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MEMORANDUM

FROM: A. Wes Siegner, Jr.

SUBJECT: ConsumerLab.com Red Yeast Rice Product Review Is in Conflict with the Law and FDA Enforcement Policy, Creating Safety Issues for Consumers and Regulatory Issues for Industry

On July 1, 2008 ConsumerLab.com, LLC (ConsumerLab) published a product review of red yeast rice dietary supplements.¹ The review is troubling because statements in the review indicate that ConsumerLab does not understand the laws and regulations enforced by the Food and Drug Administration (FDA), particularly with regard to lovastatin. In short, ConsumerLab's review is in conflict with established FDA enforcement policy for red yeast rice products and, if the review is not corrected, will result in consumers purchasing and manufacturers supplying products virtually identical to other products that FDA has warned are unsafe and illegal.

Lovastatin is a naturally occurring compound in red yeast rice, and is also the active ingredient in the approved prescription drug Mevacor™, which is prescribed for lowering cholesterol. Under the provisions of the Federal Food, Drug, and Cosmetic Act (FDC Act) and applicable case law, FDA does not permit red yeast rice dietary supplements to (1) contain anything but trace amounts of lovastatin, (2) bear claims about the levels of lovastatin in the product, or (3) bear claims concerning the product's usefulness for lowering or reducing cholesterol. Through incorrect statements and implications, the ConsumerLab review encourages consumers to purchase and

¹ The ConsumerLab product review can be obtained from the ConsumerLab website, <http://www.consumerlab.com>.

manufacturers to supply dietary supplements containing levels of red yeast rice that FDA considers illegal and unsafe, for the specific purpose of lowering cholesterol, and criticizes industry for failing to label products for lovastatin content. ConsumerLab's review informs consumers of the various levels of lovastatin in marketed products and, by connecting these levels to published research showing cholesterol lowering effects, guides consumers to purchase products that contain between 5 and 15 mg of lovastatin (or 7 to 27 mg of lovastatin and a related monacolin, the hydroxy acid form of lovastatin). FDA has determined that such levels in any dietary supplement product would cause the product to be an illegal, unsafe drug and an "adulterated" (unsafe) food "in that it bears or contains a poisonous or deleterious substance (lovastatin) which may render it injurious to health." See, e.g., Letter to Nature's Way Products (Jan. 25, 2008).²

On behalf of our clients in the dietary supplement industry, we communicated the concerns contained in this memorandum to ConsumerLab on July 17, 2008, but have been informed that ConsumerLab does not plan to withdraw or amend its product review. Therefore, we have chosen to publish this memorandum as a warning to consumers and industry. Our detailed comments and an overview of FDA policy towards lovastatin are set forth below.

I. Overview of FDA Policies For Lovastatin

FDA's current policy towards lovastatin in red yeast rice supplements stems in part from enforcement actions taken against the marketing of Cholestin™, a red yeast rice dietary supplement that contained a significant amount of mevinolin, a natural form of lovastatin, the active ingredient in the approved prescription drug Mevacor™. Cholestin was marketed by Pharmanex for use in maintaining healthy cholesterol levels. In 1998, FDA reached a final decision with regard to the marketing of Cholestin. FDA determined that Cholestin was a drug, stating that "traditional red yeast rice is fermented at temperatures that preclude the production of significant levels of lovastatin." FDA decision re: Pharmanex, Docket No. 97P-0441 (Mar. 20, 1998).

Pharmanex brought an action in federal court seeking a review of FDA's determination that Cholestin was a drug. Pharmanex, Inc. v. Shalala, 35 F. Supp. 2d 1341 (D. Utah 1999), rev'd, 221 F.3d 1151 (10th Cir. 2000), remanded 2001 U.S. Dist. LEXIS 4598, at *1 (D. Utah Mar. 30, 2001). In Pharmanex, FDA argued that, because lovastatin was the active ingredient in an approved prescription drug, it could not be marketed in a dietary supplement. FDA argued that lovastatin did not meet the definition of "dietary supplement," because a "dietary supplement" is not allowed to include an

² http://www.fda.gov/foi/warning_letters/s6692c.htm.

article “approved as a new drug” unless the article was prior to “such approval . . . marketed as a dietary supplement or as a food.” See 21 U.S.C. § 321(ff)(3)(B).

The district court rejected FDA’s argument, concluding that the relevant “article” for purposes of 21 U.S.C. § 321(ff)(3)(B) is the finished product and that, because the finished product Cholestin was different from the finished product Mevacor, the relevant article was not the same. 35 F. Supp. 2d. at 1348-1349. However, the court of appeals reversed the district court’s decision, holding that “an article that is approved as a new drug” is ambiguous and therefore, the court would defer to FDA’s interpretation of the term. 221 F.3d at 1154, 1155-56, 1159.

On remand to the District Court, the Court concluded, based on the FDA’s findings “that (1) Pharmanex manufactures ‘Cholestin’ in a manner designed to ensure that the product contains significant amounts of lovastatin, and (2) Pharmanex promotes ‘Cholestin’ for its lovastatin content,” that Cholestin “is excluded from the definition of ‘dietary supplement’” pursuant to the prohibition on marketing approved drug ingredients in dietary supplement under the FDC Act, 21 U.S.C. § 321(ff)(3)(B). 2001 U.S. Dist. LEXIS 4598, at *5.

The decision in Pharmanex is based on the facts of that case and does not prohibit the marketing of all red yeast rice supplements. The mere presence of lovastatin in red yeast rice does not disqualify such products from classification as a dietary supplement. Red yeast rice meets all the statutory criteria for dietary supplements. Red yeast rice containing lovastatin was “marketed as a dietary supplement or as a food” before the FDA approved an investigational new drug application for lovastatin and before FDA approved lovastatin as a new drug in 1987, and is, therefore, a legal dietary ingredient in dietary supplements pursuant to 21 U.S.C. § 321(ff)(3)(B). The decision in Pharmanex shows that it is the purposeful manufacturing of a product with high lovastatin levels and the marketing of the specific ingredient “lovastatin” that cause dietary supplements like Cholestin to be in violation of 21 U.S.C. § 321(ff)(3)(B).

In recent Warning Letters FDA has asserted that traditional red yeast rice products contain only trace amounts of lovastatin, and has warned industry that dietary supplements that contain more than trace amounts of lovastatin are illegal and unsafe. For example, in January 2008, FDA sent a Warning Letter to Nature’s Way Products after an FDA laboratory analysis found that the company’s red yeast rice supplements, if taken as recommended, would provide “more than 14 mg lovastatin, which is approximately 4 mg more than the lowest recommended daily dose of lovastatin in Mevacor and its generic counterparts.” Letter to Nature’s Way Products (Jan. 25, 2008). FDA found that the level of lovastatin in the product resulted in violations of multiple provisions of the FDC Act, including the food “adulteration” provisions, “in that it bears or contains a poisonous or deleterious substance (lovastatin) which may render it

injurious to health.” FDA also found that the product was an unsafe and unapproved new drug.

FDA sent a very similar letter to Swanson Health Products, notifying the company that FDA considered Swanson’s red yeast rice supplement an unsafe new drug, among other FDC Act violations, because it contained more than 5 mg of lovastatin. Letter to Swanson Health Products (Aug. 8, 2007).³ FDA has also addressed similar issues in courtesy letters sent in response to claim notifications from industry.⁴ In both the Swanson and Nature’s Way letters, FDA objected to implied and direct claims that the products would lower cholesterol, claims that FDA has consistently found to be illegal “drug” rather than legal “dietary supplement” claims.

Consistent with FDA’s statements in Warning Letters that any red yeast rice products with more than trace levels of lovastatin and related monacolins are unsafe, FDA has detained and refused entry of numerous imports of bulk red yeast rice based on FDA test results showing more than trace levels of lovastatin. In short, the agency has aggressively and consistently prohibited the marketing of any dietary supplement products with more than trace amounts of lovastatin or other monacolins naturally present in red yeast rice, the marketing of the specific ingredient “lovastatin” as contained in any dietary supplement products, or the marketing of dietary supplements generally for lowering cholesterol.

Finally, it is important in the context of the ConsumerLab product review to understand that products are regulated pursuant to the FDC Act according to the “intended use” of the product, and that different products with the same ingredients may have different intended uses depending on the claims made on the label and other factors,

³ http://www.fda.gov/foi/warning_letters/s6455c.htm. See also, Letter to Sunburst Biorganics (Aug. 7, 2007) (product, if taken as directed, provided 10 mg of lovastatin), <http://www.fda.gov/foi/warning-letters/s6456c.htm>.

⁴ FDA has challenged the claim that a firm’s red yeast rice dietary supplement “is standardized to 1.5% mixed mevinolinic acid monacolins.” See FDA Courtesy Letter to Mr. Ira L. Goldberg, President, Source Naturals (Dec. 3, 2004) (LET797, Dkt.975-0163). FDA’s letter stated that “red yeast rice products containing lovastatin are unapproved new drugs. . . . The manufacturer [sic], importation, or distribution of red yeast rice products containing lovastatin may also violate other provisions of the act. Therefore, if the mevinolinic acid monacolins that are contained in your product include lovastatin or other substances excluded from dietary supplements under [21 U.S.C. § 321 201(ff)(3)(B)], your product can not be marketed as a dietary supplement.” Id.

including product advertising.⁵ Not all red yeast rice products are intended to be consumed to affect cholesterol levels, and some of the products in the ConsumerLab review make no cholesterol-related claims.

II. Errors in ConsumerLab's Product Review

A. ConsumerLab incorrectly assumes that the intended use of all of the reviewed products is for cholesterol control, and judges the products accordingly.

ConsumerLab's review begins by acknowledging that red yeast rice "has been used as a food and a traditional medicine in China for over 1,000 years (since 800 AD)." Indeed, numerous independent research references discuss a wide range of potential health benefits attributable to red yeast rice, including effects on cholesterol but also effects on blood sugar, cardiac health, weight control and others, for which consumers might seek to consume red yeast rice dietary supplements.⁶

For unexplained reasons, ConsumerLab's review evaluates red yeast rice products with respect to only one use – "red yeast rice taken daily for two or three months lowers total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides in people with elevated cholesterol" – and then compares the tested products for this use only.

We have not undertaken a comprehensive review of the labeling and advertising for all of the products that ConsumerLab has tested and reviewed, but ConsumerLab should have undertaken such a review since the only goal of ConsumerLab's product review was to compare products for potential efficacy for lowering cholesterol (a "drug" rather than a dietary supplement claim, which dietary supplements cannot legally make in any event). Some products in the ConsumerLab review do not appear to be marketed in any way for any effects on cholesterol, and therefore are not intended for such use under the FDC Act. ConsumerLab's review will lead consumers to conclude, incorrectly, that

⁵ See 21 U.S.C. § 321(g)(1)(B) ("the term 'drug' means articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease") and (ff)(1) ("the term 'dietary supplement' means a product (other than tobacco) intended to supplement the diet). FDA's regulations include a lengthy explanation of the meaning of the term "intended uses" for drug products. 21 C.F.R. § 201.128 (the intended use of a product "may, for example, be shown by labeling claims, advertising matter, or oral or written statements" by the manufacturer or other entities responsible for distribution of the product).

⁶ See, e.g., http://www.mayoclinic.com/health/red-yeast-rice/NS_patient-redyeast.

all of the products in the review are intended to be consumed for cholesterol effects, and that some of the products are, in ConsumerLab's judgment, ineffective for that purpose.

B. ConsumerLab has misstated FDA's position on lovastatin in red yeast rice, potentially causing safety issues for consumers and confusion in the regulated industry.

In a section of the product review titled "FDA Action," ConsumerLab seeks to summarize the regulatory situation as it pertains to red yeast rice. ConsumerLab's summary contains numerous significant errors.

Perhaps most glaring is ConsumerLab's failure to recognize that the recent Warning Letters to manufacturers of red yeast rice products were the result of numerous violations of the FDC Act caused not just by cholesterol lowering claims, but also by FDA's safety concerns over elevated levels of lovastatin and related monacolins in the products at issue. As reflected in the FDA warning letters, this error, if not corrected, could have a serious negative impacts on consumers and industry alike.

ConsumerLab's review recommends that consumers "focus on products that provide a combined daily dose of lovastatin and its hydroxyl acid form similar what [sic] has been shown to work clinically to reduce cholesterol." The studies ConsumerLab sites recommend anywhere from 5 to 15 mg of lovastatin. However, FDA has made it clear that marketing dietary supplements that provide as little as 5 mg of lovastatin cause the product to be an unsafe and illegal new drug, and FDA has also noted that products with more than the trace levels of monacolins naturally occurring in red yeast rice are adulterated, unsafe foods because of the adverse effects associated with higher levels of lovastatin.

In short, ConsumerLab's review will lead consumers to purchase illegal products with levels of monacolins that FDA has found to be unsafe. FDA has repeatedly warned manufacturers who market products with lovastatin levels that exceed trace amounts that "[f]ailure to promptly correct these violations may result in legal action without further notice, including, without limitation, seizure and injunction." See, e.g., Letter to Nature's Way Products (Jan. 25, 2008).

C. ConsumerLab's review is not sufficiently clear that labeling red yeast rice dietary supplement products as to lovastatin content or with claims to lower cholesterol is illegal.

Although the ConsumerLab review acknowledges that there are "regulatory issues" with listing levels of monacolins in red yeast rice products, the review implicitly criticizes dietary supplement companies for not listing the amount of lovastatin in the

supplements. The review states that “[t]here are no standards for amounts of lovastatin and other monacolins in red yeast rice dietary supplements” and, since red yeast rice products “do not indicate the levels of lovastatin and other monacolins, it is very difficult to compare products.” This criticism is in error in light of the Pharmanex decision and subsequent actions that prohibit any mention of lovastatin or related compounds on the label of dietary supplement products. By failing both to fully inform the public of the legal issues that are involved and to clarify that it is illegal to sell dietary supplements that are standardized for monacolins or that list the amounts of lovastatin or monacolins, ConsumerLab erroneously paints the dietary supplement industry in a negative light.

Finally, the ConsumerLab review creates confusion about the types of claims that are permitted for red yeast rice supplements. FDA consistently takes enforcement action against red yeast rice supplements that claim to improve or lower cholesterol or lipid levels. In the Warning Letter to Swanson Health Products, FDA stated that Swanson Health Product’s red yeast rice supplements were drugs under the terms of the FDC Act “because they are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease” as a result of product claims to “keep your blood lipid levels within a healthy range” and to lower total plasma cholesterol. Letter to Swanson Health Products (Aug 8, 2007). Without an explanation of what claims are acceptable under the law, consumers will have no real understanding of how to compare different red yeast rice products and will unwittingly look for products with cholesterol lowering claims such as those discussed in the ConsumerLab review.

III. Conclusion

The ConsumerLab product review of red yeast rice supplements makes incorrect statements about the law and FDA enforcement policy, and creates general confusion about the marketing of red yeast rice products. Most important, the review encourages consumers to purchase dietary supplements with high levels of monacolins that FDA has determined to be unsafe. Finally, the review could cause serious regulatory problems for companies that may try to market products that are illegal. As a result of our communications with ConsumerLab, we hope that the company will have a better understanding of FDA’s policy towards red yeast rice dietary supplements and will revise its product review accordingly.