

## Opportunity to Respond to Questions

This form provides the opportunity to respond to the questions posed in the Background Paper: Joint FAO/WHO Development of a Scientific Collaboration to Create a Framework for Risk Assessment of Nutrients and Related Substances.

Responses may be typed in to the form directly or appended as an 'attachment' to each question (use 'Upload file'). Fields with asterisks are required. Responses and your name/organization will be available for public viewing.

---

### *Name/Organization*

#### Title

Dr

#### First name \*

Klaus

#### Last name \*

Kraemer

#### Name of Organization (Use 'None' if none) \*

BASF Aktiengesellschaft

#### Affiliation Category (Click on bar to select a sector) \*

Industry

#### Today's Date \*

09/12/2004

---

### ***Question 1***

The Background Paper discusses the possibility that hazard identification and hazard characterization have global relevance, while exposure assessment and risk characterization are relevant to populations. If such a conceptual framework for the four steps is appropriate, then scientific principles could be organized and considered along these same lines.

**Question 1a: Is the distinction between global relevance and population relevance for the four risk assessment steps a meaningful consideration for the purposes of developing an international nutrient risk assessment approach? (Please indicate why or why not)**

**Question 1b: If so, please provide specific suggestions about how best to further articulate and make good use of the differences in identifying the scientific principles for nutrient risk assessment.**

---

### ***Question 2***

Hazard identification and characterization involve a number of decision points that require scientific judgment in order to derive a UL. Please provide input as to how guidelines for these judgments can be developed for the following decision points:

**Question 2a: Criteria for the evaluation of the quality and utility of relevant scientific evidence.**

**Question 2b: Extrapolation to various age/gender groups.**

Question 2c: Determination and use of uncertainty factors.

Question 2d: Other

---

***Question 3***

The conduct of exposure assessment and risk characterization also requires sound scientific principles that can be applied to the various decision points, including but not limited to compilation and collection of intake data and decision-making for summarizing the potential for harm.

Question 3a: Please provide input on general scientific principles relevant to the process of determining exposure for a nutrient or related substance.

Question 3b: Please provide input on general scientific principles for the characterization of the severity and the degree to which intakes exceed the UL or other aspects of risk characterization.

---

***Question 4***

The Background Paper reflects a 'thought process' and is intended to inform a longer process for the development of a technical expert workshop. Clearly the process will benefit from additional input.

**Question 4a: Please provide comments on other general factors or considerations that could be taken into account during the process of identifying principles for nutrient risk assessment.**

(attachment)

Contact: Klaus Kraemer, PhD.

Phone: +49 621 60 28712

E-mail: [klaus.kraemer@basf-ag.de](mailto:klaus.kraemer@basf-ag.de)

December 9<sup>th</sup>, 2004



## Introduction

The BASF Aktiengesellschaft commends the FAO/WHO for taking the initiative necessary to critically evaluate the safety of nutrients and related substances and appreciates the opportunity to comment on the Nutrient Risk Assessment Project. In general, BASF believes it is appropriate for the FAO/WHO to undertake the effort to better determine what kinds of information are needed in order to make more accurate and credible assessments of safety within the meaning of the "reasonable expectation" standard for nutrients and related substances. We believe the goal of this effort should be to create processes and requirements (framework) that more uniformly and reproducibly allow for a safety determination of nutrients and related substances (new dietary ingredients).

As a transnational manufacturer and supplier of dietary ingredients, BASF has had a long history of providing safe and beneficial supplemental nutrition to the marketplace. Informed consumers seek to supplement their daily diets with those dietary ingredients that they believe will meet their own individual dietary needs. Responsible manufacturers strive to produce only products that are known to be safe because a defined body of peer-reviewed, published information permits such a conclusion by an expert panel. Responsible manufacturers act responsibly by conducting a thorough review of the safety of those ingredients that they choose to market. The guidelines for undertaking these reviews and making these determinations are based upon a notion of sound scientific principles that should be common among those in the industry. This notion is arguably not consistently or equally applied by industry. BASF is supportive of a meaningful harmonized standard of safety for nutrients and new dietary ingredients.

The assessment of the safety of a food ingredient or a new dietary ingredient intended for dietary supplements should involve a critical evaluation by properly qualified and experienced experts of the published information on the particular substance and chemically related substances. The assessment is based upon adequate review of credible scientific data derived from appropriate studies that are designed to determine if there are adverse biological effects of the ingredient or supplement at use levels that have adequate margins of safety. The assessment shall be data-driven and omit risk management actions. An assessment of safety can be made in the absence of a less than complete complement of data by relying on the expertise of experienced professionals and we believe a clear objective of this evaluative exercise should be to create the correct and acceptable balance of data requirements that are appropriate for certain

**Deleted:** such as the  
*precautionary principle*

classes of new dietary ingredients.

### **Use of Expert Panels to Establish Reasonable Expectation of Safety**

BASF supports the use of some form of the Generally Regarded as Safe (GRAS) model. At BASF, we have used the self-affirmed GRAS process successfully for a number of dietary supplement ingredients. Other industries have successfully used GRAS procedures to examine the safety of products destined for the marketplace with a potential for widespread human exposure. Most notable among these is the Cosmetic Ingredient Review that was established nearly 30 years ago.

Food safety experts assembled as a GRAS panel should be able to reliably evaluate available, published information on safety and conclude whether the available information supports the safety of a nutrient and new dietary ingredients under specific conditions of use. In addition, the experts should also address the issue of general recognition of safety and conclude that there is general recognition (other experts in the respective fields would come to the same conclusion) or there is not.

These panels of recognized experts (national/international recognition, proper training and experience) would be identified as GRAS experts. Their credentials and reputations should be such that they are not challengeable. The individuals who comprise GRAS panels could be in the employ of the manufacturer or be independently selected by a disinterested third party upon the request of the manufacturer. The format for reviewing the data that is germane to making a determination of safety should remain flexible enough to accommodate the particular individual characteristics of the nutrient or related compound and to the expected dietary exposure parameters. Sufficient flexibility in the self-GRAS determination process should be retained in order to develop GRAS determination models that are most effective for evaluating a variety of classes of nutrients that may have characteristics in common.

The concept of "GRAS," as found in the food additive definition (US Food Drug and Cosmetic Act, Section 201(s)), provides a touchstone for a discussion since this has worked effectively for decades and has broad support and credibility among the scientific and regulated industry communities.

Under a contract with the US FDA, the Food the Nutrition Board (FNB) of the National Academies of Science Institute of Medicine (IOM) initiated a project "Dietary Supplements: A Framework for Evaluating Safety". In April 2004, the FNB published the framework for evaluating dietary supplement ingredients. The framework for evaluating the safety, outlines a science-based process for assessing supplement ingredients, even when data about a substance's safety in humans is scarce. The framework includes a methodology to review the available peer-reviewed literature with regard to the role of the dietary supplement ingredients in health, taking into consideration methods other expert bodies have used to categorize and review supplement safety and efficacy issues.

The use of any of these panels or variation of these could be an efficient means of providing the finest and most critical evaluation of the safety of new dietary ingredients for dietary

peer-reviewed journals as critical reviews. GRAS determinations and supporting information would be submitted to the respective regulatory bodies as part of a review process. In this way, more credibility is added and consumer confidence is improved, and the regulators having the distinct advantage of having the final decision on the entry of new dietary ingredients to the market

## Conclusion

BASF believes it is important for the FAO/WHO to provide clarity and routine in the risk assessment of nutrients and new dietary ingredients. While there are numerous studies that could be required, we do not believe the FAO/WHO needs to create a “checklist” of data requirements for each nutrient or related compound. BASF recommends that the FAO/WHO consider how the use of expert safety panels could be used to optimize the process of new dietary ingredient safety reviews. BASF looks forward to working with all interested parties and the FAO/WHO to create an improved system that will maintain consumer confidence in the safety of this class of products.

## Other resources

Risk assessment in general:

Institute of Medicine of the National Academies, 2004: "Dietary Supplements: a framework for evaluating safety"  
<http://www.iom.edu/report.asp?id=19578>

Renwick AG. Et al. 2004. Risk-benefit analysis of micronutrients. *Food Chem Toxicol* 42:1903-1922

Use of epidemiological studies (see question 2a):

Federal Focus, Inc. London Principles for Evaluating Epidemiologic Data in Regulatory Risk Assessment: <http://www.fedfocus.org/science/london-principles.html>, Principles for Evaluating Epidemiologic Data in Regulatory Risk Assessment, ISBN 0-9654148-0-9, and "Recommendations for Implementing the 'London Principles' and for Risk Assessment Guidance", Federal Focus 1996

Hertz-Picciotto I. 1995. Epidemiology and quantitative risk assessment: A bridge from science to policy. *Amer J Pub Health* 85:484-91

**Deleted:** Further to be addressed:¶  
Precautionary Principle shall not apply in risk assessment – tool of the risk managers¶  
Risk assessment of single compounds rather than mixtures¶  
Nutrients deserve specific approach¶  
Do not derive RDA-based limits ¶

**Field Code Changed**

**Field Code Changed**

BASF Aktiengesellschaft  
Ludwigshafen, Germany

---

**Question 4b: Please provide other comments on the content of the Background Paper.**