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March 2, 2001

Dockets Management Branch  
Food and Drug Administration  
5630 Fishers Lane  
Room 1061  
HFA-305  
Rockville, Maryland 20852

**RE: FDA's Refusal to Grant Meeting Requested by Raisio Benecol Ltd. (Docket No. 00P-1276)**

Dear Madam/Sir:

Arent Fox submits this letter to the Food and Drug Administration ("FDA" or "the Agency") on behalf of Raisio Benecol Ltd., Raisio, Finland ("Raisio"), to memorialize the Agency's refusal to grant our request for a meeting to further clarify issues raised in Raisio's comments to the Interim Final Rule for Health Claims for Plant Sterol/Stanol Esters and Coronary Heart Disease ("Interim Final Rule").

Raisio strenuously objects to FDA's refusal to meet, and wishes to preserve its objection. We therefore request that this letter be placed in the administrative record for the above-referenced docket.

**Chronological Account of Events**

On November 22, 2000, Raisio submitted comments to the Interim Final Rule. In the Interim Final Rule, the Agency set the minimum qualifying level of plant stanol esters at 2.0 g/d stanols, but set the minimum qualifying level of plant sterol esters at 0.8 g/d sterols, a significantly lower dose than that for plant stanol esters. In its comments, Raisio requested that FDA approve a health claim for stanol esters at a level of 0.8 g/d stanols, so that stanols and sterols would have the same minimum dose requirement.

As previously explained in Raisio's comments, scientific studies support a health claim for plant stanol esters at a dose at least as low as 0.8 g/d stanols. One of the arguments raised by Raisio in support of a lower dose is the reduction, at that lower dose, of plasma levels of Apolipoprotein B ("Apo B"), a marker of LDL cholesterol that allows precise and direct measurements as compared to the normally used calculated measurement of serum LDL cholesterol level. Plasma ApoB level is considered a reliable marker in evaluating the risk of cardiovascular disease. The role of Apo B in determining the minimum dose of stanols required to produce a statistically significant cholesterol-lowering effect is highly complex.

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Therefore, as soon as Raisio was able to ensure the availability of experts with extensive knowledge of Apo B, we requested a meeting with FDA to help clarify for the Agency these complex scientific issues. The goal of this meeting was to assist the Agency to understand these issues so that it could fairly evaluate the merit of the arguments raised in Raisio's comments.

In mid-January 2001, I telephoned Dr. Lynn Larsen, Director of the Division of Nutrition Science and Policy, CFSAN, and informed him of our desire to schedule a meeting with him and his staff to clarify certain complex scientific points in Raisio's comments. Dr. Larsen responded to my request by instructing me to submit our meeting request to him in writing. Therefore, on January 25, 2001, I submitted a written meeting request to Dr. Larsen.

On February 15, 2001, one of my partners, Brian Waldman, called Dr. Larsen, and, once again, explained that we believed it was important that FDA meet with us and our experts to discuss some of the scientific and technical issues raised in Raisio's comments. During that conversation, Dr. Larsen expressed concern that if FDA were, in fact, to meet with Raisio, the company might present new information in addition to clarifying the points raised in Raisio's comments. He explained that such an eventuality might require FDA to re-open the comment period, something the Agency wanted to avoid. Mr. Waldman reiterated that Raisio did not wish to present any new or additional information, but rather only to provide clarification on the material that it had previously submitted during the notice and comment period.

On February 21, I telephoned Dr. Larsen to follow up with him on his conversation with Mr. Waldman. Dr. Larsen told me that Raisio's comments would have to stand on their own, without additional clarification, because the Agency had decided not to meet with us. Later that afternoon, Louisa Nickerson, an attorney in FDA's General Counsel Office, telephoned me to confirm FDA's decision to refuse our request for a meeting. Ms. Nickerson stated that the Agency's decision as to whether to grant a meeting request lies within the discretion of the Agency, and the Agency had decided to reject our request.

#### **Objection to FDA's Denial of Meeting Request**

As stated at the outset, we strenuously object to FDA's denial of our request for a meeting. We believe that a meeting would benefit FDA, and therefore the public health, because it would assist FDA in making a reasoned decision in its response, not only to Raisio's request for a lower dose for stanols, but also to the same request made in several other comments to the Interim Final Rule submitted by other companies. We believe that such a

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meeting is important for two main reasons: (1) to clarify scientific issues so that no confusion about the comments can result; and (2) to make the most efficient use of Agency resources.

#### **Clarification of Scientific Issues**

A meeting with FDA would benefit the Agency's decision-making on the Interim Final Rule because it would offer the Agency an opportunity to meet with those experts in the field who could discuss with FDA the results of the studies reviewed in Raisio's comments. It is critical for Raisio that these studies be fully clarified in order to ensure that the Agency understands the scientific justification for a dose of stanol esters that is similar to that granted sterols.

The disparity in the minimum qualifying dose for sterols and stanols is scientifically unsupported, and is therefore inequitable. It creates the illusion that sterols are clinically superior to stanols. As consistently noted in several of the comments to the Interim Final Rule submitted by various third parties, including the American Heart Association, such a notion is flatly false and belied by the scientific evidence. Indeed, Raisio believes that the studies, when viewed collectively, demonstrate unequivocally that the cholesterol-lowering effect of stanols is at least equal to that of sterols. Despite this equivalency, the Interim Final Rule sets the minimum qualifying dose of stanols at a much higher level than sterols.

Moreover, as also noted in several of the other comments, the disparity in qualifying levels between stanols and sterols will likely result in consumer confusion. Such consumer confusion poses the serious risk that consumers, befuddled by the purported differences in stanols and sterols, will avoid both stanol- and sterol-containing products entirely. Clearly, such a result defeats the purpose of the health claim — to wit, to make these products, and information about the health benefit associated with them, readily accessible to consumers so that they may avail themselves of such benefit, thereby decreasing the risk of CHD in the United States.

#### **Efficient Use of Agency Resources**

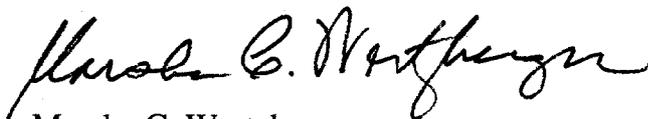
A meeting between FDA and Raisio would allow FDA to conserve scarce Agency resources by availing itself of all relevant information prior to finalizing the Interim Final Rule. If FDA rejects the opportunity to collect and consider such information concurrently with its review of the comments, Raisio may have to seek additional administrative or judicial remedies once the rule becomes final. It would be far less resource intensive for FDA to fully interrogate the available data rather than have to respond to a later petition to

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amend the health claim rule or to a legal challenge. Raisio would be most concerned should the final rule continue to incorporate the disparity between qualifying levels for stanols and sterols that currently exists. Indeed, Raisio might be compelled to file a petition to amend the health claim immediately after the final regulation issues, opening the entire review process for the stanol/sterol health claim all over again immediately after the final regulation issues. The delay associated with FDA's consideration of such a petition would create yet another obstacle to consumer access to truthful information concerning the tremendous health benefit that these products offer.

For the foregoing reasons, we strenuously object to FDA's denial of Raisio's request for a meeting, and ask that our objection be added to the administrative record.

Very truly yours,



Marsha C. Wertzberger

cc: Mr. Rabbe Klemets  
Mr. Tapio Palmu  
Mr. Ingmar Wester  
Dr. Lynn Larsen  
Louisa Nickerson, Esq.