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ILSI North America

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Leila G. Saldanha, PhD
Department of Health and Human Services
Office of Dietary Supplements
6100 Executive Boulevard
Rm 3B01, MSC 7517
Bethesda, MD 20892

Dear Dr. Saldanha:

Re: Proposed Definition of Bioactive Food Components (69 Federal Register 55821, September 16, 2004)

The North American branch of the International Life Sciences Institute (ILSI North America) would like to thank you for the opportunity to comment on the proposed definition of bioactive food components and applauds the Department of Health and Human Services (DHHS) for providing this opportunity for scientific input.

The North American branch of the International Life Sciences Institute (ILSI North America) is a public, non-profit scientific foundation. ILSI North America advances the understanding and application of scientific issues related to the nutritional quality and safety of the food supply, as well as health issues related to consumer self-care products. The organization carries out its mission by sponsoring relevant research programs, professional education programs and workshops, seminars, and publications, as well as providing a neutral forum for government, academic, and industry scientists to discuss and resolve scientific issues of common concern for the well-being of the general public. ILSI North America's programs are supported primarily by its industry membership.

The ILSI North America Technical Committee on Food Components for Health Promotion was formed in January 1994 to increase understanding of the role of food components in human health promotion; monitor research and promote efforts of scientists from industry, government, and academia related to the development and application of such food components; and disseminate these findings. Included is a lisitng of much of the relevant scientific work the committee has sponsored over the years as well as selected publications from other ILSI branches from around the world.

The ILSI North America Project Committee on Flavonoids is a new group to ILSI North America formed in 2004 to address the effects of dietary flavonoids on heart health. Both committees would like to submit the following comments for your consideration.

We suggest:

1. Clarifying the need for a definition and its intended use
2. Removing the descriptive term 'bioactive', or changing it to 'physiologically-active'
3. Modifying the definition

It is stated that there is an interest in establishing a definition for 'bioactive food components' as a first step toward developing approaches that might be used to assess their health effects. However, it is not clear why the definition is necessary. As background, the Food Components Committee spent a significant amount of time talking with the scientific community to work on the definition of "functional food." Although a working definition was finally drafted, it seemed the dialogue around the definition took away from resources that could have been spent on research. As an international organization, ILSI recognizes the international implications of this issue and itself tried to develop a definition. In the end, this effort resulted in a list of attributes, instead of a definition.

Further clarification on why such a definition is needed and how it will be used needs to be clearly articulated. Definitions tend to set boundaries, and unless the reasons for the definition are clear, those boundaries can be arbitrary and artificial. Definitions may be used for strategic planning for scientific research, international arenas, and/or by regulatory agencies. Again, we urge DHHS to be thorough in spelling out the exact intended use and reason behind this definition as one definition may not be universally applicable.

A challenge arises over use of the term 'bioactive', -- defined by Webster (1) as having "any effect on, interaction with, or response from living tissue," which invariably associates the food component with biologic or pharmacologic activity. For this reason, the term 'bioactive' is not helpful in describing food components that are directly or indirectly physiologically active and result in health promotion or reduction in the risk of disease. For this reason, we believe a more scientifically accurate term would be "physiologically-active" food components. It might be useful to conduct consumer research to explore reactions to any proposed terminology.

The DHHS Working Group proposed definition is:
"Constituents in foods or dietary supplements, other than those needed to meet basic human nutritional needs, that are responsible for changes in health status." This definition presents several scientific concerns that can be remedied by appropriate word substitutions, as will be seen in the modified definition developed following consideration of the posed questions.

ILSI North America proposes an alternate definition that addresses several scientific concerns that can be remedied by appropriate word substitution as follows:

> Physiologically-active food components: Food components demonstrated to result, directly or indirectly, in a consistent positive physiological response linked to health promotion, or reduction in risk of disease, as measured through utilizing appropriate methodology and biomarkers.

What categories/classes of compounds should and should not be considered as bioactive food components?

> Most, if not all, components found in food can be considered 'bioactive'. These natural constituents in food can be separated into distinct categories or classes by expression of their bioactivity. Those determined to cause, directly or indirectly, a consistent deleterious physiological response, as measured through *in vitro* or *in vivo*

studies utilizing appropriate methodology and biomarkers, should not be considered in the proposed definition. This would include toxins and other contaminants.

On the other hand, food components resulting in positive physiologic benefits, either directly or indirectly, should be the focus of this definition. In order to be comprehensive, the definition should be as inclusive as possible. We do recognize that at high enough doses any component could potentially have a harmful effect, but that is not the focus here.

To further note how complicated the inclusion and exclusion criteria really are, it is impossible to completely include or not include all compounds that fall under the main classes of plant secondary compounds. For example, one might argue that monoterpenes should not be considered as 'bioactive' food components because they are responsible for the smell and flavor of many plant foods, in particular herbs and spices. On the other hand, certain monoterpenes have anti-plaque bacteria properties, and does this fit into the proposed definition of a bioactive food component as improving overall health status?(2) Some monoterpene flavor compounds are also suspected carcinogens. Therefore each component has to be looked at individually not as a class.

Should essential nutrients be included as bioactive food components?

Yes, classically, some physiologically-active food components have been called nutrients--essential nutrients for life, and other nutrients for health currently classified as non-essential.

Should synthetically derived components used in fortified foods and dietary supplements be considered under this definition?

Yes, food components that are synthetically derived forms of natural compounds should also be considered under this definition. For example, synthetic vitamins are food components with beneficial physiologic activities.

Again, thank you for the opportunity to provide comments and we look forward to working with you on the scientific issues surrounding the definition and its use.

Sincerely,

Richard M. Black, PhD
Executive Director, ILSI North America
Representing the compilation of comments received from the ILSI North America Technical Committee on Food Components for Health Promotion and the ILSI North America Project Committee on Flavonoids

Enclosure, Listing of ILSI sponsored scientific work

References: 1. Webster's New Universal Unabridged Dictionary. Barnes and Noble, Inc. 1996
2. J Dent Res. 1992 Jul;71(7):1431-8.