Example: Indicators Considered for EAR for Vitamin A

- Dark adaptation
- Serum/plasma retinol concentration
- Isotope dilution
- Relative dose-response/modified relative dose-response
- Conjunctival impression cytology
- Immune function

EAR for Vitamin A Using Dark Adaptation

- Pooled four studies (13 individuals)
- EAR = 300 RAE/day (vs. 625)
- But, CV = 40%; therefore, no RDA established using dark adaptation.

AIs

1) Lack of dose response data (chromium)
2) Uncertainty of the physiologic significance of indicators that are sensitive to the nutrient’s status (vitamin K)
Highest Priority (I)

1) Identification of new functional and biochemical endpoints that indicate sufficient and insufficient body stores (vitamin A; vitamin K; iron; chromium)

Vitamin K

1) Role in bone health (3 interventions)
2) Undercarboxylated osteocalcin
3) New: Roles in cardiovascular health and brain function

Highest Priority (I)
Highest Priority (I)

1) Identification of new functional and biochemical endpoints that indicate sufficient and insufficient body stores (vitamin A; vitamin K; iron; chromium)

2) Identification of new functional and biochemical endpoints that indicate nutrient toxicity (iron and oxidative status; iron content of ferritin; hepcidin; vitamin A and bone toxicity; zinc [? which systems])

Highest Priority (II)

3) The identification and (quantified) effects of interactions between micronutrients and other food components: vitamins A & K; calcium & zinc; zinc & phytate

4) What effects age, sex, race, pregnancy, and lactation have on nutrient utilization/turnover: vitamin A, vitamin K, zinc, and iodine.
Example: Criteria for Vitamin A - (ug/day)

<table>
<thead>
<tr>
<th>Life Stage</th>
<th>Criterion</th>
<th>EAR</th>
<th>RDA</th>
<th>AI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 mo</td>
<td>human milk content</td>
<td>400</td>
<td>500</td>
<td></td>
</tr>
<tr>
<td>7–12 mo</td>
<td>extrapolated from 0-6 mo</td>
<td>210</td>
<td>300</td>
<td></td>
</tr>
<tr>
<td>1–3 y</td>
<td>extrapolated from adults</td>
<td>275</td>
<td>400</td>
<td></td>
</tr>
<tr>
<td>4–8 y</td>
<td>extrapolated from adults</td>
<td>445</td>
<td>600</td>
<td></td>
</tr>
<tr>
<td>9–13 y, M</td>
<td>extrapolated from adults</td>
<td>420</td>
<td>600</td>
<td></td>
</tr>
<tr>
<td>9–13 y, F</td>
<td>extrapolated from adults</td>
<td>630</td>
<td>900</td>
<td></td>
</tr>
<tr>
<td>14–18 y, M</td>
<td>extrapolated from adults</td>
<td>625</td>
<td>900</td>
<td></td>
</tr>
<tr>
<td>&gt; 18 y, M</td>
<td>adequate body stores</td>
<td>500</td>
<td>700</td>
<td></td>
</tr>
<tr>
<td>&gt; 18 y, F</td>
<td>adequate body stores</td>
<td>700</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Zinc RDAs and ULs, mg/d

<table>
<thead>
<tr>
<th></th>
<th>RDA</th>
<th>UL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>4-8</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

Progress Made on High Priority Questions (I)

1) Effect of vitamin A status on plant carotene conversion (Am J Clin Nutr 72: 455-465)

2) Vitamin A activity of plant foods
Vitamin A Value of Plant β-C to Retinol in Humans

<table>
<thead>
<tr>
<th>Vitamin-rich vegetable</th>
<th>Calculated trans-β-C from</th>
<th>Total AUC response to</th>
<th>Vitamin A reference dose for adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweet potato</td>
<td>2 x 2.25 mg trans-β-C/d; 2 x (0.685 mg or 0.375 mg retinol)/d</td>
<td>30 : 1</td>
<td>60 : 1</td>
</tr>
<tr>
<td>Indian spinach</td>
<td>2 x 2.25 mg trans-β-C/d; b-carotene oil capsule, 2 x 2.25 mg trans-β-C/d</td>
<td>21 : 1</td>
<td>10 : 1</td>
</tr>
<tr>
<td>β-carotene capsule</td>
<td>2 x 2.25 mg trans-β-C/d; b-carotene oil capsule, 2 x 2.25 mg trans-β-C/d</td>
<td>15 : 1</td>
<td>1 : 1</td>
</tr>
</tbody>
</table>

Mean changes of total body stores of vitamin A before and after a 60 day intervention in adult men as compared with the mean changes in the retinyl palmitate group of adults.

Sweet potato, n = 14
Indian spinach, n = 14
β-carotene capsule, n = 14
Retinyl palmitate, n = 14

Progress Made on High Priority Questions (II)

3) Vitamin K content of foods
4) Improved classification of iron loading syndromes with identification of the central role of hepcidin (down regulator of iron transporter)

New High Priority Questions (I)

1) Vitamin A and gene expression profiles
2) Menaquinones- bioavailability and metabolism
3) Role of vitamin K in sphingolipid synthesis and metabolism
New High Priority Questions (II)

5) Examine the relationship between iron status and infection (malaria, HIV, TB)

6) Examine the potential for high iron cereal and legume crops (produced by varietal selection or genetic engineering) to improve iron nutrition

7) Examine the potential for high β-carotene crops (genetic engineering) to improve vitamin A nutrition

New High Priority Questions (III)

7) Develop biomarkers of zinc status (genomic, proteomic) to correlate with functional outcomes (e.g. immunity). Biomarkers may be gene product e.g. derived from zinc influenced systems such as zinc transporter proteins.

Production of Intrinsically Labeled Golden Rice
Cr, Cu and Ultratrace Minerals (Ar, Bo, Mn, Mo, Ni, Si, Vn)

1) Bioavailability and turnover

2) Physiological and psychological functional consequences of deficiency (e.g. boron & bone health, arsenic & methylation)