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November 28, 2005 () 7 5 2 5 DEC 15 P1:57

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Comments on Qualified Health Claims in Food Labeling and the FDA Report entitled "Effects of Strength of Science Disclaimers on the Communication Impacts of Health Claims"- Docket No. 2005N-0413

Dear Sir:

My name is Sin Hang Lee, M. D., and I am the petitioner for the qualified green tea health claim under FDA Docket No. 2004Q-0083. I would like to comment on the FDA's Qualified Health Claims in Food Labeling program (the Program) and the recently released report entitled "Working Paper - Effects of Strength of Science Disclaimers on the Communication Impacts of Health Claims by the Division of Social Sciences, Office of Regulations and Policies, CFSAN" (the Working Paper), based on my personal experience. In my opinion, the Working Paper fails to address the real problems of the Program. Its very conclusion ***"that the results suggest that text sentences using adjectives do not correctly convey to respondents the intended strength of science"*** has wrongly put the emphasis on "text sentences" while the real issue is the strength of science. The ineffective language used in the health claims is a symptom of improper execution of the Program. Its pathology is best demonstrated by a postmortem analysis of the FDA green tea health claim decision, a real case that the authors of the Working Paper have carefully avoided as they chose calcium/orange juice, omega-3/tuna, selenium/eggs, and lycopene/spaghetti sauce to formulate their hypothetical language for the survey.

The qualified green tea health claim published by the FDA on June 30, 2005 is extremely confusing to consumers [1]. It is the result of deviation from established rules, unjustified handling of relevant scientific data, inadequate medical scientific knowledge of the review staff and personal bias of the regulators of the FDA, elaborated in further details as follows.

1. FDA deviated from its own rules in formulating the qualified health claim language

FDA bastardized its own guidelines by inserting a new adjective "highly unlikely" to over-reach its non-scientific conclusion for a green tea health claim. The FDA guidelines are well documented in "Standardized Qualifying Language for Qualified Health Claims" of the "Guidance for Industry and FDA- Interim Procedures for Qualified Health Claims in the Labeling of Conventional Human Food and Human Dietary Supplements" of July 10, 2003 (Interim Guidance). Based on the released Working Paper, the term "unlikely" appears to have been coined by the Division of Social Sciences, Office of Regulations and Policy of the CFSAN as an arbitrary "Response Scale" (Table 4. Communication Outcome Measures) for the 1,920 respondents to grade their perceived relevant health benefits in a theoretical, experimental scheme of wording and word order similar but not identical to those listed in FDA's Interim Guidance for qualified health claims. The word "unlikely" is not part of the standardized claim language in the Interim Guidance. In approving a qualified health claim, the FDA's use of "highly unlikely" to qualify a potential event is confusing and misleading to the American consumers. The language in the FDA June 30, 2005 letter of enforcement discretion on the green tea/breast and prostate cancer claims communicated to the public by Mr. Michael M. Landa, an FDA lawyer, is cited *verbatim* as follows:

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“Based on FDA's review of the strength of the total body of publicly available scientific evidence for a claim about green tea and reduced risk of breast cancer, FDA ranks this evidence as the lowest level for a qualified health claim. For the reasons given above, FDA concludes that it is highly unlikely that green tea reduces the risk of breast cancer.”

“Based on FDA's review of the strength of the total body of publicly available scientific evidence for a claim about green tea and reduced risk of prostate cancer, FDA ranks this evidence as the lowest level for a qualified health claim. For the reasons given above, FDA concludes that it is highly unlikely that green tea reduces the risk of prostate cancer.”

Webster's New Collegiate Dictionary defines "unlikely" as "improbable", meaning "not likely to be true". For the FDA to endorse a "not likely to be true" health claim to be used as food label is an insult to the intelligence of all educated American consumers.

The Interim Guidance has provided three levels of language, categories B, C and D, to rank the strength of the scientific evidence for the qualified health claim if the evidence supporting the health claim approved by the FDA fails to meet the “significant scientific agreement” requirements for a category A unqualified health claim. Category D is the lowest level, but none of the categories contains the word "unlikely" in its definition. The insertion of the words “highly unlikely” into an approved qualified health claim, even of the lowest level scientific strength, is a deviation from the Interim Guidance.

2. FDA broke its own rules by using "illegitimate" data as weighing evidence

Without consulting with the petitioner or other medical scientists, the FDA reviewer violated the agency's own rules by selectively handpicking two poorly designed studies that were published after January 27, 2004, the official closing date of the petition, as negative weighing evidence [2, 3] to downgrade the positive evidence in the two accepted studies supporting green tea as an effective functional food against breast cancer and prostate cancer. This quasi-legal maneuver gave the FDA regulator justification to insert the predetermined adjective "highly unlikely" into an approved green tea cancer health claim, a decision that the regulators could no longer delay after six unprecedented deadline postponements. According to the rules governing the review process, all scientific evidence under consideration by the FDA should be posted on the FDA's Dockets Management website for public view and public comments during the official comment period to maintain transparency and responsiveness of the review process. The flawed marginal studies that do not show that drinking green tea reduces the risk of breast cancer and prostate cancer were not even published until after the official closing date of the petition. They were not posted on the FDA Dockets Management website. The inclusion of these late publications as negative weighing evidence without posting them for public view and public comments violated the FDA's own rules. If these "illegitimate" data were excluded, the FDA would have to agree that it is highly likely that green tea may reduce the risk of breast cancer and prostate cancer, a category B qualified health claim the regulator apparently does not want to endorse.

3. FDA reviewer did not have adequate medical knowledge to review the green tea cancer health claim petition

The FDA assigned a staff with inadequate medical scientific background to review the petition for a health claim linking a potential relationship between green tea consumption and cancer prevention.

The FDA reviewer ignored the pharmacodynamics data in the world's literature that shows that a certain quantity of green tea of certain strength, commonly expressed in terms of (-)-epigallocatechin gallate (EGCG) level, must be regularly consumed to achieve the expected benefits of cancer prevention or cancer risk reduction. These pharmacodynamics data have been recommended and published by the National Cancer Institute (NCI) for the design of protocols in cancer research and in human clinical trials

[4]. Without the basic knowledge in pharmacology and in dose dependence between a bioactive substance and a targeted pathophysiological condition, the FDA regulator discarded the pharmacodynamics data of the NCI as inadmissible evidence for consideration, a trial lawyer tactic applied in science.

Another example of improper manipulation of scientific data by the FDA lawyer, Mr. Michael M. Landa is the fact that he dismissed two highly significant intervention studies showing green tea as an effective dietary factor for preventing or delaying recurrence of the malignant tumor in stage I and stage II breast cancer patients [5, 6]. In his letter of enforcement discretion, Mr. Landa emphasized on the one hand that “intervention studies provide the strongest evidence for an effect.” On the other hand, he claimed that “no intervention studies were submitted by the petitioner relating green tea and cancer risk reduction.” This last statement is a blatant distortion of facts because the two submitted intervention studies were rejected for further consideration by Mr. Landa himself. He argued that the study subjects in these two reports had already been diagnosed with breast cancer and therefore the studies are not acceptable as intervention studies extrapolated for a healthy population. This legal manipulation of science is remarkable since all intervention studies are conducted on human subjects with an established diagnosis of the targeted disorder. This is the very definition of intervention. There is no need for intervention in a “healthy” population. Mr. Landa was totally ignorant of the fact that the medical literature is replete with intervention studies in cancer research using cancer recurrence rate as the endpoint for evaluation of a potential effective dietary factor. The American Cancer Society has had a Breast Cancer Dietary Intervention Project in this country for many years, using dietary intervention to reduce the recurrence rate of breast cancer as part of the prevention measures [7]. A simple PubMed internet search with the words “intervention studies, cancer recurrence” shows all the articles related to this subject.

The lack of logic is astonishingly apparent in the letter of enforcement discretion. For example, on review of the green tea prostate cancer data, Mr. Landa wrote in his findings:

“Two case-control studies evaluated green tea and prostate cancer risk (Jian et al., 2004; Sonoda et al., 2004). Both studies received high methodological quality ratings. Jian et al. (2004) evaluated green tea intake and prostate cancer using 130 cases and 274 controls from China.

Drinking three cups of green tea per day was significantly associated with a reduced risk of prostate cancer; odds ratio 0.27 (95% CI 0.15-0.48). Sonoda et al. (2004) included 140 Japanese prostate cancer cases and controls. Drinking two to ten cups of green tea per day was not significantly associated with prostate cancer risk; odds ratio 0.67 (95% CI 0.27-1.64). “

However, based on his findings, Mr. Landa made the following conclusion:

“One weak and limited study does not show that drinking green tea reduces the risk of prostate cancer, but another weak and limited study suggests that drinking green tea may reduce this risk. Based on these studies, FDA concludes that it is highly unlikely that green tea reduces the risk of prostate cancer.”

Any person with a rudimentary understanding of medical science can see that Mr. Landa’s above findings do not lead to his conclusion. First of all, “high methodological quality ratings” is not an appropriate descriptive characterization of a “weak and limited study”. An odds ratio 0.27 (95% CI 0.15-0.48) means a reduction of prostate cancer incidence rate of 73% that is statistically significant. An odds ratio 0.67 (95% CI 0.27-1.64) means a reduction of prostate cancer incidence rate of 33% that is statistically not significant. Since both of the FDA-accepted studies with high methodological quality ratings have found a beneficial effect of green tea in reducing prostate cancer risk, although one with more significant result than the other, a “highly unlikely” conclusion cannot be established.

4. FDA allowed lawyers to inject personal bias in the review process

The FDA is a Federal agency entrusted with an enormous power to determine what foods the American consumers will eat and what medicines they will take to manage their health. The FDA should assign staff members with adequate scientific background to review the data submitted for the qualified health claim petitions. This program is new and its regulations are still evolving. The reviewing staff should look at all scientific data according to the FDA regulations without personal bias against or in favor of a particular food substance being considered. If a regulator or a scientist assigned to review an issue has an *a priori* opinion on the matter to be reviewed that might influence his or her objective evaluation of the data, he or she should be excused from the assignment.

In a sworn statement made by a medical doctor representing a group of pathologists and oncologists in New Haven, who solicited support of the FDA to be used as a legal ground to expel an M. D. partner from a group practice for maintaining an internet website that advocates green tea to be considered by cancer patients and their doctors as a potentially effective, non-toxic dietary supplement for cancer controls, the then chief counsel, Mr. Daniel Troy was quoted as stating ***“Your partner’s engaged in criminal activity, he could go to jail. My advice to you is to get as far away from this as you possibly can.”*** [8]. This legal opinion was rendered by the FDA chief counsel against using green tea as a dietary supplement for cancer control in February 2003, almost one year before the green tea qualified health claim petition was filed. At that time, a conclusion against using green tea by the medical profession to help control cancer had already been made at the FDA regulators’ office, without review of any scientific evidence.

The public record also shows the following relevant events in connection with the history of the review process on the green tea qualified health claim petition.

August 1, 2004- Mr. Michael M. Landa became Deputy Director for Regulatory Affairs, Center for Food Safety and Applied Nutrition (CFSAN). Mr. Landa served as Deputy Chief Counsel under Mr. Daniel Troy prior to his current appointment.

October 26, 2004- Dr. Kathy Ellwood, director of Division of Nutrition Programs and Labeling informed the petitioner that the original FDA decision deadline date, October 29, 2004, could not be met because review by other division had not been completed. However, no scientific issues were raised.

November 28, 2004- Daniel E. Troy, the then FDA chief counsel, resigned.

April 26, 2005- Mr. Sheldon T. Bradshaw, the newly appointed FDA Chief Counsel informed petitioner that he found the voluminous file of the green tea qualified health claim petition sitting in the Chief Counsel’s office for several months and needed time to review it. Therefore, the FDA announcement could not meet the then new deadline set for April 29, 2005.

June 30, 2005- Mr. Michael M. Landa officially signed off the green tea cancer health claim petition as a rejection and a reluctant approval for breast cancer and prostate cancer with an ambiguous claim language.

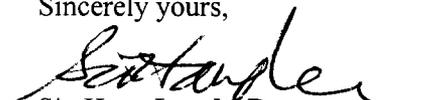
It appears that the final FDA green tea qualified health claim language was constructed by Mr. Daniel E. Troy and Mr. Michael M. Landa at the Chief Counsel’s office before Mr. Troy’s departure from the FDA. The FDA should conduct an internal investigation to determine to what extent the ambiguity of the green tea health claim language that has caused such great confusions in the lay media and among the American consumers has been influenced by the personal bias of Mr. Daniel E. Troy and Mr. Michael M. Landa, acting as agents of a group of healthcare providers in New Haven.

In summary, the report entitled "Working Paper - Effects of Strength of Science Disclaimers on the Communication Impacts of Health Claims by the Division of Social Sciences, Office of Regulations and Policies, CFSAN" does not address the real issues of the Qualified Health Claims in Food Labeling of the FDA. In order to better serve the interest of the consumers, the review of qualified health claim petitions

should be conducted by medical scientists according to established scientific principles and protocols. Peer review should be incorporated in the process. The final decision should be made according to science, not to be influenced by personal opinions of the regulators. The conclusion and the claims should be supported by the findings in science and should be made according to the FDA regulations without arbitrary deviation. The strength of science disclaimers should be based on science as stipulated in the FDA guidance. Quasi-legal manipulation of the disclaimer language by the Office of Regulation staffed by a bunch of lawyers is not the proper approach to convey science-based information to American consumers for managing their health.

Thank you for posting this letter on the Dockets Management website for public information.

Sincerely yours,



Sin Hang Lee, M.D.

References (excluding FDA official documents)

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8. Superior Court Case Docket No. CV-03-0478695-S, State of Connecticut. Deposition of Paul Fiedler, M.D. on July 11, 2004 for a group of medical doctors in New Haven, Connecticut.

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