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Subject: Exemptions for Investigational Use

This written submission is made following the public hearing held December 5, 2006 on Conventional Foods Being Marketed as “Functional Foods.” Our comment addresses a need which is central to claims made for functional foods but has broader implications to other food labeling and food safety issues. It is recognized that current manpower restraints are so severe within the Center for Food Safety and Applied Nutrition at the US Food and Drug Administration that it may not be feasible to implement the action that is being proposed at this time. However, the proposed action has significant benefit to both consumers and the regulated industry.

One of the issues that have not been addressed at public hearing on “Functional Foods” is the need to facilitate clinical research on the efficacy of the food in providing a public health benefit. A growing problem is securing approval to conduct clinical research when the substance of interest has not been approved as a food additive or been determined to be GRAS. Often such substances would be considered to have no or minimal risk to human subjects in a carefully controlled study. The establishment of a procedure to assess the adequacy of safety data for conducting clinical studies prior to food additive approval or GRAS determination would encourage the acquisition of needed scientific data.

The informal definition of a “functional food” has as its central tenant that the food promotes a benefit in lowering a health risk or enhances a structure or function in the human body. Therefore the fundamental characteristics concerning functional foods which set these foods apart from all other foods are the claims made for them. The central question is: Does the consumption of the food provide enhanced performance and or health benefits for humans? Although the primary concern must be the safety of long-term consumption of a functional food, data on the efficacy of consumption is essential to

claims. While safety assessments can be made using data derived from animal studies, compositional data and physical properties, efficacy determinations must rely on data derived from studies involving humans.

In some instances epidemiology data may provide sufficient efficacy data for products that have been approved as food additives or recognized as GRAS and have a significant period of use by a segment of a human population. However, such observational studies must have sufficient statistical reliability to warrant recognition of efficacy for the health benefit. Unapproved food additives and new substances under consideration for GRAS determination will likely lack necessary efficacy data for making functional food claims. In recent years securing approval from an Institutional Review Board (IRB) has become a major impediment to conducting human clinical trials for efficacy determination prior to completing the safety evaluation of the substance. IRB approval of studies that use federal funding to conduct clinical research is often contingent on recognition that the substance to be tested has been determined to be safe for intended use. Further even IRB approval for industrial funded research is often forced to observe this practice because the institution is supported by other federal grants and or contracts and the institution has a policy to be in compliance with federal guidelines.

This dilemma has the tendency to discourage the development of functional foods that may have significant benefits to consumers. Currently the timeline associated with bringing a product with a novel ingredient to market is long because safety and efficacy research can not be done at the same time. The uncertainty of a substance's efficacy may in some instance have a negative effect on the decision to pursue the safety evaluation. On the other hand the acquisition of positive efficacy data would encourage the petitioner to pursue necessary safety data.

In many cases the risk of causing harm from testing the efficacy of a new substance for which limited safety data is available or a new use of a traditional ingredient in a well-controlled human study may be very small or non-existent. The amount of risk if any can often be minimized by the health of study participants, the amount of medical monitoring and the study design. The United States Congress in its wisdom recognized this need when the Food Additive Amendment was added to the Federal Food Drug and Cosmetic Act in 1958. Authority was given to the Agency to promulgate regulations exempting unapproved food additives for investigational use. The text of this provision follows:

Unsafe Food Additives

SEC. 409. [21 U.S.C. 348] (a) A food additive shall, with respect to any particular use or intended use of such additives, be deemed to be unsafe for the purposes of the application of clause (2)(C) of section 402(a), unless—

Exemptions for Investigational Use

(j) Without regard to subsections (b) to (i), inclusive, of this section, the Secretary shall by regulation provide for exempting from the requirements of this section any food additive, and any food bearing or containing such additive, intended solely for investigational use by qualified experts when in his opinion such exemption is consistent with the public health.

It is recognized that proposed regulations for enabling the use of this provision in the Act were not promulgated both because of urgency with respect to other Agency priorities and petitioner needs. Essentially the Agency was relying on the IRBs at research institutions to assure that adequate safety data were available to proceed testing with clinical trials. However, most IRBs are not structured to perform this task. Also there was a perceived need to not further encumber petitioners with added burden in the face of limited benefit for obtaining food safety data from clinical trials. However, the need for human data to verify functional food claims adds new urgency to propose regulations for this provision of the FD&C Act that have not existed before.

It is recognized that the proposed regulation would only be useful if the process for granting an exemption can be accomplished in a timely manner and with reasonable expenditure of resources by both the petitioner and the Agency. Therefore it is proposed that a system be implemented in which the petitioner with the use of an expert panel independently make a safety assessment for conducting clinical studies. Provided that the findings of the assessment indicate minimal or no risk the petitioner could make a submission of the safety assessment to the FDA. The Agency would respond within a specific time if there were exceptions to the safety assessment. In the absence of the Agency objection the findings in the safety assessment the petitioner would have an exemption for investigational use of the unapproved food additive. Such an exemption could be revoked at any time should new data be obtained which indicated that the risk of conducting well controlled clinical studies is unacceptable.

Respectfully submitted,

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