

The Practice of Risk Assessment for Food Additives

Workshop on Risk Analysis for
Processed Food Manufacture
May 15, 2010
Mumbai, India

Henry B. Chin, PhD
Senior Director Food Safety

The Coca-Cola Company

Outline

- Describe the components of risk assessment
- Describe regulatory guidelines
- Describe actual applications from previous experiences
- “Golden Rule” – all uses of food additives should comply with relevant laws and regulations AND be safe



Available Regulatory Guidelines

- USFDA
 - <http://www.fda.gov/Food/FoodIngredientsPackaging/FoodAdditives/default.htm>
- EFSA Guidelines
 - http://www.contactalimentaire.com/fileadmin/ImageFichier_Archive/contact_alimentaire/Fichiers_Documents/Avis_de_AESA/EFSA_-_List_of_guidance_guidelines_and_working_documents1.pdf
- JECFA Guidelines
 - <http://www.inchem.org/documents/ehc/ehc/ehc70.htm>
 - <http://www.who.int/ipcs/food/principles/en/>
- FSANZ
 - http://www.foodstandards.gov.au/_srcfiles/Food%20Additives%20Guidance%20Document%20final.pdf

WHO Definition of Risk Analysis

Risk Analysis Framework



Risk Analysis Components (Codex)

- Risk Assessment: A scientifically based process consisting of the following steps: 1) hazard identification, 2) hazard characterization, 3) exposure assessment, and 4) risk characterization
- Risk Management: The process, distinct from risk assessment, of weighing policy alternatives, in consultation with all interested parties, considering risk assessment and other factors relevant for the health protection of consumers and for the promotion of fair trade practices, and, if needed, selecting appropriate prevention and control options.
- Risk Communication: The interactive exchange of information and opinions throughout the risk analysis process concerning risk, risk-related factors and risk perceptions, among risk assessors, risk managers, consumers, industry, the academic community and other interested parties, including the explanation of risk assessment findings and the basis of the risk management decisions.

“Within risk analysis, a functional separation between risk assessors and risk managers is necessary to ensure scientific objectivity of the risk assessment process”

Risk Assessment Components

- Hazard Identification
- Hazard Characterization
- Exposure Assessment
- Risk Characterization



Hazard Identification

- The potential to cause an adverse health effect
 - Chemical Hazards
 - Heavy metals, pesticide residues, solvents
 - Composition
 - Microbiological hazards
 - Pathogens (not spoilage organisms)
 - Physical hazards
 - Choking hazards, irritants

Hazard Characterization

- Toxicology of the additive (JECFA, EFSA, INCHEM, FDA)
- Processing effects/Storage Effects
 - Degradation products of chemicals
 - Reduction or Elimination of Pathogens
 - Microbiological stability
- Determine an Acceptable Daily Intake level, ADI
 - Usually 100 times less than the NOAEL

Exposure Assessment

- Intended uses and use levels of the additive
- Determine the Estimated Daily Intake (EDI) of the additive from all sources
 - Need to determine likely use levels in food and amounts of food consumption
 - Recognizing the most sensitive population

Risk Characterization

- Compare the EDI to the ADI
 - Usually want an additional margin of safety between EDI and ADI

Sources of technical data

- Information required to support an application can be derived from many sources and will depend on whether the application is for a new food additive or for a change to the use of an established food additive.
- A new food additive may be new to all global markets and, in this case, the data will be recently generated and provided by the sponsoring company. For a food additive which is new only to Australia and New Zealand, data may be available from sources other than the sponsoring company.
- Data on the safety assessment and dietary exposure of the food additive may be available following an international assessment by JECFA. Alternatively, assessment reports may be available from national government food regulatory agencies such as the USFDA or EFSA.

*“Food Additives Guidance Document”, FSANZ

Examples of the Process

- New Uses for Previously Approved Ingredients
 - Use of hydrogen peroxide to sterilize Polypropylene
 - Use of Chlorine Dioxide in water to wash fruits
 - GRAS Food Additive Notification
- Previous regulatory approvals
 - Hydrogen peroxide approved as a bleaching agent for various foods, as a sterilant for polyethylene packaging surfaces
 - Basis of previous approvals: toxicology of hydrogen peroxide is well known, minimal residual levels of peroxide, no significant oxidation products in food
 - Chlorine dioxide (as substitute for chlorine) approved for washing poultry
 - Basis of approval: toxicology of chlorine dioxide was known, no significant residual levels of chlorine dioxide or perchlorate present washed poultry, no significant oxidation products in poultry

Regulatory Petition for Hydrogen Peroxide on Polypropylene

- Proposed Use: A solution of concentrated hydrogen peroxide is applied to the surface of a polypropylene package that will be used for food. H₂O₂ is removed by hot air.
 - Based upon previously approvals need to demonstrate that less than 0.5 ppm residual H₂O₂ would be present in packages at time of filling-developed analytical method capable of routinely being used.
 - Needed to show that under the conditions of use no significant oxidation of the PP would occur and that no significant changes in the possible migration of chemicals from PP would occur
 - Surface analysis studies and extraction studies
 - Petition contained updated literature review on hydrogen peroxide and updated environmental impact assessment
 - New use was approved.

New Use for Hydrogen Peroxide

- Hazard Identification
 - Known from previous work
 - Any changes due to this use? (composition, pH, microbiological issues, processing conditions)
- Hazard Characterization
 - Known from previous use (updated literature review)
- Exposure Assessment
 - Determine additional intake due to new use
- Risk Characterization
 - Compare new EDI to ADI

Petition for New Use for Chlorine Dioxide

- Proposed Use: Chlorine dioxide (generated by specified means) is added to potable water to aid in the washing of raw fruits and vegetables.
 - Update literature search on toxicology of chlorine dioxide and other possible chlorine containing compounds
 - Primary questions to address
 - Residual levels of chlorine containing compounds, primarily perchlorate
 - Determine whether treatment produced undesirable effects in the fruits and vegetables, e.g., loss of nutrients, oxidation products
 - Conducted studies using fruits and vegetables selected to represent a cross section of possible pH, nutrients, physical and chemical characteristics
 - Developed analytical methods capable of detecting parts per billion levels of perchlorate in water and extracts from these foods
 - Examined products for loss of key nutrients, analyzed products for indications of oxidative damage
 - Environmental Impact Assessment

New Use for Chlorine Dioxide

- Hazard Identification
 - Known from previous work
 - Any changes due to this use? (composition, pH, microbiological issues, processing conditions)
- Hazard Characterization
 - Known from previous use (updated literature review)
- Exposure Assessment
 - Determine additional intake due to new use
- Risk Characterization
 - Compare new EDI to ADI

Example-New Use for “Direct” Additive

GRAS NOTIFICATION

for

**CONJUGATED LINOLEIC ACID (CLA)-RICH OIL
FOR USE IN CERTAIN FOODS**

Submitted by: Lipid Nutrition
P.O. Box 4
1520 AA, Wormerveer
The Netherlands

GRAS-Risk Assessment

This section summarizes a determination by a panel of experts qualified by scientific training and experience to evaluate the safety of substances added to food ("Expert Panel") that CLA-Rich Oil is generally recognized as safe (GRAS) by scientific procedures for its intended use as described herein

CLA-Rich Oil is a food grade preparation derived from processed safflower oil. It consists of approximately 78% total conjugated linoleic acid (CLA) isomers and 74% of an approximately 50:50 mixture of cis-9,trans-11 and trans-10,cis-12 CLA isomers ("50:50 mixture"). CLA-Rich Oil is intended to be added to certain specified foods within the general categories of soy milk, meal replacement beverages and bars, milk products and fruit juices. CLA-Rich Oil would be added to these foods at a level of 1.5 g per serving.

GRAS-Risk Assessment

- 4.0 METHOD OF MANUFACTURE
 - 4.1 Manufacturing Process
 - 4.2 Product Specifications (Chemical and Microbiological)
 - 4.2.1 Chemical Specifications
 - 4.2.2 Microbiological Specifications
 - 4.3 Product Analysis
 - 4.3.1 Chemical Analysis of CLA-Rich Oil
 - 4.3.2 Microbiological Analysis of CLA-Rich Oil
 - 4.4 Stability Testing
- 5.0 INTENDED USE OF CLA-RICH OIL IN FOOD
- 6.0 ESTIMATED DIETARY CONSUMPTION OF CLA FROM INTENDED FOOD USES OF CLA-RICH OIL
 - 6.1 Background Dietary Intake of CLA
 - 6.2 Estimated Consumption of CLA from Intended Food Uses of CLA-Rich Oil
 - 6.2.1 Consumption Estimate of CLA Based on Historical Food Use
 - 6.2.2 Consumption Estimate of CLA Based on Intended Use

GRAS-Risk Assessment

- 7.0 INFORMATION TO ESTABLISH THE SAFETY OF CLA-RICH OIL
 - 7.1 Introduction
 - 7.2 Absorption, Distribution, Metabolism, and Excretion (ADME)
 - 7.2.1 Absorption and Distribution
 - 7.2.2 Metabolism
 - 7.2.3 Excretion
 - 7.2.4 Summary and Conclusions (ADME)
 - 7.3 Preclinical Toxicological Studies
 - 7.3.1 Introduction
 - 7.3.2 Acute Toxicity Studies
 - 7.3.3 Subchronic Toxicity Studies
 - 7.3.4 Chronic Toxicity / Carcinogenicity Studies
 - 7.3.5 Mutagenicity
 - 7.4 Additional *In Vitro* and Animal Studies
 - 7.5 Clinical Studies
 - 7.5.1 Introduction/Overview
 - 7.5.2 Cardiovascular Disease
 - 7.5.3 Insulin Sensitivity and Glucose Metabolism
 - 7.5.4 Maternal Milk Fat
 - 7.5.5 Summary with respect to Clinical Studies
 - 7.6 Summary and Conclusions

GRAS-Risk Assessment

8.0 SUMMARY OF GRAS STATUS

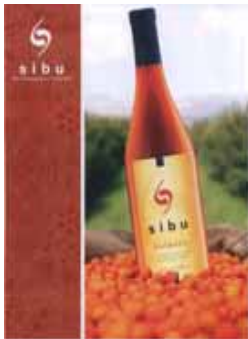
- 8.1 The GRAS Determination is Based on Generally Available Information, and Corroborated by Unpublished Information
- 8.2 The GRAS Determination is Based on a Consensus Among Qualified Experts
- 8.3 GRAS Determination

Key Learnings

- Take a science based approach, understand the basis of previous approvals, justify intended use, identify information gaps
- Consult with the regulatory agency early in the process to ensure that the work will address their likely questions
- Stay engaged with the regulatory agency through the process
- The science must be of the highest quality, capable of standing on its own merits
- Focus on the needs
- Understand that risk assessment is only one-third of the process of risk analysis
 - Providing information for risk management
 - Need to understand Risk Communication

Special Risk Assessments

- Novel Foods
- New Technologies



Notable Exceptions

- Threshold of Toxicological Concern

- Below an amount that can be determined scientifically as unlikely to be harmful

- ILSI Europe, ILSI NA

R. Kroes et al., Food and Chemical Toxicology, 42 (2004), 65-83

- FDA Policy – Threshold of Regulation for Food Contact Materials

<http://www.fda.gov/Food/FoodIngredientsPackaging/FoodContactSubstancesFCS/cm093685.htm>

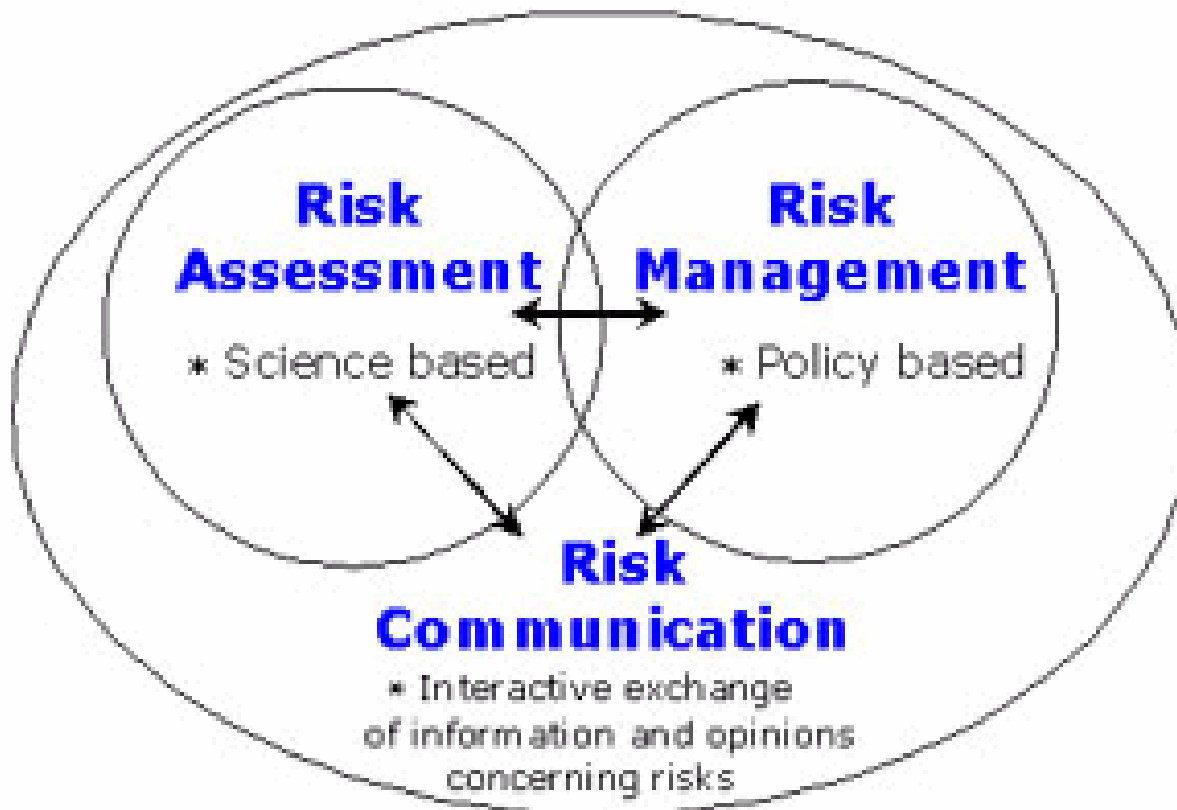
Importance of Separation between Risk Assessment and Risk Management

- Concepts of Risk-Risk and Risk-Benefit
- Nothing is without risk,
 - Reasonable estimation of safety
- Benefit considerations are part of the risk management process
 - Example-WHO/FAO Expert Consultation on Benefits and Risk of Chlorine Containing Disinfectants in Food Processing



WHO Definition of Risk Analysis

Risk Analysis Framework



Importance of Risk Communication- Survey of risk literature (UKFSA)

- Risk and Benefits-majority are “moderately risk tolerant”-question of control
 - Perceived risks center on health, **uncertainty**, environment
 - People often fail to identify any tangible benefits
- General attitudes
 - Attitudes towards science
 - Cultural values
 - Attitudes toward health and nutrition
 - Attitudes toward food

Importance of Risk Communication- Survey of risk literature (UKFSA)

- Emotion-limited knowledge and pre-existing values combine to cause emotional responses. People tend to form negative associations and are inclined to assume the worst.
- Prior knowledge and effects of information-negative information carries more weight, people more likely to accept a viewpoint from a source which shares a similar outlook
- Trust-
 - Media, government, industry least trusted (U.K.)
 - People expect to rely on “experts” (scientists and regulators) to make decisions, but at the same time do not trust them
 - Most trusted are friends, family, and health professionals.

Source: An Evidence Review of Public Attitudes to Emerging Food Technologies, FSA 2009

Questions?