Approaches to Assess the Health Effects of Bioactive Food Component: Cardiovascular Disease

Paula R. Trumbo, Ph.D.
Division of Nutrition Programs and Labeling
Assessing the Health Effects for What?

- Health Claims for Food Labeling

  Causal *relationship* between a nutrient or food and a disease (e.g., risk reduction) – effective dose may or may not be identified depending on whether it is a health claim (required) or qualified health claim* (depending on the available evidence) and if there is a Daily Value.

  *Qualified health claims require less scientific evidence than health claims*

- Dietary Reference Intakes (DRI)

  Recommended intake levels (e.g., RDA) and tolerable upper intake levels

  Identify an *intake level* to achieve a health benefit (e.g., disease risk reduction)
Application of Animal Data

• Useful in understanding the mechanism by which the bioactive food component has a beneficial role in human health

• Useful in identifying potential surrogate endpoints

• Useful in the safety evaluation of bioactive food components and for setting a tolerable upper intake level (DRI)

• Not useful in setting recommended intake levels or reviewing the evidence for a health claim
Essentiality of Surrogate Endpoints

Evidence that is considered useful for setting a DRI or allowing a health claim includes human intervention studies that measure:

**Validated Surrogate Endpoints**

- CHD – LDL and total cholesterol, blood pressure

**Incidence of the Disease**

- Myocardial infarction, ischemia, atherosclerosis, cardiovascular/sudden death

Surrogate endpoints may not be essential, but would eliminate conducting very long and expensive intervention studies on incidence
Essentiality of Surrogate Endpoints

• Very helpful in the evaluation of the relationship between a nutrient (bioactive food component) and a disease (CHD) (Health Claim).

• Very helpful in setting recommended intake levels - Estimated Average Requirement (EAR)* which is required to set a Recommended Dietary Allowance (RDA) – Difficult to establish an EAR based on “incidence” data

*EAR is the average daily intake level estimated to meet the requirement (provide a health benefit) for 50% of individuals in a particular life stage and gender group.
Case: Omega 3 DHA/EPA and CHD

- NO DRI set for EPA or DHA

- There was credible evidence for a qualified health claim*, but not for a health claim

*Qualified health claims require less credible evidence than health claims, therefore requiring qualifying language
Evidence for EPA and DHA

While most intervention studies on incidence showed a benefit,

- Conducted in **diseased** populations (e.g., prior coronary event)

- Endpoints measured were **not validated surrogate endpoints**

- Involved **fish**, rather than EPA/DHA
Surrogate endpoints for CHD,

- One surrogate endpoint for EPA/DHA – blood pressure

- EPA/DHA not effective on blood pressure in healthy individuals, average dose to see a benefit in individuals with hypertension and hypercholesterolemia > 4g/day

- Studies conducted on other endpoints, not useful (e.g, LDL, restinosis, plaque stability)

- Included other nutrients besides EPA/DHA (n-6 fatty acids)
Evidence for EPA/DAH

- Strongest evidence for EPA/DHA and CHD for the general population is from observational studies

- EPA and DHA or some other component in fish?
  
  Insufficient for an EAR/RDA or health claim on nutrient
  
  Sufficient for an Adequate Intake* or qualified health claim*

*Requires less scientific evidence than an RDA or health claim
For future studies to be relevant for DRIs and Health Claims

• Identify animal models for evaluating safety and for identifying potential surrogate endpoints for a specific bioactive food component.

• Validate these potential surrogate endpoints in healthy humans.

• Conduct **controlled human** intervention studies in which the subjects are **healthy or at high risk** (e.g., hypercholesterolemic) and the specific bioactive food component is evaluated at multiple doses.

• If surrogate endpoints are not available, then will need to conduct intervention studies that measure disease incidence in healthy or high risk populations.