NCCAM Colloquium: Industrial Perspective

"Industry and the Role of NCCAM in the Development of Complementary and Alternative Medicine Products for the US Market"

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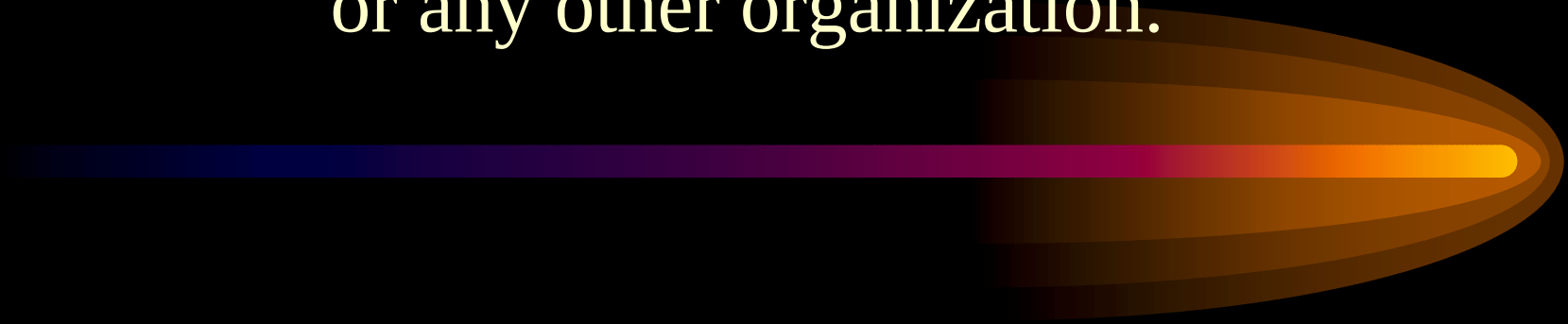


NIH NCCAM - Industry Colloquim

Questions

- *What* **is** *the "industry"?*
- *How does the industry perceive CAM?*
- *What are the needs of the industry?*
- *What role can NIH play in the development of CAM by industry?*

U.S. Regulatory Agencies

- FDA
- FTC
- USDA
- DEA
- ATF
- US Customs
- FWS

U.S. Regulation

- **FDA**
  - **foods, drugs, biologics, cosmetics, medical devices, radiation producing devices**
  - **labeling of regulated products**
  - **advertising & promotion of Rx drugs**
- **FTC**
  - **advertising & promotion of foods, devices, OTC drugs**
  - **advertising of practices, procedures**
- **EPA**
  - **pesticide tolerances**
- **USDA**
  - **commodities, animal vaccines**

Products Used in CAM
Foods

- conventional foods, teas
- spices, “food additives”
- dietary supplements

Products Used in CAM
Drugs

- botanical drugs
- homeopathic drugs
- off-label use of conventional drugs
- use of products not currently marketed as drugs (e.g., foods, dietary supplements)

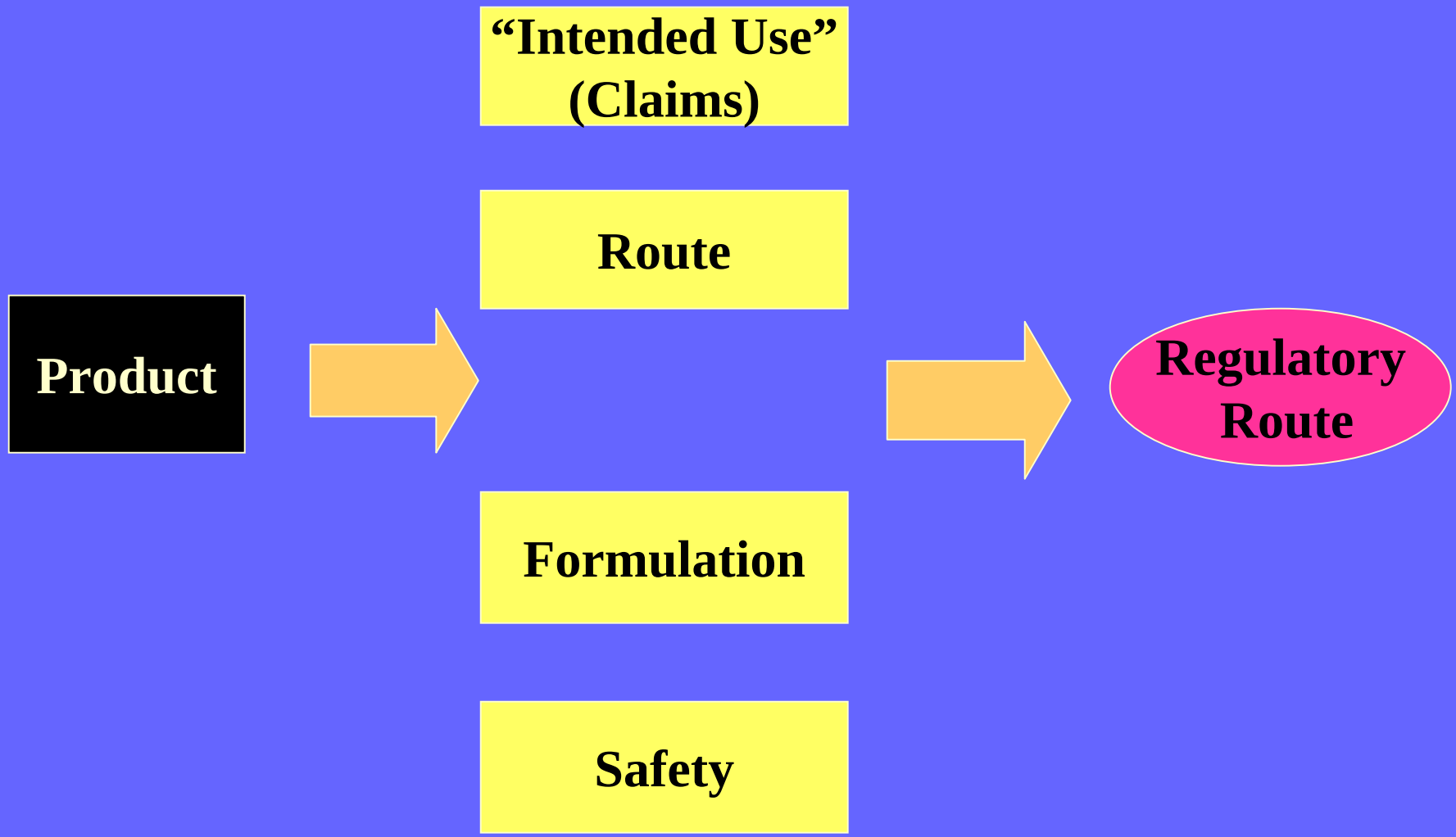
Products Used in CAM
Biologics

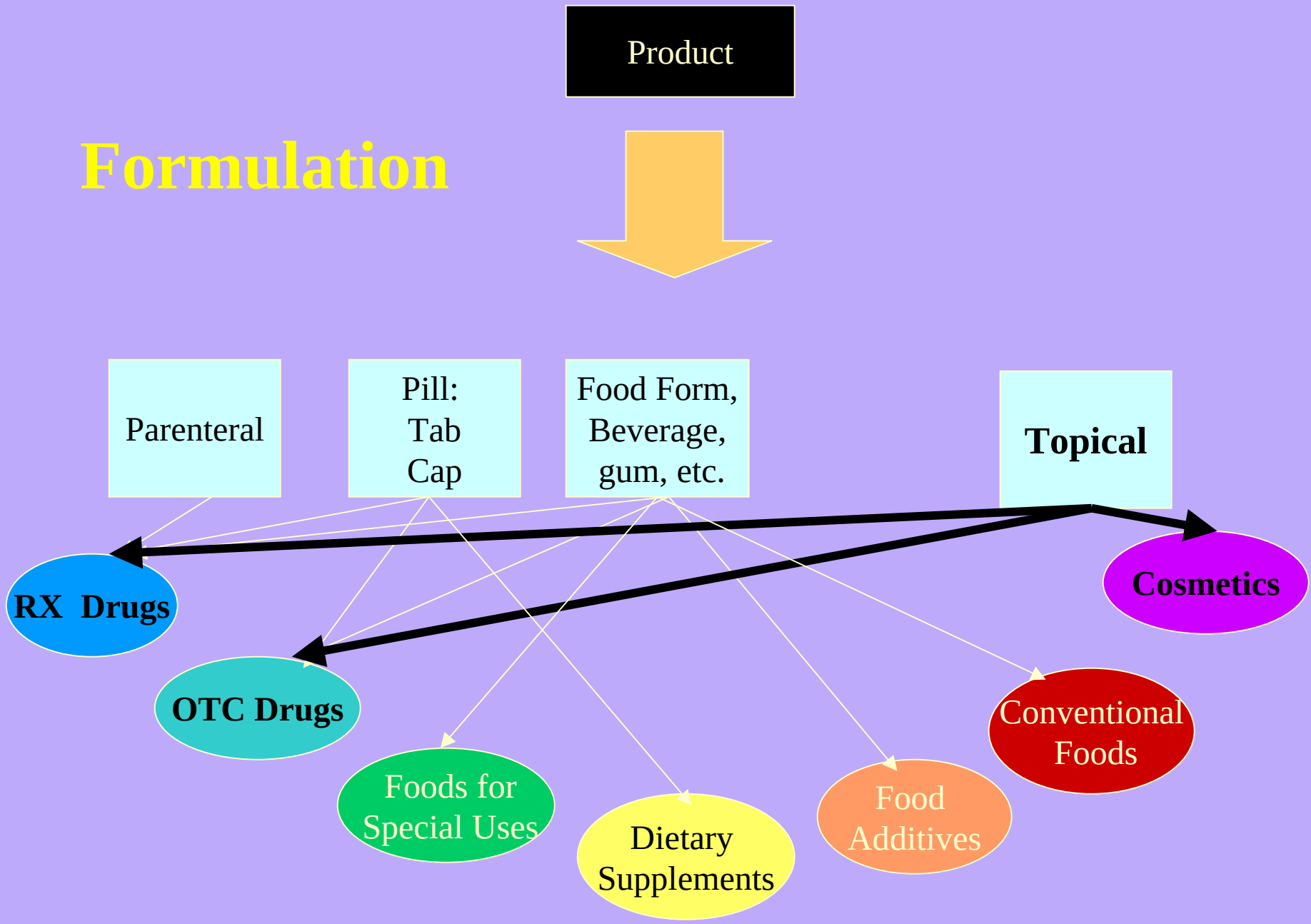
- vaccines(e.g., Coley's toxin; allergenic --to pollens, grasses)
- antibodies (colostrom, whey)
- cytokines (homeopathic, etc.)
- blood-derived products
- diagnostic test kits related to blood-borne diseases (e.g., HIV, hepatitis)

Products Used in CAM
Medical Devices

- acupuncture devices (needles, etc.)
- biofeedback
- electromagnetism
- all diagnostic test-kits not regulated as biologics (e.g., heavy metal screens)
- radiation and light

Factors in the Selection of Regulatory Route

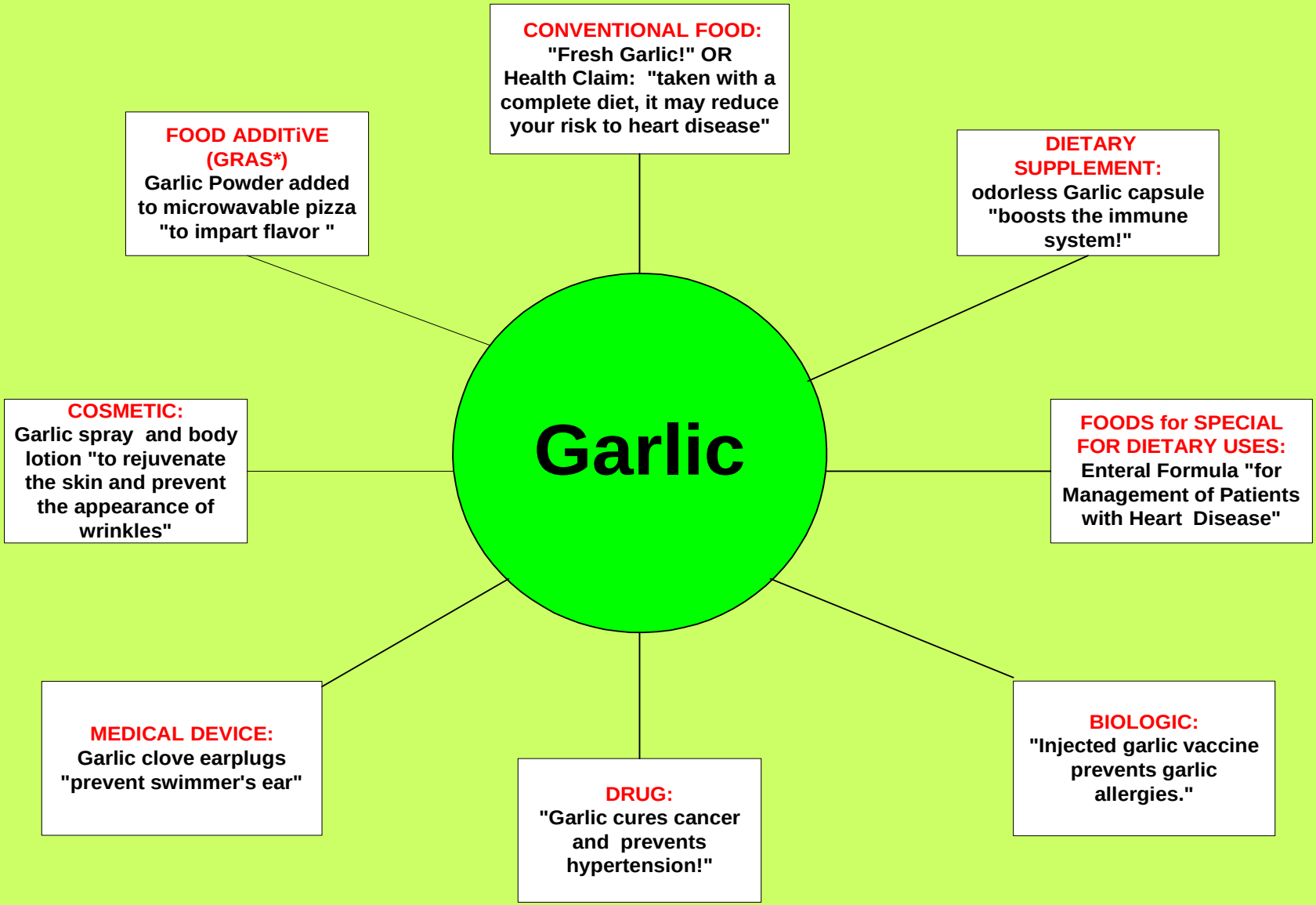



Product
Formulation
Parenteral
Pill:
Tab
Cap
Food Form,
Beverage,
gum, etc.
Topical
RX Drugs
OTC Drugs
Cosmetics
Foods for
Special Uses
Dietary
Supplements
Food
Additives
Conventional
Foods

Intended Use Defines the U.S. Regulatory Classification

Example: Claims for Garlic Products

From: FA Hoffman and T Garvey IV; Textbook of Legal Medicine, 5th ed/ 2001



*** Garlic is Generally Recognized As Safe (GRAS) based on its common use in food prior to January 1, 1958. 21 CFR 570.30(a)(1).**

What *is* the “Industry?”

More than one industry

Regulated Industries producing CAM products:

- Food
- Dietary Supplement
- Herbal
- OTC Pharmaceutical
- Rx Pharmaceutical
- Device
- Diagnostic
- Biologics
- Cosmetic
- Veterinary

Botanicals: A "Growing" Market

Consumer sales in $Millions all retail channels, direct sales, MLM, mail order, practitioner sales

- 1994 $ 2,020
- 1995 $ 2,470
- 1996 $ 2,990
- 1997 $ 3,530 **> 100% ↑**
- 1998 $ 3,980 **in < 6 years**
- 1999 $ 4,400
- 2000 $ 4,800
- **Source: Nutrition Business Journal 2001**

POTENTIAL US MARKETS
for Botanicals 1998 (1997) in $ Billions

- **Prescription Drug Market** **$ 81.3 (94.0)**

  Source: Pharmaceutical Research and Manufacturers of America

- **OTC Drug Market** **$ 16.7 (16.7)**

  Source: Consumer Healthcare Products Association
  (Nonprescription Drug Manufacturers Association)

- **Supplement Market** **$ 25.8 (10.4)**

  Source: Nutrition Business Journal

- **Current Botanical Market** **$ 3.9 (3.2)**

  Source: Nutrition Business Journal

Adapted from Floyd E. Leaders, Jr. - Botanical Enterprises, Inc.

Factors Influencing the Development of CAM Products

How the FDA perceives CAM:

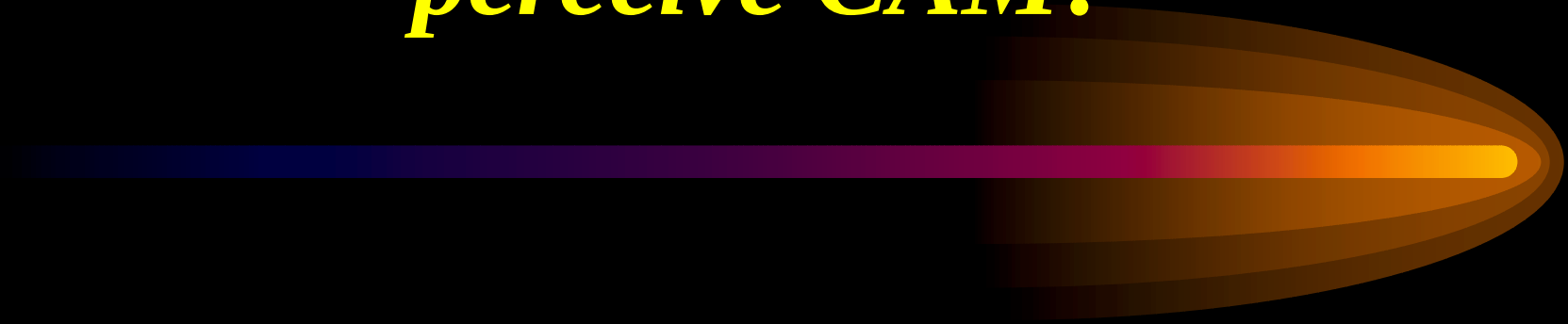
FDA has no legal, regulatory, or policy definition of

"complementary" or "alternative" medicine.

“There are no alternative products ----
only alternative sponsors.”

F Hoffman, Pfizer, Inc. 5/01

How does the industry perceive CAM?



Industry Perceptions

Mainstream industries are-----

mainstream!

US Industry Perceptions of CAM

Product Factors

- Quackery?!?-- no scientific rationale; no "proof of concept"
- too available to the public
- unavailable/ "not invented here" (inventor is unwilling to release details of product or procedure; foreign owned)

US Industry Perceptions of CAM

Milieu

Regulatory confusion

- DSHEA Structure/Function claims
- no dietary supplement GMPs
- ?CMC section of IND for complex products
- foreign regulatory pathways don’t match up to US

US Industry Perceptions of CAM

Barriers

- unusable “data”: product sold for a use for which it is was not intended (i.e., GMP issues)
- individualized intervention - not generalizable for product labeling
- other, e.g., environmental (protection, biodiversity)

US Industry Perceptions of CAM

Industry Factors

- outside core competencies
  - (e.g., foods being used as drugs)
  - no expertise (medical botanists; naturapaths; homeopaths)
- scale up (local or environmental impact)

US Industry Perceptions of CAM

Marketing Factors

- no proprietary insulation (e.g.,unpatentable)
- culturally unrecognized or novel indication
- cost of development outstrips ROI (e.g., commodity pricing)
- distribution is outside usual channels (e.g., health food stores)

What are the needs of the industry?

What role can NIH play in the development of CAM by industry?

US Industry Stakeholders

In search of...

- adequate “size of the opportunity”
- validation of “proof of concept”
- assurance of regulatory outcome
- sustainability of intellectual property
- competitive advantage
- ROI

US Industry Stakeholders

Preclinical Needs

- characterization/standardization the "product" (includes nomenclature, taxonomy)
- mechanism of action
- "modeling studies" (in vitro/animals)
- safety (pharmacology/toxicology)

US Industry Stakeholders

Clinical Needs

- Defining and Confirming Safety
  - collection/analysis of prior human use
- Defining and Confirming Efficacy
  - scientific plausibility of response
  - strength of association (dose/response; temporal)
  - reproducibility of outcome measurements
  - breadth of response (extrapolation beyond current/historical use)

Historical Perspective

Role of the

NIH Office of Alternative Medicine:

- Acupuncture devices
- Botanical drugs

NIH
Office of Alternative Medicine

RFA (FY94):

- 800 “letters of intent”
- >400 grant applications received
- 2 dozen grants with regulated products for indications: to “diagnose, treat, prevent, mitigate or cure” disease

Acupuncture Needles
Status - 1994

- unapproved at change in law [5/76] thus: “investigational” Class 3 medical devices
- no interested company resulted in:
  - no manufacturing controls or assurances
  - no labeling
  - not reimbursed

NIH - OAM

Acupuncture Needles

- NIH OAM - FDA Symposium on Acupuncture Devices (Apr 1994)
- focus: outstanding regulatory issues
- participants: academia, industry, NIH, FDA
- resulted in 5 Citizen Petitions to FDA

Acupuncture Needles
Status - 1996

FDA reclassification of acupuncture needle devices (4-01-96), results in:

- legally marketed devices
- labeling review
- GMPs
- new research >> new products

NIH- Office of Alternative Medicine

Botanical INDs

- 3 grants required INDs:
  - Columbia U - post menopausal symptoms
  - Emory - topical plantar warts
  - SF AIDs Clinic - chronic sinusitis w/HIV+
- All multiple Chinese herbals regimens

NIH-OAM

NIH-FDA Symposium 12/94

"What Role (if any) might Botanicals play in US Healthcare?"

- How are botanicals used today?
- How do we know they work?
- How do we know they are safe?
- How do we know what they are?
- What are the incentives and barriers to bringing botanicals to the US market?

Drug Information Association Botanical Conferences

- DIA (w/NIH, FDA): 3/95 - Worldwide Use
- DIA (w/NIH, FDA, USP): 4/96 - Chemistry, Taxonomy, Nomenclature
- DIA (w/NIH, FDA): 1/97- Pharm/Toxocology
- DIA (w/NIH, FDA): 11/97-Clinical/Regulatory
- DIA (w/FDA): 2/98 [Cape Town]- Trade/patent
- DIA (w/ FDA): 3/99 Pharmacoeconomics

Botanical Drugs: FDA's Activities

- Guidance for Industry for development of Botanical Drugs [8/10/00]
- Revising its regulations [i.e., Combination Rule
- Proposed Rules: Use of foreign marketing experience for OTC monographs[12/20/99]

NIH - Office of Alternative Medicine

Transparency of the Process

If NIH-funded,

grantees would acknowledge existence of their INDs----

clarification of the regulatory pathway

Botanicals as Future Drugs in the US marketplace

- > 100 investigational new drug (IND) applications now in the system

Summary
NCCAM's Role

- Fund/conduct "proof of concept" and mechanism of action studies through SBIR grants, etc.
- stimulate evolution of US regulation by:
  - encouraging transparency of the process
  - supporting public discussion

Summary

NCCAM's Role--contd.

- New approaches for evaluating technologies that work through unusual unconventional mechanisms
- Support quality and standards development (e.g., Botanical Center Grants)
- Technology assessment (Consensus Conferences)
- Identify unmet clinical and consumer needs
- Identify/support needs of independent investigators

F Hoffman, Pfizer, Inc. 5/01