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**CONFIDENTIAL COMMUNICATION****PURSUANT TO FRE****VIA EMAIL** [dtroy@oc.fda.gov](mailto:dtroy@oc.fda.gov)

Dan Troy  
Chief Counsel  
Food and Drug Administration  
5600 Fishers Lane  
Room 605, GCF-1  
Rockville, MD 20857

Dear Dan:

This letter responds to your request at our meeting of November 24, 2003 that I supply you with a further explanation concerning the agency's distinction between so-called "prevention" claims and so-called "treatment" claims, the former constituting ones FDA has said can be processed as health claims, the latter constituting ones FDA has said cannot be so processed. As you know, we take issue with this distinction finding no basis in the statute or legislative history underlying it to support such a distinction. As we see it, the term "health claim," defined in pertinent part in 21 U.S.C. 343(r) as any statement that "characterizes the relationship of a nutrient to a disease or health related condition," embraces any claim of treatment, prevention, cure, or mitigation. Without waiving this point, we nevertheless here proceed to explain why interpreting the chondroitin sulfate/ glucosamine claims before the agency as "treatment" claims conflicts with the agency's own definition of treatment claims and its prior precedent.

In its letter dated May 26, 2000, FDA first explained its position that the health claims provision of the statute does not embrace "claims for treatment of existing disease." There, then CFSAN Director Levitt asked "whether a claim about an effect on an existing disease is within the scope of the food labeling health claims provision of the FFDCA" (May 26, 2000 letter at 1). He characterized the saw palmetto extract claim there in issue as one "to relieve the symptoms of an existing disease" (May 26, 2000

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letter at 2)<sup>1</sup>. He concluded that "claims about effects on existing diseases do not fall within the scope of the health claim provisions in 21 U.S.C. § 343(r) and therefore may not be the subject of an authorized health claim" (May 26, 2000 letter at 3). This position has since become the precise one taken by the Department of Justice on FDA's behalf both at the trial level (see, e.g., Government's Motion to Dismiss at 27) and at the appellate level (see, e.g., Government's Opposition Brief at 27 and 39) in the saw palmetto case. The Government's Opposition brief containing that definition was appended to its October 3, 2003 decision letter on the glucosamine/chondroitin sulfate claims.

The claim in issue in the saw palmetto case concerns the effects of saw palmetto extract on reducing symptoms of mild BPH (urine flow, nocturia, and voiding urgency), not on reducing the risk of those symptoms. It differs from earlier claims FDA reviewed in that it does not concern disease risk reduction or prevention in healthy populations. For example, each of the claims in the Pearson v. Shalala case were framed in terms of disease risk reduction in healthy populations: consumption of antioxidant vitamins may reduce the risk of certain kinds of cancers; consumption of fiber may reduce the risk of colorectal cancer; consumption of omega-3 fatty acids may reduce the risk of coronary heart disease; and .8 mg of folic acid in a dietary supplement is more effective in reducing the risk of neural tube defects than a lower amount in foods in common form.

All of the chondroitin sulfate/glucosamine claims before the agency are likewise worded in terms of disease risk reduction in healthy populations (either referring to reduction in the risk of a disease or to reduction in the risk of disease conditions (joint pain, tenderness, and swelling; joint degeneration; cartilage deterioration)). The chondroitin sulfate/glucosamine claims are thus aimed at the general population and focus on disease risk reduction in that population. They are not aimed at parties with disease. The claims have been chosen intentionally to focus on disease risk reduction in healthy populations, not on treatment of diseased populations. We think a fair reading of the language of the actual claims begets that conclusion.<sup>2</sup>

<sup>1</sup> The saw palmetto claim reads: "Consumption of 320 mg daily of Saw Palmetto extract may improve urine flow, reduce nocturia and reduce voiding urgency associated with mild benign prostatic hyperplasia (BPH)."

<sup>2</sup> The claims concern the nutrients effects on reducing the risk of (1) osteoarthritis; (2) osteoarthritis-related joint pain, tenderness, and swelling; (3) joint degeneration; and (4) cartilage deterioration. Everyone is worded in terms of disease risk reduction, not treatment. They are:

Glucosamine may reduce the risk of osteoarthritis.

Chondroitin sulfate may reduce the risk of osteoarthritis.

Glucosamine and chondroitin sulfate may reduce the risk of osteoarthritis.

Glucosamine may reduce the risk of osteoarthritis-related joint pain, tenderness and swelling.

Chondroitin sulfate may reduce the risk of osteoarthritis-related joint pain, tenderness and swelling.

Glucosamine and chondroitin sulfate may reduce the risk of osteoarthritis-related joint pain, tenderness and swelling.

Glucosamine may reduce the risk of joint degeneration.

Chondroitin sulfate may reduce the risk of joint degeneration.

Glucosamine and chondroitin sulfate may reduce the risk of joint degeneration.

Glucosamine may reduce the risk of cartilage deterioration.

Chondroitin sulfate may reduce the risk of cartilage deterioration.

Glucosamine and chondroitin sulfate may reduce the risk of cartilage deterioration.

Thus it has been the position of the FDA until its letter concerning the glucosamine/chondroitin sulfate claim (dated October 3, 2003) that claims worded in terms of disease risk reduction are eligible for evaluation as health claims. The new position asks the reader to presume the plain language of the claims not to be the claims' true meaning, rather, the claims are said to mean what certain of the evidence underlying them can be interpreted to mean: i.e., disease treatment. Thus disease risk reduction claims are transformed through creative construction into disease treatment claims. That is said to follow logically from the fact that the science upon which the disease risk reduction claims are based is extrapolated, in certain instances, from treatment studies. That, we think, wholly illogical and a precedent counter to the goal of facilitating the dissemination of accurate information about the nutrient-disease relationship. It is also inconsistent with the agency's prior decisionmaking.

The argument that reliance on studies concerning the effects of nutrients in diseased populations transforms claims worded in terms of disease risk reduction into treatment claims appears for the first time in the agency's October 3, 2003 letter on the chondroitin sulfate/glucosamine claims. Until that letter, evidence from treatment studies had been used routinely by the agency and the petitioners in supporting differing positions on the credibility of scientific evidence concerning disease risk reduction claims. Consider two examples.

In the phosphatidylserine/dementia and phosphatidylserine/cognitive dysfunction claim context<sup>3</sup>, the scientific evidence supporting the risk reduction claims there in issue came from treatment studies (dealing with patients suffering from Alzheimer's, dementia, and senility). There, as here, there was no rigid line identifying when a person first contracted the diseases in question. Rather, the presence of a constellation of symptoms accounted for diagnosis of dementia and cognitive dysfunction; similarly, a constellation of symptoms accounts for diagnosis of osteoarthritis. There is no bright line demarcation at which we may say a person first contracted cognitive dysfunction of dementia. Likewise, here, there is no bright line demarcation at which we may say a person first contracted osteoarthritis. The diseases symptomology is multifaceted and chronic along a continuum and is preclinical until many symptoms coexist making the presence of the disease undeniable to diagnosticians. Yet, because credible evidence supports the role of phosphatidylserine in retarding loss of key parameters of mental function (a reasonable scientific extrapolation from the treatment studies), the phosphatidylserine claims were allowed. So too here, and on far greater evidence, credible evidence supports the role of glucosamine and chondroitin sulfate in retarding loss of joint function and mobility (a reasonable scientific extrapolation from the treatment studies but also from numerous other animal and *in vitro* studies) by supporting, rebuilding, and repairing the cartilage matrix.

Also, for example, it was a centerpiece of FDA's argument to the district court in the antioxidant vitamin/cancer claim case that there were no studies documenting that

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<sup>3</sup> It is important to bear in mind that the evidence supporting the chondroitin sulfate/glucosamine claim is substantially greater than the credible evidence supporting the phosphatidylserine claims.

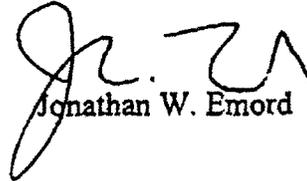
antioxidants interfered with cancer progression in diseased populations studied (evidence FDA thought indispensable to finding significant scientific agreement and to avoiding misleadingness). See, Whitaker v. Thompson, Government's Opposition to Plaintiff's Motion for Preliminary Injunction, US District Court for D.C., Case No. 01CV01539 (GK) filed 10/12/01. FDA was thus arguing that the antioxidant vitamin/cancer claim could not be made based on epidemiological evidence of risk reduction in the general population; rather, FDA demanded proof that antioxidants blocked cancer progression (i.e., FDA demanded proof of beneficial antioxidant effects in treatment studies). We present that point not to suggest that FDA was correct in its position, but to reveal that FDA has historically extrapolated from treatment studies when evaluating disease risk reduction claims and has found that evidence palpable proof, even beyond credible evidence. Indeed, extrapolating from treatment studies to the prevention context is a mainstay of modern science, a basic and common method employed by scientists in the evaluation of research, as became clear at the November 24, 2003 meeting.

In sum, the chondroitin sulfate/glucosamine claims are classic disease risk reduction claims, not treatment claims. The fact that our scientists extrapolate from treatment studies to the disease risk reduction context does not transform the claims into treatment claims. Adherence to the position taken in the October 3, 2003 letter errs not only because the claims are plainly worded in terms of disease risk reduction but also because that adherence requires acceptance of the unscientific proposition that extrapolation from treatment studies to the disease risk reduction context is an illegitimate scientific exercise. To the contrary, that extrapolation is legitimate and common in the scientific community.

Finally, adherence to the position taken in the October 3, 2003 letter creates a Hobson's choice for would-be petitioners. Under the October 3, 2003 letter, would-be petitioners understand that reliance on treatment studies will risk FDA recharacterization of risk reduction claims as treatment claims, rendering the claims ineligible for health claim review. But, alas, direct proof that a substance frustrates progression of a basic disease mechanism such that it could fend off initiation of that disease in the healthy is credible scientific evidence of such an effect and may well be the best evidence. Yet, despite that fact, a petitioner henceforth may have to discount that evidence in favor of reliance on less direct proof of beneficial effects (e.g., epidemiological evidence of hypothesized risk reduction in healthy populations, animal studies, or *in vitro* studies). Reliance on less direct proof may cause FDA to require use of a more draconian disclaimer (a C or D level disclaimer in the lexicon of the qualified claims guidance). Yet, imposition of that disclaimer will mislead in instances where, as in the present, the evidence is extremely strong of an actual disease risk reducing effect: repair and rebuilding of the cartilage matrix.

Thank you for this opportunity to explain in greater detail why we think it folly for the FDA to presume claims worded in terms of disease risk reduction are treatment claims solely on the basis that scientists extrapolate from treatment studies to the disease risk reduction context. If any further questions arise, please feel free to give me a call. We look forward to hearing from you.

Sincerely,



Jonathan W. Emord

cc: Dan Thomson;  
Todd Crowley;  
DeLois Shelton