden in challenging the FDA's action under the APA.

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[1] *See Nutraceutical v. Von Eschenbach*, 459 F.3d 1033 (10th Cir. 2006).

[2] 21 U.S.C. §§ 301–399 (2000 & Supp. 2006).

[3] Publ. L. No. 103-417, 108 Stat. 4325 (1994) (codified as amended in scattered sections of 21 U.S.C.).

[4] 5 U.S.C. §§ 500–584, 701–706 (2000 & Supp. 2006).

BACKGROUND

Regulatory Framework

The FDCA gives the FDA authority to "promulgate regulations for the efficient enforcement of [the FDCA]."[5] The DSHEA, which Congress enacted in 1994, amended the FDCA. In the DSHEA, Congress instructed the federal government to "take swift action against products that are unsafe or adulterated."[6]

The DSHEA defines a dietary supplement as adulterated (and, therefore, unmarketable in the United States), if it "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."[7] At issue is the FDA's regulation of EDS under the "unreasonable risk" provision of this statute.

FDA's Rulemaking

As early as 1995, the FDA, faced with some evidence of the adverse effects of EDS on health, discussed the potential public health problems arising from EDS use. Ephedrine alkaloids belong to a pharmacological group of chemical stimulants. In the United States, manufacturers marketed EDS as a substance helping people to lose weight, increase energy, and enhance athletic performance. By January 1997, the FDA had received more than 800 reports of injuries and illnesses associated with EDS use. At this time, the FDA began reviewing scientific studies

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[5] 21 U.S.C. § 371(a).

[6] DSHEA, 108 Stat. at 4326.

[7] 21 U.S.C. § 342 (f)(1)(A).

and holding meetings on the safety of EDS. Also in 1997, the FDA began a rulemaking process, soliciting public comment on a proposed rule containing the FDA's contemplated formulation and labeling restrictions for EDS.

In brief, the FDA proposed that EDS would be considered adulterated if it contained eight or more milligrams of ephedrine alkaloids per serving or if its labeling recommended use resulting in an intake of eight or more milligrams within six hours, or twenty-four or more milligrams as a total daily intake. Additionally, the rule proposed to (1) prohibit labeling that would require a long-term intake of EDS to attain the purported effect, (2) prohibit manufacturers from combining ephedrine alkaloids with other stimulants, (3) require warning statements directing consumers not to take EDS for longer than seven days and alerting them to possible drug interactions, (4) require additional warning statements to advise at-risk consumers of the risks of EDS, and (5) require claims encouraging excessive, short-term intake to include a warning that the recommended intake could cause serious, adverse health effects.

In conjunction with the publication of its proposed rule, the FDA published the administrative record it had compiled to that point — a record containing 221 scientific and other references, as well as information on some of the adverse event reports the FDA had received. Later that same year, after the FDA received additional adverse event reports and found some omissions in the initial administrative record, the FDA reopened the period for public comment and made an additional record available to the public. Over the course of the next seven years, the FDA continued to compile and review scientific literature on EDS and continued to receive adverse event reports from the public.

In August 1999, the General Accounting Office issued a report concluding the FDA was generally justified in its consideration of EDS safety issues. However, the GAO recommended the FDA "provide stronger evidence on the relationship between the intake of dietary supplements containing ephedrine alkaloids and the occurrence of adverse reactions that support the proposed dosing level and duration of use limits."[8] Consequently, the FDA hired an expert to conduct further research on the health effects of EDS. Then, based on the report of the GAO as well as comments the FDA had received on the EDS restrictions it proposed, the FDA withdrew part of its proposed rule in April 2000. The agency stressed that its decision to withdraw part of its proposal did not limit its discretion to take action regarding EDS. Rather, it reflected the FDA's decision "to reconsider, with public input, whether any dietary ingredient level or duration of use limit for [EDS] is appropriate or whether alternative measures should be considered."[9] The FDA also announced the public availability of additional EDS-related scientific information and adverse event reports, and it again invited interested parties to submit comments and new information supporting the safety of EDS. Later, the FDA extended (and, at one point, reopened) this comment period. And, in August 2000, a public meeting was held to discuss the safety of EDS.

After more scientific evidence about the risks of EDS came to light, the FDA — for the fifth time — invited comment on its EDS proposal. With this invitation, the FDA proposed a

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[8] Dietary Supplements Containing Ephedrine Alkaloids, Withdrawal in Part, 65 Fed. Reg. 17,474, 17,475 (Apr. 3, 2000) (internal quotations omitted).

[9] *Id.*

warning statement for EDS. Tracking the language of § 342(f)(1) of the DSHEA, the FDA also stated that it intended to consider

> whether in light of current information FDA should determine that dietary supplements containing ephedrine alkaloids present a 'significant or unreasonable risk of illness or injury under conditions or use recommended or suggested in labeling, or if no conditions of use are suggested or recommended in the labeling, under ordinary conditions of use.'[10]

In whole, the administrative record on EDS comprises more than 132,000 pages. The FDA received more than 48,000 comments during its notice-and-comment periods, and the FDA collected information on about 19,000 complaints or adverse events from EDS use. During the course of this rulemaking process, Nutracuetical responded to the FDA's request for comments several times, requesting regulatory exemptions for low-dose EDS.

On April 12, 2004, the FDA's final rule regarding EDS took effect. Under the final rule, parties can no longer market EDS in the United States — the FDA banned EDS at all dosage levels. In reaching the final rule, the FDA noted that it looked at the "well-known pharmacology of ephedrine alkaloids, the peer-reviewed scientific literature on the effects of ephedrine alkaloids, and the adverse events reported to have occurred in individuals following consumption of dietary supplements containing ephedrine alkaloids."[11] In the final rule, the FDA described, in detail, the short-term and long-term medical risks EDS pose to consumers. For instance, it cited evidence of increased blood pressure and resulting conditions such as stroke, heart attack, death,

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[10] Dietary Supplements Containing Ephedrine Alkaloids; Reopening of the Comment Period, 68 Fed. Reg. 10,417, 10,419 (Mar. 5, 2003) (quoting 21 U.S.C. § 342(f)(1)(A)).

[11] Final Rule Declaring Dietary Supplements Containing Ephedrine Alkaloids Adulterated Because They Present an Unreasonable Risk, 69 Fed. Reg. 6788, 6788 (Feb. 11, 2004).

and increased morbidity from heart failure and abnormal heart rhythms. Ultimately, the FDA concluded "[t]he best clinical evidence for a benefit [from EDS use] . . . supports only a modest short-term weight loss, insufficient to positively affect cardiovascular risk factors or health conditions associated with being overweight or obese."[12] The FDA determined, based on its risk-benefit analysis, that under all ordinary or recommended conditions of use, EDS present an "unreasonable risk of illness or injury."[13] Accordingly, in the final rule, the FDA classified EDS as an adulterated substance under the DSHEA.

Procedural Background

In April 2005, this court (Campbell, J.) granted summary judgment to Nutraceutical on its claim that the FDA's final rule banning the sale of EDS violated 21 U.S.C. § 342(f)(1). Specifically, this court found the FDA's use of a risk-benefit analysis to support the final rule was contrary to Congress' intent and that the FDA failed to establish EDS posed an unreasonable risk of illness or injury at a dose of ten milligrams or less a day. The defendants appealed. On August 17, 2006, the Tenth Circuit reversed this court's decision and directed the court to enter summary judgment for the defendants and against Nutraceutical. Specifically, the Tenth Circuit held that "Congress unambiguously required the FDA to conduct a risk-benefit analysis under DSHEA."[14] According to the Tenth Circuit, the FDA had demonstrated that *any dose* of EDS posed an unreasonable risk of illness or injury, so the FDA's decision to ban EDS completely

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[12] *Id.* at 6789.

[13] *Id.* at 6788.

[14] *Nutraceutical*, 459 F.3d at 1038.

was justified.[15] The Tenth Circuit remanded the case, and it was reassigned to the undersigned judge. In accordance with the Tenth Circuit's mandate, this court entered summary judgment for the defendants with regard to Nutraceutical's statutory challenge to the FDA's ban of EDS. This court then ordered further briefing on Nutraceutical's two remaining causes of action. Nutraceutical filed a motion for summary judgment on these two causes of action on December 20, 2006. The defendants responded by filing a cross-motion for summary judgment on January 18, 2007.

SCOPE AND STANDARD OF REVIEW

In its pleadings, Nutraceutical seeks review of procedural and substantive components of the FDA's final rule, under the APA.[16] Specifically, Nutraceutical asserts (1) the FDA violated the APA by neglecting to adequately follow publication and comment requirements when adopting its final rule, and (2) the FDA acted in an arbitrary and capricious manner in violation of the APA when it banned EDS but failed to bring other products that contain ephedrine alkaloids, such as food and traditional Asian medicines, within reach of the final rule.

Although Nutraceutical requests judicial review of agency action under the APA, it styles its motion as a motion for summary judgment. The defendants respond in kind, but point out that "[r]eviews of agency action in the district courts must be processed *as appeals*."[17] The use of summary judgment procedures in administrative appeals is prohibited because such procedures

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[15] *Id.* at 1040–43.

[16] *See* 5 U.S.C. §§ 553, 706.

[17] *Olenhouse v. Commodity Credit Corp.*, 42 F.3d 1560, 1580 (10th Cir. 1994).

"are conceptually incompatible with the very nature and purpose of an appeal."[18] In light of this, the court has treated the motions of Nutraceutical and the defendants as cross-appeals. Consequently, the court has substantively reviewed the administrative record to assess the FDA's actions and has considered no evidence outside of the administrative record and no *post hoc* rationalizations of counsel.[19]

Section 701 of the APA provides courts with authority to review agency actions unless there is a statutory prohibition on such review or the action is committed to agency discretion as a matter of law.[20] Neither prohibition appears to be at issue here. In a case such as this one, the "essential function of judicial review is a determination of (1) whether the agency acted within the scope of its authority, (2) whether the agency complied with prescribed procedures, and (3) whether the action is otherwise arbitrary, capricious, or an abuse of discretion."[21] The FDA's authority is not at issue here, but Nutraceutical challenges its compliance with procedures and the arbitrariness and capriciousness of its action pursuant to the APA.

Section 706 of the APA governs judicial review of both formal and informal agency action. This section mandates that the

> reviewing court . . . hold unlawful and set aside agency action, findings, and conclusions found to be —

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[18] *Id.*

[19] *See id.*

[20] *Thomas Brooks Chartered v. Burnett*, 920 F.2d 634, 641–42 (10th Cir. 1990) (construing 5 U.S.C. § 701 (a)(1)–(2)).

[21] *Olenhouse*, 42 F.3d at 1574.

(A) arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law;

(B) contrary to constitutional right, power, privilege, or immunity;

(C) in excess of statutory jurisdiction, authority, or limitations, or short of statutory right;

(D) without observance of procedure required by law . . . .[22]

Although a presumption of regularity attaches to agency decisions, the presumption does not prevent courts from conducting "a thorough, probing, in-depth review."[23]

DISCUSSION

The parties have asked the court to determine whether the FDA's promulgation of the final rule was inconsistent with APA requirements; specifically, the notice-and-comment requirement and the prohibition against arbitrary and capricious agency action. The court finds the FDA's process and its final rule to be compliant with the APA's notice-and-comment requirements. Further, the FDA acted consistently with the statutory scheme by excluding non-dietary supplement products containing ephedrine alkaloids from the reach of the final rule. Accordingly, the court finds Nutraceutical has failed to meet its burden in challenging the FDA's action under the APA.

I. THE FDA'S COMPLIANCE WITH PRESCRIBED PROCEDURES — NOTICE AND COMMENT

Nutraceutical first alleges the FDA's rulemaking was invalid because it failed to comply with the APA's publication requirements and comment requirements. With regard to publication, Nutraceutical provides no support for its objections. The APA contains broad and

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[22] 5 U.S.C. § 706.

[23] *Citizens to Preserve Overton Park v. Volpe*, 401 U.S. 402, 415 (1971).

comprehensive publication requirements for agencies.[24] But Nutraceutical fails to indicate which provision the FDA violated or to offer any evidence to support such a claim. Instead, Nutraceutical's failure-to-publish argument seems more like a sufficiency-of-notice argument under 5 U.S.C. § 553, so the court addresses it as such.

With regard to notice and comment, Nutraceutical generally objects to the FDA's alleged failure to comply with the APA's requirements and Nutraceutical alleges pointed and specific notice-and-comment failures by the FDA. In particular, Nutraceutical objects to the FDA's alleged announcement of a consolidated standard in its proposed rule, then rejection of that standard in its final rule, and to the FDA's alleged failure to follow notice-and-comment procedures before adopting a risk-benefit analysis. In addition, Nutraceutical claims that in violation of notice-and comment procedures, the FDA rejected the requirement from its proposed rule that harm from EDS be established causally, and it created a standard for all dietary supplements in the final rule instead of limiting the standard to EDS, as in the proposed rule.

A. *General Challenge to Notice-and-Comment Procedures*

Section 553 of the APA sets forth the procedures agencies must follow in rulemaking.[25] First, the agency must give notice of the proposed rulemaking:

> General notice of proposed rule making shall be published in the Federal Register, unless persons subject thereto are named and either personally served or otherwise have actual notice thereof in accordance with law. The notice shall include . . . either

[24] *See* 5 U.S.C. § 552.

[25] *See id.* § 553.

> the terms or substance of the proposed rule or a description of the subjects and issues involved.[26]

But "the notice need not specifically identify 'every precise proposal which [the agency] may ultimately adopt as a final rule.'"[27] Notice is adequate if it allows for meaningful public participation by "'fairly appris[ing] interested persons' of the nature of the rulemaking."[28]

After the agency provides the requisite notice, it must provide an opportunity for comment: "the agency shall give interested persons an opportunity to participate in the rule making through submission of written data, views, or arguments with or without opportunity for oral presentation."[29] The APA requires only limited opportunity to participate — no more. To impose on the FDA more stringent procedural requirements than called for in § 553 would violate the Supreme Court's direction that agencies must have discretion to formulate their own procedures.[30]

After an agency subjects a proposal to this notice-and-comment process, it often publishes a final rule. But it is not unusual for an agency's final rule to differ from its proposed rule. Change is often a natural result of the notice-and-comment procedure:

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[26] *Id.* § 553(b).

[27] *Chemical Mfrs. Ass'n v. EPA*, 870 F.2d 177, 203 (5th Cir. 1989) (quoting *United Steelworkers of Am. v. Schuylkill Metals*, 828 F.2d 314, 317 (5th Cir. 1987)).

[28] *United Steelworkers of Am. v. Marshall*, 647 F.2d 1189, 1221 (D.C. Cir. 1980) (quoting *Am. Iron & Steel Inst v. EPA*, 568 F.2d 284, 293 (3d Cir. 1977)).

[29] 5 U.S.C. § 553(c).

[30] *See Vermont Yankee Nuclear Power Corp. v. Natural Res. Defense Council*, 435 U.S. 519, 543 (1978).

> That an agency changes its approach to the difficult problems it must address does not signify the failure of the administrative process. Instead, an agency's change of course, so long as generally consistent with the tenor of its original proposals, indicates that the agency treats the notice-and-comment process seriously . . . .[31]

The rule allowing an agency to make changes to its proposed rule after the notice-and-comment period has ended, without requiring the agency to elicit a new round of comments, is "well settled and sound."[32] "To hold otherwise would 'lead to the absurdity that in rule making under the APA the agency can learn from the comments on its proposals only at the peril of starting a new procedural round of commentary.'"[33] Generally, if the final rule is a "logical outgrowth" of the proposed rule, the notice of proposed rulemaking will be sufficient to forecast the final rule.[34]

In this case, the FDA provided the public with generous notice that it planned to regulate EDS under 21 U.S.C. § 342(f)(1)(A). The FDA published its proposed rule in the Federal Register in 1997, flagging its concerns about the safety of EDS.[35] In total, the EDS rulemaking process spanned seven years and included five comment periods — the FDA received over 48,000 comments. During this time, the FDA continued to release additional scientific evidence

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[31] *Am. Med. Ass'n v. United States*, 887 F.2d 760, 767 (7th Cir. 1989).

[32] *Beirne v. Sec'y of the Dep't of Agric.*, 645 F.2d 862, 865 (10th Cir. 1981).

[33] *Id.* (quoting *Int'l Harvester Co. v. Ruckelshaus*, 478 F.2d 615, 632 n.51 (D.C. Cir. 1973)); *see also Small Refiner Lead Phase-Down Task Force v. EPA*, 705 F.2d 506, 546–47 (D.C. Cir. 1983).

[34] *See Small Refiner*, 705 F.2d at 547; *see also Am. Mining Congress v. Thomas*, 772 F.2d 617, 637 (10th Cir. 1985).

[35] Dietary Supplements Containing Ephedrine Alkaloids, 62 Fed. Reg. 30,678 (June 4, 1997).

as well as information on the ever-increasing, EDS-related complaints and adverse event reports submitted to the FDA.

These extensive notice-and-comment efforts easily meet APA requirements, even though the FDA's final rule differed from the proposed rule, because the final rule was a logical outgrowth of the 1997 proposal. Indeed, it would seem odd for the FDA to continue to endorse its proposed rule after reviewing such an extensive and long-spanning record. The notices in the Federal Register between 1997 and 2004 more than adequately revealed the subject matter of the final rule and foreshadowed the probable outcome. In other words, in light of the Federal Register notices, the final rule was foreseeable. First, both the proposed rule and the final rule address the adulteration of EDS and degree and type of restrictions necessary to manage the risks of EDS. And from 1997 until 2004, the FDA repeatedly gave notice that it was specifically considering whether the FDA should find EDS adulterated (and, therefore, prohibited) under 21 U.S.C. § 342(f)(1)(A). In both the final and the proposed rules, the FDA cited the adulteration standard of § 342(f)(1)(A) as a basis for its regulatory authority. Also, in the record accompanying the proposed rule, the FDA discussed the specific range of alternatives it had available to it. As one option, the FDA considered "[b]an[ning] dietary supplements that contain ephedrine alkaloids."[36] Expounding on this option, the FDA pointed to a significant reduction in the expected number of adverse events that would result from such a ban. This notice alone amply alerted the public that the FDA might adopt a final rule that included any strategy

[36] *Id.* at 30,705.

available under the DSHEA to regulate EDS and it forecast the possibility that the FDA would ultimately decide to ban EDS.

The unfolding of the "comment" process also lends support to the conclusion that the FDA's notice was adequate. Each of the five times it opened up comment periods, the FDA specifically requested information about the safety of EDS. And when the FDA solicited comments in March 2003, it requested comments on whether EDS posed an unreasonable risk of illness or injury under § 342(f)(1)(A), forecasting its use of this standard in the final rule. Additionally, the comments submitted to the FDA demonstrate the adequacy of the notice. For example, a number of comments submitted specifically address a risk-benefit analysis when discussing "unreasonable risk." Such comments, while not determinative of the adequacy of the notice, provide support for a finding that the final rule was a logical outgrowth of the proposed rule.[37] Therefore, although the extent of the regulatory restrictions in the final rule differed from the proposed rule, the progression to the final rule was predictable.

Nutraceutical's own participation in the rulemaking process belies its claims that the FDA provided statutorily inadequate notice or failed to comply with comment requirements. Nutraceutical was repeatedly involved in the process — from 1997 to the time the FDA promulgated the final rule — submitting detailed comments. That the FDA was unpersuaded by Nutraceutical's requests to exempt its product from regulation does not call into question the sufficiency of the FDA's notice-and-comment procedures. Nutraceutical had notice the FDA might adopt any degree of regulation required to address its concerns about the safety of EDS and

[37] *See Shell Oil Co. v. EPA*, 950 F.2d 741, 757 (D.C. Cir. 1991).

Nutraceutical had a full and fair opportunity to comment on all significant issues during the rulemaking process.

In sum, the court cannot find the notice-and-comment procedures the FDA followed to be violative of § 553 or to be otherwise constitutionally impermissible. The FDA fairly apprised interested parties of the nature of the rulemaking and provided them with a meaningful opportunity to participate.

B. *Specific Challenges to Notice-and-Comment Procedures*

In addition to making a general challenge to the sufficiency of the notice-and-comment procedures afforded by the FDA, Nutraceutical specifically objects to the FDA's alleged announcement of a consolidated standard in its proposed rule, then rejection of that standard in its final rule. And Nutraceutical argues the FDA should have subjected its adoption of a risk-benefit analysis to notice-and-comment procedures. Further, Nutraceutical claims the FDA violated notice-and-comment requirements by moving from a causal requirement in its proposed standard to no such requirement in its final rule, and by announcing a standard for all dietary supplements in the final rule even though it limited the proposed rule to EDS.

1. Rejection of a Consolidated Standard

Nutraceutical argues the FDA violated the APA by failing to provide notice and an opportunity to comment on its alleged change from a "consolidated" standard in its 1997 proposal to a risk-benefit analysis in its final rule. At the outset, this particular challenge appears to be foreclosed because it is a new argument — Nutraceutical did not raise this alleged policy change in its complaint or its statement of the causes of action remaining. In both documents,

Nutraceutical alleged only that the FDA "failed to provide advance notice and opportunity for public comment on its new risk/benefit standard" in violation of the APA.[38] This omission forecloses Nutraceutical's argument, since the purpose of the parties' briefs and this order is to deal with the remaining issues in the case — not to address new arguments.

Even if Nutraceutical had properly made this allegation, the claim fails on the merits. Nutraceutical's claim fails because the FDA never expressed an intent to rely on a consolidated standard and never actually relied on such a standard. This undercuts Nutraceutical's entire argument, because unless the FDA used a consolidated standard or expressed an intent to rely on such a standard, the FDA could not reject or alter the standard. And the FDA would have no requirement to provide notice or request comment on a nonexistent standard. Nutraceutical contends that in the FDA's proposed rule, it combined the adulteration standard of "injurious to health" from § 342(a)(1), with both the "significant risk" and "unreasonable risk" standards from § 342(f)(1)(A). This newly-created standard, argues Nutraceutical, consolidated standards for dietary supplements and conventional foods into one. The FDA responds that it referred to both the "injurious to health" standards and the "significant or unreasonable risk" standards as independent bases for finding EDS to be adulterated, but it never consolidated the two standards.

In its proposed rule, the FDA tentatively determined that, to effectively address the risks of EDS, several measures needed to be addressed, including: (1) limiting ephedrine alkaloids to less than eight milligrams per serving; (2) requiring the label to limit ephedrine alkaloids to an intake of less than eight milligrams in a six-hour period and a total daily intake of less than

[38] Compl. 11, ¶ 46 (Docket No. 1).

twenty-four milligrams; (3) requiring the label to state that the product should not be used for more than seven days; and (4) prohibiting the use of ingredients with stimulant effects in combination with EDS. The FDA specifically cited to § 342(f)(1)(A) in its discussion of the each of these four factors. With regard to the first measure, the FDA also determined that a finding of adulteration possibly could be supported by § 342(a)(1) because a level of ephedrine alkaloids higher than eight milligrams may make the supplement injurious to health.

Nutraceutical stretches things too far by claiming this citation to two different provisions of the FDCA as authority for the FDA's proposal somehow creates a new policy or consolidated standard. The plain language of the proposed rule supports the FDA's claim that the standards remain distinct. Nutraceutical repeatedly cites the following language from the proposed rule:

> Based on the available evidence and the likely sources of measurement error around estimated intake levels, the agency tentatively concludes that the use of dietary supplements containing 8 mg or more ephedrine alkaloids per serving may render the dietary supplement injurious to health. The agency also tentatively concludes that consumption of dietary supplements that contain this level or more of ephedrine alkaloids presents a significant and unreasonable risk of illness or injury under the conditions of use recommended or suggested in the labeling . . . .[39]

But the court fails to see how this passage supports Nutraceutical's claim. Nowhere does the FDA state (or even imply) it adopted a standard combining § 342(a)(1) with § 342(f)(1)(A). Rather, the FDA again referred to two possible grounds for its regulatory approach. It tentatively concluded EDS containing eight or more milligrams of ephedrine alkaloids might be injurious to health under § 342(a)(1). It *also* tentatively concluded these same EDS posed both a significant and an unreasonable risk under § 342(f)(1)(A). This wording does not indicate a combined

[39] Dietary Supplements Containing Ephedrine Alkaloids, 62 Fed. Reg. at 30,693.

standard of "injurious to health" and "significant risk" and "unreasonable" risk, nor does it indicate the FDA consolidated the standards applicable to conventional foods with those applicable to dietary supplements. This citation to and use of two independent grounds of authority provided notice the FDA might rely on either or both of the provisions in the final rule — it did not constitute an adoption of a consolidated standard.

As further evidence that the FDA had endorsed a standard (the consolidated standard) and departed from it, Nutraceutical cites to the FDA's statement in the final rule that it was pronouncing an unreasonable risk standard for the first time. Nutraceutical repeats the "first time" language again and again in its pleadings, as if the phrase somehow magically proves the FDA utilized statutorily inadequate notice-and-comment procedures. But the defendants persuasively explain that with this language, the FDA was simply noting that it had not removed products from the market under the DSHEA's adulteration of dietary supplements provision before.

This explanation is consistent with and supported by the FDA's own language in the administrative record. In the final rule, the FDA explained that it used its rulemaking authority to address EDS because it was "articulating a standard for unreasonable risk under 402(f)(1)(A) [§ 342(f)(1)(A)] of the act for the first time and because it is more efficient to declare these products adulterated as a category than to remove them from the market in individual enforcement actions."[40] In other words, the FDA simply observed that because it was interpreting the adulteration standard of § 342(f)(1)(A) for the first time, it used its rulemaking

[40] Final Rule, 69 Fed. Reg. at 6794.

power (with the attendant notice-and-comment procedures) — not that it was articulating a brand new standard for the first time in the final rule. In sum, nothing in this passage supports Nutraceutical's contention that the FDA utilized, then rejected, a consolidated standard in favor of the risk-benefit standard.

Nutraceutical also argues the FDA conflated or combined the standards of "significant" with "unreasonable" when discussing the degree of risk pursuant to § 342(f)(1)(A). Specifically, Nutraceutical argues the FDA's reference, in its 1997 proposal, to the "significant *and* unreasonable" risk posed by EDS,[41] establishes that the FDA initially interpreted § 342(f)(1)(A) as containing a single adulteration standard. In other words, Nutraceutical alleges the FDA viewed "significant" and "unreasonable" as conjunctive, rather than as disjunctive standards. According to Nutraceutical, by focusing on the unreasonable risk posed by EDS in the final rule, the FDA divorced these concepts. Because the FDA did not provide notice or request comment on this change, argues Nutraceutical, it was impossible to foresee the FDA's reliance on the unreasonable risk standard in the final rule. Again, Nutraceutical's argument founders on the plain language in the administrative record. Multiple times in the record accompanying the proposed rule, the FDA referred to the adulteration standard as requiring a showing of a significant *or* an unreasonable risk. Only in the FDA's conclusory section did it refer to the risk as significant *and* unreasonable. In doing so, the FDA merely expressed its opinion that EDS would be adulterated under both prongs of § 342(f)(1)(A) — that the risk was significant and it was unreasonable. It is illogical to argue that because the FDA used "and" between the terms

[41] Dietary Supplements Containing Ephedrine Alkaloids, 62 Fed. Reg. at 30693.

instead of using separate sentences, the FDA failed to recognize the independent nature of the terms or to give "significant risk" a meaning separate and independent from "unreasonable risk."[42]

In short, Nutraceutical's argument that the FDA adopted, then rejected, a consolidated standard without providing for sufficient notice and comment fails. Because a consolidated standard never existed, it is impossible for the FDA to have departed from the standard without sufficient allowance for notice and comment.

2. Risk-Benefit Analysis

Nutraceutical next alleges the FDA failed to comply with the notice-and-comment requirements of the APA by defining "unreasonable risk" under § 342(f)(1)(A) in the final rule as requiring a risk-benefit analysis. Nutraceutical argues the FDA needed to provide notice and solicit comments with respect to its intent to use the risk-benefit interpretation and the weight it intended to assign to each term. The defendants respond that the FDA was not required to subject its risk-benefit standard to notice-and-comment procedures because it rests on a congressional statute rather than an FDA initiative.

Under the APA, notice-and-comment requirements apply to substantive rules established via rulemaking.[43] A substantive rule is a rule that "'establishes a standard of conduct which has

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[42] Insofar as Nutraceutical argues the FDA erred by failing to give full weight to the significance of the risk under § 342(f)(1)(A), the argument fails. The Tenth Circuit decided "unreasonable risk" had independent meaning and the FDA met its statutory burden under DSHEA by regulating EDS pursuant to the phrase "unreasonable risk." *See Nutraceutical*, 459 F.3d at 1039–40, 1044.

[43] *See* 5 U.S.C. § 553.

the force of law.'"[44] Interpretive rules, on the other hand, are subject to no such requirements.[45] To hold that an agency must follow notice-and-comment procedures when interpreting statutory language would lead to unreasonable results. It would effectively require agencies to submit their interpretations of each word in the statutes over which they have enforcement authority to the public for comment. Only after receiving comment and releasing an official interpretation of each statutory term could the agency undertake notice and comment on its proposed regulation — its substantive rule. Following Nutraceutical's logic, an agency could technically be required to submit for public comment its definitions of the terms it used to define statutory terms. This type of requirement would make timely rulemaking impracticable. Agencies have inherent authority to interpret terms in statutes over which they have enforcement authority, and mere interpretations of statutory language are not subject to the notice-and-comment provisions of the APA.[46]

The interpretation of the phrase "unreasonable risk" falls squarely within the FDA's inherent authority to interpret statutory terms it has authority to enforce. Congress imposed the requirements and standards at issue with its enactment of the DSHEA. The plain language of the DSHEA directs the FDA to "restrict distribution of dietary supplements which pose *any risk* that is unreasonable in light of its *potential benefits*."[47] By interpreting and implementing the

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[44] *Am. Mining Congress*, 671 F.2d at 1263 (quoting *Pac. Gas & Elec. Co. v. Fed. Power Comm'n*, 506 F.2d 33, 38 (D.C. Cir. 1974)).

[45] *See* 5 U.S.C. § 553(b).

[46] *See York v. Sec'y of Treasury*, 774 F.2d 417, 420 (10th Cir. 1985).

[47] *Nutraceutical*, 459 F.3d at 1038 (emphasis added).

"unreasonable risk" standard as requiring a risk-benefit analysis, the FDA did not make new law. It interpreted a specific statutory term, but imposed no new requirements and made no discretionary judgment as to how to implement a statutory mandate. Only the final EDS rule is a substantive rule which establishes "a standard of conduct which has the force of law."[48] But as discussed before, the final rule was appropriately subject to the APA's notice-and-comment requirements with regard to the FDA's consideration of whether to find EDS adulterated under § 342(f)(1)(A).

The Tenth Circuit's opinion on appeal further obviates any argument that the FDA violated the APA by failing to give notice of its intended use of a risk-benefit analysis. The Tenth Circuit determined that in assessing whether EDS poses an unreasonable risk of illness or injury, "Congress unambiguously required the FDA to conduct a risk-benefit analysis under DSHEA."[49] In other words, the "unreasonable risk" standard absolutely requires the risk-benefit analysis the FDA used[50] — the FDA interpreted the term correctly and simply followed congressional directive.[51] Therefore, the risk-benefit interpretation of "unreasonable risk" was a logical outgrowth of the proposed rule — a proposal which relied in part on the "unreasonable risk" standard. As a side note, to the extent that any of Nutraceutical's contentions reargue the

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[48] *Am. Mining Congress*, 671 F.2d at 1263.

[49] *Nutraceutical*, 459 F.3d at 1038.

[50] *See id.*

[51] *Id.* at 1043.

statutory meaning of "unreasonable risk" or the FDA's adoption of a risk-benefit analysis, the court rejects them in light of the Tenth Circuit's decision on the appeal.

In sum, Nutraceutical conflates the FDA's interpretation of the statutory standard of "unreasonable risk" with the creation of a new standard. Although the final rule is substantive, in light of the language of the DSHEA, the FDA's interpretation of "unreasonable risk" cannot be called substantive rulemaking. Because the FDA's interpretation of "unreasonable risk" in § 342(f)(1)(A) constitutes an interpretive rule, as opposed to a substantive rule, the FDA had no requirement to subject the adoption of the risk-benefit analysis of "unreasonable risk" to notice-and-comment procedures.

3. Causation and Scope Objections

Finally, Nutraceutical alleges that in violation of the APA's notice-and-comment requirements, the FDA moved from a requirement to establish harm from EDS causally in the proposed rule to no such requirement in the final rule, and the FDA limited the proposed rule to EDS but created a standard for all dietary supplements in the final rule. Both arguments are meritless.

Nutraceutical supports its contention that the proposed rule required proof EDS caused harm by citing the FDA's discussion of adverse event reports. But in this discussion, the FDA never adopted a causal standard. Instead, the FDA legitimately assessed the underlying causal relationship of EDS with adverse events in order to avoid the "serious misinterpretation of data" that may spring from "inappropriately assuming that a cause and effect relationship exists

between a particular exposure and a particular adverse event."[52] Neither this assessment nor the FDA's use of adverse event reports (essentially, complaints that EDS caused harm) to support its EDS restrictions transforms the FDA's risk standard into a causation standard. The proposed rule never required (or even implied) actual harm had to be established by causation. Instead, both the proposed rule and final rule focused on the *risk* of harm, in accordance with the plain-language requirement of § 342(f)(1)(A). As but one example of this focus, in the proposed rule, the FDA specifically noted that adverse events from EDS "occur in individuals who have no apparent *risk* factors, or who are unaware that they are at *risk*."[53]

At some points in its pleadings, Nutracuetical presents a slightly different twist to this same argument. Rather than claiming the FDA first required proof EDS caused harm, then rejected this requirement, Nutraceutical alleges the FDA adopted, then rejected, a standard "where harm *could be* proven causally."[54] This variation of the theme fails to help Nutraceutical. That the proposed standard allegedly could be proven causally and the final standard could not is a non-issue in light of the fact that the FDA never adopted a causal component. In other words, this variation in how the standards could be met does not change the sufficiency of the notice-and-comment procedures the FDA afforded or undermine the predictability of the final rule.

The administrative record similarly fails to support Nutraceutical's claim that the final rule covered all dietary supplements while the proposed rule applied only to EDS. The plain

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[52] Dietary Supplements Containing Ephedrine Alkaloids, 62 Fed. Reg. at 30,689–90.

[53] *Id.* at 30,693 (emphasis added).

[54] Pls.' Reply in Supp. of Mot. for Summ. J. 2 (Docket No. 54) (emphasis added).

language of the proposal and the final rule constitutes the clearest evidence that both rules applied only to EDS. First, the proposed rule was entitled "Dietary Supplements Containing Ephedrine Alkaloids,"[55] and the final rule was entitled, "Final Rule Declaring Dietary Supplements Containing Ephedrine Alkaloids Adulterated Because They Present an Unreasonable Risk."[56] Next, the language within the final rule specifically brings EDS within its ambit, not other dietary supplements: "[t]his final rule applies to dietary supplements containing ephedrine alkaloids."[57] Indeed, the FDA responded to a comment challenging the "unreasonable risk" standard by explaining the limited reach of its rule: "We are using our general rulemaking authority . . . to issue a regulation applying the ["unreasonable risk"] standard in the context of a particular category of dietary supplements — those that contain botanical ephedrine alkaloids."[58] Nutraceutical cites to no language in the final rule indicating an intent to create a new adulteration standard for all dietary supplements. If, with its argument, Nutraceutical is objecting to the effect the FDA's adoption of a risk-benefit analysis of "unreasonable risk" might ultimately have on the regulation of other dietary supplements pursuant to § 342(f)(1)(A), Nutraceutical's objection also fails. The FDA explicitly limited its rulemaking and the reach of its final rule to EDS. It is unreasonable to ask the FDA to predict future reverberations of its interpretation of "unreasonable risk" on other products. The FDA provided notice in the Federal

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[55] Dietary Supplements Containing Ephedrine Alkaloids, 62 Fed. Reg. at 30,678.

[56] Final Rule, 69 Fed. Reg. at 6788.

[57] *Id.* at 6793.

[58] *Id.* at 6796.

Register and accepted comments from all interested parties. All who believed they might be disadvantaged by this approach had the chance to be heard.

Ultimately, because the FDA's proposed rule did not include a causal component to establish harm, and the final rule applied only to EDS and did not create a standard for all dietary supplements, the FDA had no requirement to subject either "change" to notice-and-comment procedures.

II. THE FDA's REGULATION OF EDS ONLY — ARBITRARY AND CAPRICIOUS CHALLENGE

In addition to its notice-and-comment challenges, Nutraceutical calls the FDA's bar of EDS arbitrary and capricious since the FDA did not similarly prohibit ephedrine alkaloids in conventional foods or traditional Asian medicines. The defendants respond that the FDA simply and permissibly followed Congress' scheme by only prohibiting EDS.

"The APA reflects the principles of *Chevron* and 'provides that agency action must be set aside if the action was arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law' or if the action failed to meet statutory, procedural, or constitutional requirements."[59] Under this "arbitrary or capricious" standard, the court's review is "'narrow and deferential.'"[60] Regulations are presumed to be valid, and are subject only to rational basis review.[61] Agency action will be set aside only

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[59] *Nutraceutical*, 459 F.3d at 1038 (quoting *Valley Cmty. Pres. Comm'n v. Mineta*, 373 F.3d 1078, 1084 (10th Cir. 2004)).

[60] *Id.* (quoting *Slingluff v. Occupational Safety & Health Review Comm'n*, 425 F.3d 861, 866 (10th Cir. 2005)).

[61] *Id.*

> if the agency has relied on factors which Congress has not intended it to consider, entirely failed to consider an important aspect of the problem, offered an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise.[62]

When applying the arbitrary and capricious standard, the court focuses on the rationality of the decisionmaking process of the agency, not the rationality of the agency's actual decision.[63] From the facts in the record, the court must be able to conclude the agency's action was the product of reasoned decisionmaking.[64]

Contrary to Nutraceutical's claims, the FDA's separate regulation of EDS is not arbitrary or capricious because it is consistent with the regulatory scheme of the DSHEA. Agency power to make rules "carries with it the responsibility . . . to remain consistent with the government legislation."[65] The DSHEA requires the FDA to regulate dietary supplements differently than conventional foods — conventional foods and other drug products are subject to their own statutory and regulatory requirements, including some requirements to which dietary supplements are not always subject. And while some provisions of § 342 apply to all foods, certain provisions (such as § 342(f)(1)(A)) apply solely to dietary supplements and their ingredients.[66] Section 342(f)(1)(A), therefore, does not apply to conventional foods or traditional Asian medicines. In

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[62] *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983).

[63] *Olehouse*, 42 F.3d at 1575.

[64] *Id.*

[65] *Morton v. Ruiz*, 415 U.S. 199, 232 (1974).

[66] *See* 21 U.S.C. § 342(f)(1)(A).

other words, conventional foods and other types of products cannot be found adulterated under the unreasonable-risk provision of the DSHEA — and it is impossible for products to be arbitrarily exempted from a rule that could never have applied to them. Congress drew these regulatory distinctions, not the FDA. Considering that Congress specifically provided for this separate regulation of dietary supplements, the FDA's regulation of EDS separately from other ephedrine-alkaloid products is consistent with the statutory scheme. In its rulemaking, the FDA simply followed Congress' determination that dietary supplements be subject to a standard — the "unreasonable risk" standard — that does not apply to conventional foods. The court cannot say that by following Congress' provision, the FDA acted unreasonably or that it acted in an arbitrary or capricious manner.

Even if Congress' statutory scheme had not provided for separate and distinctive regulation of dietary supplements, the FDA's regulation of EDS (and not other ephedrine-alkaloid products) falls well within its discretion. In the absence of a congressional directive, much of the decision of when to regulate a specific substance, what substance to regulate, and how, must necessarily be left up to the FDA.[67] And in this case, the FDA faced a congressional directive to "take swift action against products that are unsafe or adulterated."[68] Thus, the court cannot say it was unreasonable for the FDA to focus on regulating EDS before focusing on the regulation of other products containing ephedrine alkaloids. The FDA had comprehensively reviewed the risks of EDS and, as the Tenth Circuit noted,

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[67] *See Vermont Yankee*, 435 U.S. at 543.

[68] DSHEA, 108 Stat. at 4326.

> [t]he FDA's extensive research identified the dose level at which ephedrine alkaloids present unreasonable risk of illness or injury to be so minuscule that no amount of EDS is reasonably safe. The FDA reasonably concluded that there is no recommended dose of EDS that does not present an unreasonable risk.[69]

As early as 1995, the FDA was faced with evidence of the adverse effects of EDS, and during its rulemaking, the FDA obtained information on about 19,000 complaints related to the use of EDS. There is no indication the FDA faced any similar evidence of the adverse effects of other products containing ephedrine alkaloids or that any similar impetus existed with regard to such products.

Indeed, the FDA considered the use of other products containing ephedrine alkaloids in its rulemaking, but noted that "conditions of use are so different."[70] "Not only are dietary supplements marketed for different uses than the traditional use of *Ephedra*, most dietary supplements are marketed in a form that is different than the form in which it has been traditionally used."[71] Because of these differences, the FDA found the use of ephedrine alkaloids in traditional Asian medicine would not forecast the safety or effects of EDS.[72] Ultimately, therefore, the court cannot say the FDA's decision to prohibit EDS without similarly prohibiting ephedrine alkaloids in conventional foods or traditional Asian medicines was unreasoned or otherwise arbitrary or capricious.

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[69] *Nutraceutical*, 459 F.3d at 1043.

[70] Dietary Supplements Containing Ephedrine Alkaloids, 62 Fed. Reg. at 30,705.

[71] *Id.*

[72] *Id.*

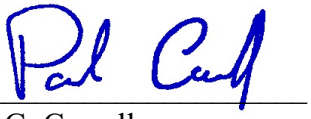
In short, the FDA acted in accordance with the statutory scheme by restricting the application of its final rule to EDS and restricting the scope of its regulatory activities to EDS. And even if no clear statutory scheme had existed, the FDA has authority to reasonably dictate the timing, scope, and manner of its own regulatory priorities. In other words, the FDA is free to proceed one step at a time.

CONCLUSION

The court finds the FDA's rulemaking with regard to EDS to be procedurally and substantively proper. Consequently, Nutraceutical's motion for summary judgment / appeal [#45] is denied, and the defendants' cross-motion for summary judgment / cross-appeal [#50] is granted. The Clerk's Office is directed to enter judgment accordingly and to close this case.

DATED this 16th day of March, 2007.

BY THE COURT:



Paul G. Cassell
United States District Judge