Dietary Supplements and a Method for Determining Safety and Efficacy

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Toxicology 101
“All things are toxic, it is only a matter of dose…”

Dioxin - 0.00006 g
Cobra venom - 0.0115 g
Strychnine - 0.12 g
Morphine - 0.1 g
Water - 6000 g
Alcohol - 600 g

Increasing Dose
Vit. A: An Example of Dose-Response Toxicology 102: A substance may have more than one effect

- Normal
  - Erythema
  - Alopecia
  - Eczema

- Toxic
  - Hemorrhage
  - Bone exostoses
  - Fractures
  - Death

- Deficiency
  - Night blindness
  - Xerophthalmia
  - Inanition
  - Death

The therapeutic range is indicated by an upward arrow labeled CSF pressure.
Concentration of Foods May be a Risky Business
Drivers for the Dietary Supplement Health and Education Act

• FDA’s charter is safety of the consumer
  – DS were potentially very dangerous
  – DS were drugs and, if not, unapproved food additives

• Consumer driving forces
  – Quality of life issues
  – Lionizing of natural remedies
  – Reaction to high cost of drugs
  – Conspiracy theories about “big pharma”

• Industry argument – protect R&D & ROI
  – Encourages enterprise, competition & better products
FDA needed Congress to provide some flexibility

**DSHEA and New Rule Set**

- DS are not drugs, not food additives
- Food and a certain presumption of safety
- “Grandfathered” substances, only ‘new’ substances must be ‘notified’
- Lower hurdle for demonstration of safety
- Burden of proof – on FDA
- No provision for data confidentiality
DSHEA (§201ff)
Dietary Supplements may be:

(1) **Nutrients**: Vitamin, mineral, amino acid
(2) **Food components**: “…a dietary substance for use by man to supplement the diet by increasing the total dietary intake…”
(3) **Products or fractions**: “…a concentrate, metabolite, constituent, extract, or combination of any ingredient.”
(4) **Catchall**: an herb or other botanical

Dietary supplement may **not** be:

Tobacco, drug, biologic or a substance for which IND issued…
Not Much Progress Since 1994
How to Break the Log Jam?
Three Options

1. Keep status quo & FDA only in reactive mode – no additional funding
2. Health Independence Information Act - HR 4004 – FDA not involved in decision
3. Supplement FDA efforts with independent experts – FDA oversight of decision
A System For Resolution - Option #3: A Combination of Incentives and Oversight

1. Supplement FDA efforts with the use of Independent Experts
2. Expand Notification program & recognize opinions of experts
3. Permit a term of exclusivity
Supplement FDA efforts with Independent Experts

Precedent

- GRAS (Generally Recognized As Safe) for food ingredients
- GRASE (…safe and effective) for drugs
- FDA Advisory Committees
1. Supplement FDA efforts with the use of Independent Experts

Confidential submission To Agency

Dossier Approved by Independent Experts

(1) Safety & Proposed claim
(2) Supporting evidence

Criteria Reviewed by Agency

*Claim & supporting evidence* (Limited Review Criteria)
- Experts qualified “...by training and experience…"
- Rationale supporting claim
- Credibility of supporting data
1. Supplement FDA efforts with the use of Independent Experts

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Decision By Agency

Criteria Reviewed by Agency

Claim & supporting evidence (Limited Review Criteria)
- Experts qualified “...by training and experience…"
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- Credibility of supporting data

Inadequate

No Public Notice Returned to Submitter
2. Expand Notification program & recognize opinions of experts

1. Confidential submission To Agency

   Dossier Approved by Independent Experts

   (1) Safety & Proposed claim
   (2) Supporting evidence

2. Criteria Reviewed by Agency

   Claim & supporting evidence (Limited Review Criteria)
   - Experts qualified “by training and experience…”
   - Rationale supporting claim
   - Credibility of supporting data

   Decision By Agency

   No objection
   - FDA Website
     - Product identity
     - Claim
     - Manufacturer
     - Safety data

   Inadequate

   Public Notice By Agency

   No Public Notice

   Returned to Submitter
3. Permit a term of exclusivity

1. Confidential submission To Agency
   - Dossier Approved by Independent Experts
     - (1) Safety & Proposed claim
     - (2) Supporting evidence

2. Criteria Reviewed by Agency
   - Claim & supporting evidence (Limited Review Criteria)
     - Experts qualified “...by training and experience...”
     - Rationale supporting claim
     - Credibility of supporting data
   - Decision By Agency
     - No objection
     - Inadequate
   - Public Notice By Agency
     - FDA Website
       - Product identity Claim
       - Manufacturer Safety data

3. No Public Notice Returned to Submitter
   - Efficacy data Confidential
Resolution

• Consumers
  – Empowerment - greater access to new discoveries/enhancement of QoL
  – Drug cost savings
• Industry
  – Free speech assured
  – Return on investment
• FDA
  – Ensure consumer safety
  – Ensure efficacy (no mis-labeling)
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