FDA's Science Needs

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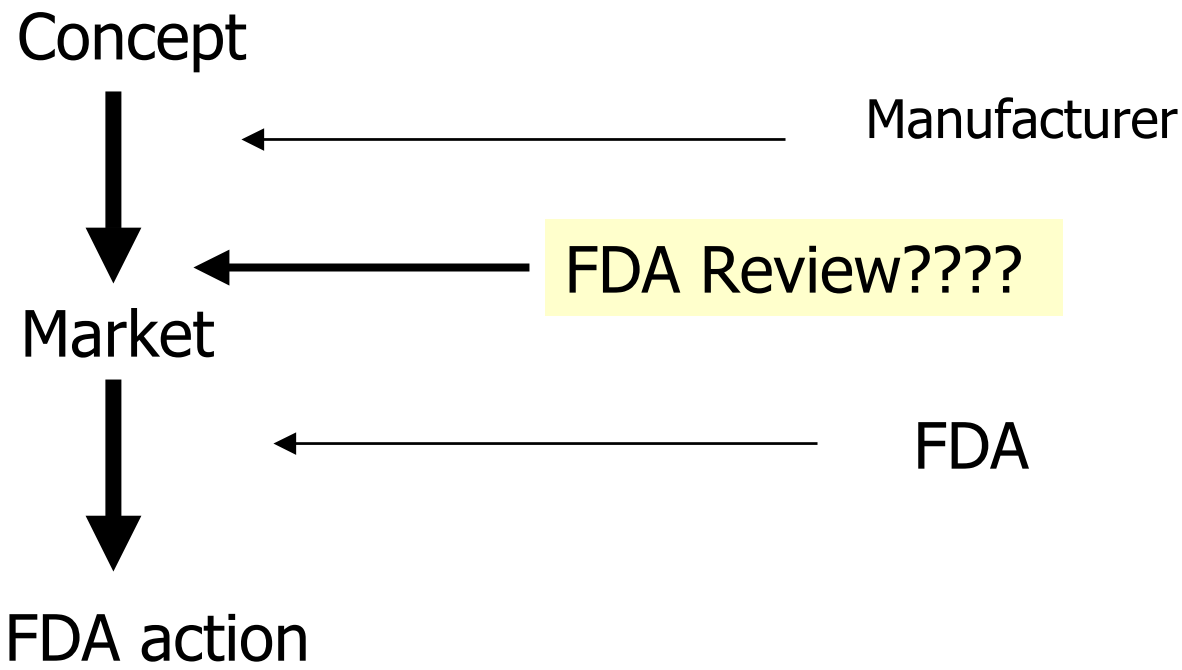
Legislative Assumptions

- History of Safe Use
- Public Health Benefit
- Significant or unreasonable risk under conditions of use

Regulatory Framework

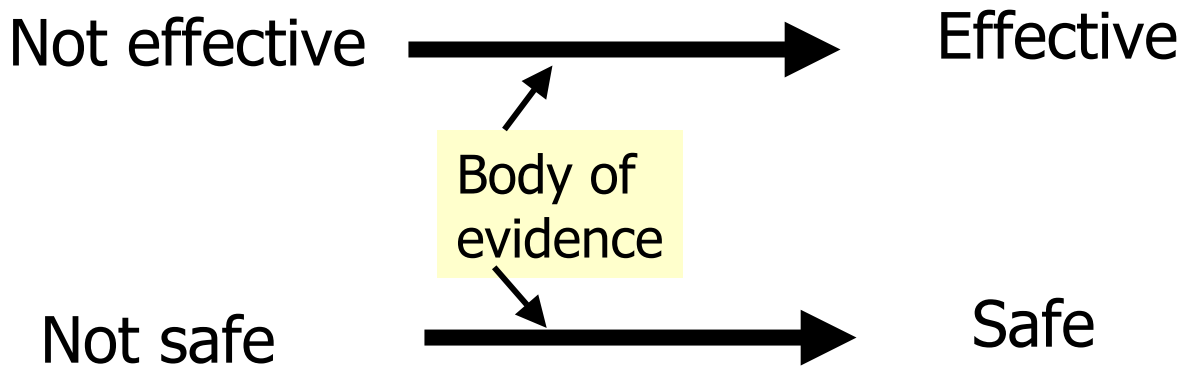
	Supplements	**Drugs**
Regulation	Food	Drug
Users	General; healthy	Sick; symptomatic
Safety	Risk	Risk/benefit
Claims	Risk reduction; Structure/ function	Treat, cure, mitigate, prevent

Who Bears the Burden?



What is the Starting Point?

Null hypothesis



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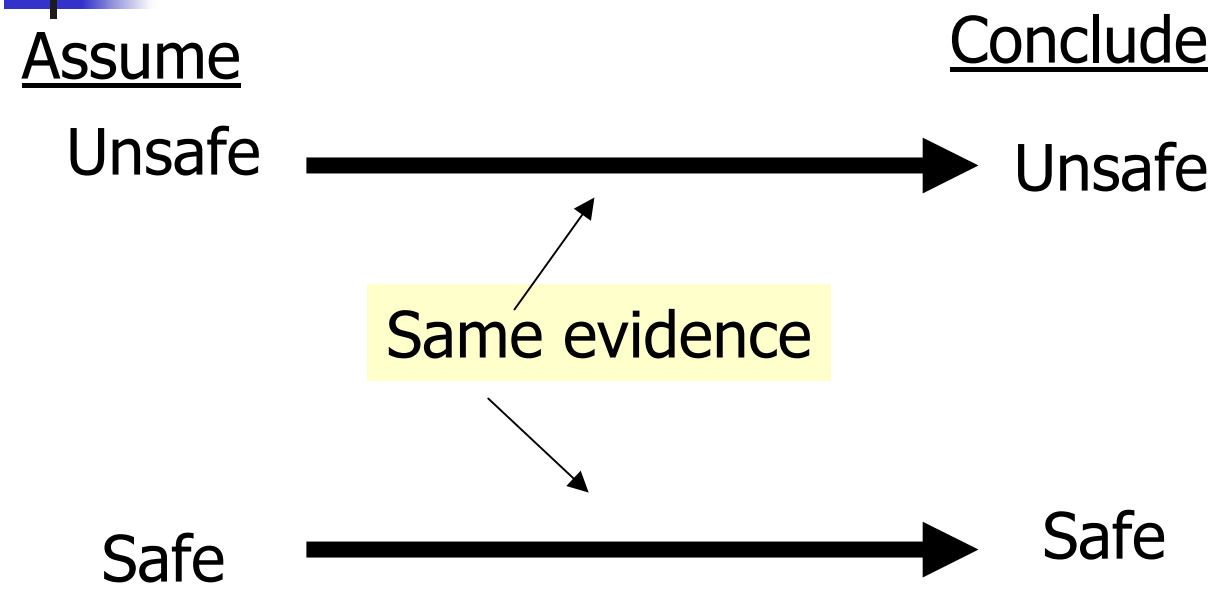

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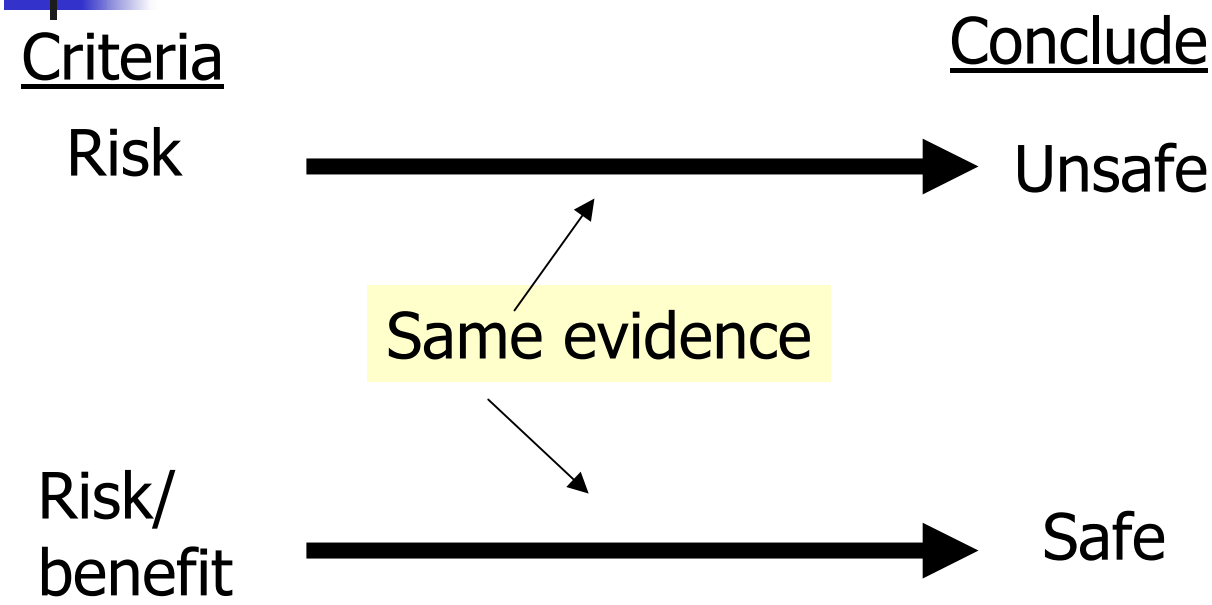

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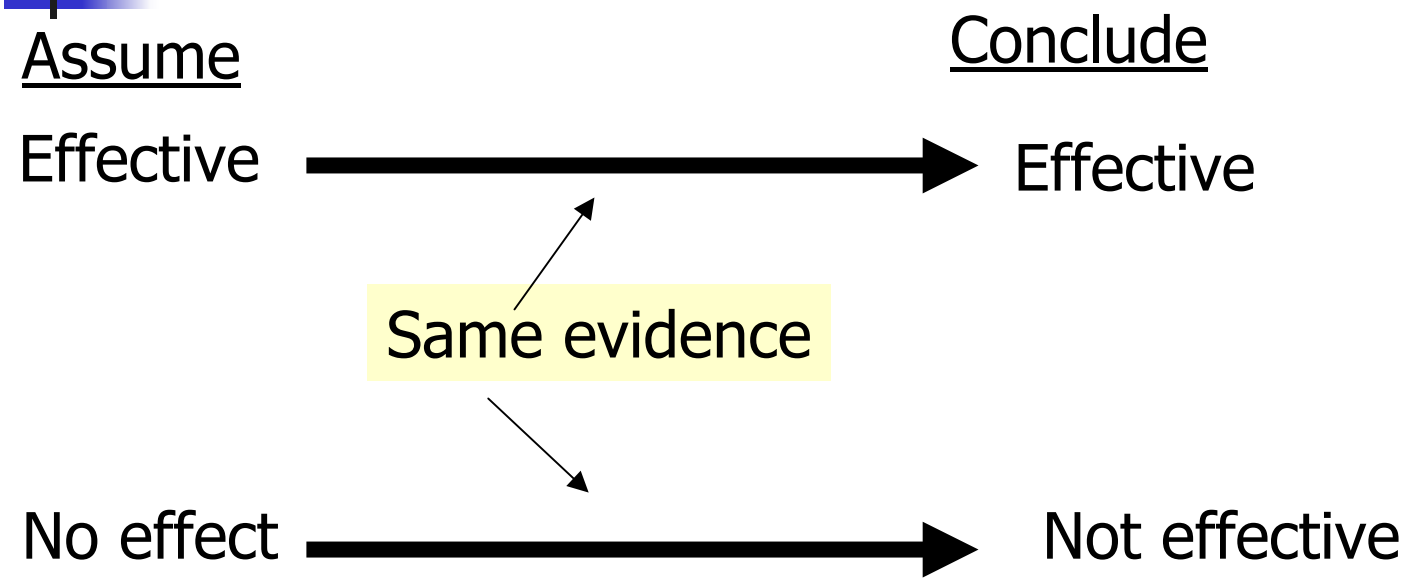
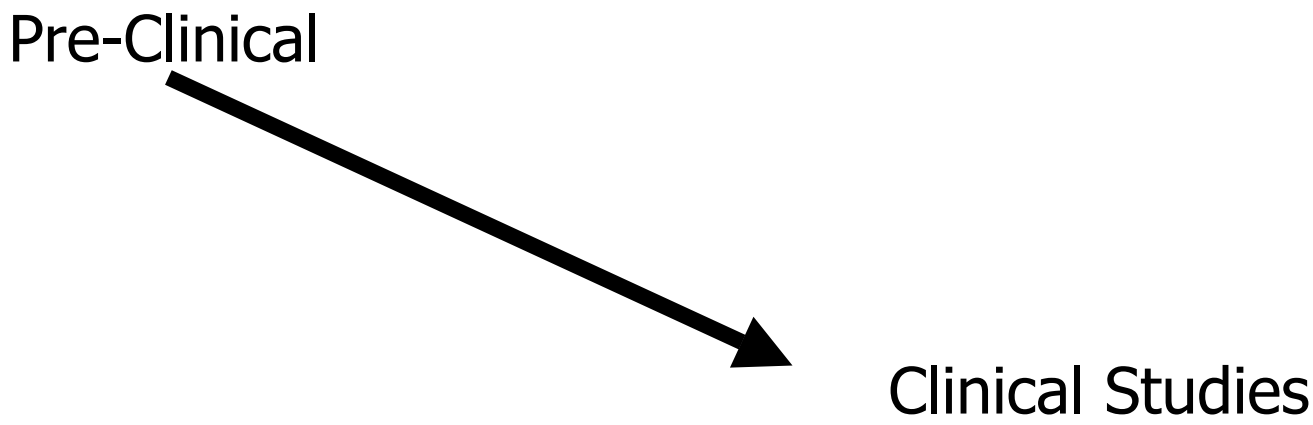


"Usual" Scientific Process



For substance to be marketed under anticipated conditions of use

“Reality” – Scientific Evidence

History of use
-
Efficacy studies
-
Observational data

Safe

“Reality” – Scientific Evidence

History of use
-
Drug efficacy study
-
Observational data

Effective as a supplement

“Reality” -- Available Evidence

- Generalize:
  - Single high dose to lower dose
  - Short term to long term use
  - High risk to general population
  - One product to all products

Post-market Safety Challenges

- Under- and incomplete-reporting
- Product composition
- Consumer:
  - Use patterns
  - Individual sensitivities
- Causality
- Biological plausability

Ephedra: Adrenergic activity

	α	β_1	β_2	CNS
Eph	+	++	++	++
PSE	+	+	+	+
PPA	++	+/-	+/-	++
Nor-eph	+++	+	0	0

Interactions: Soy Protein

- Net Effect?
  - Daidzen
  - Genistein
  - Equol
  - Gut flora
  - Soy protein matrix

Interactions

- Active Ingredients/Product:
  - Mean: 22
  - Range: 1 to >50
- Multiple products used

Use Conditions

- Concurrent rapid weight losses
- Physical exertion/dehydration
- Concurrent illnesses
- Interactions with drugs and foods
- Interactions within individual products

Evaluation strategies

- Generic vs. product specific
- Pre-market systematic approaches
- Post-market monitoring and surveillance
  - Biomarkers
  - Product composition and use patterns

Research Needs

- Relevance to supplement use as a food
- Individual sensitivities/idiosyncrasies
- Drug and food interactions
- How use conditions alter potential for toxicity

Research Needs

- Validation of analytical methods
- Validation of rapid screening tests
- Validation of animal models
- Validation of "interpretable" biomarkers for population monitoring and surveillance
- Relative effects

Safety Research Needs

- Link to adverse events
- Relevant to conditions of use
- Biological plausibility
- Relative toxicities

Summary

- General population
- Risk reduction, not treatment etc.
- Risk, not risk/benefit
- Research:
  - Pre-market
  - Post-market