BIOE 301

Lecture 19

http://www.npr.org/templates/story/story.php?storyId=1579643

Zantrex-3

- One of the most popular weight loss supplements currently sold in the US
  - One month's supply: $50
  - Millions of bottles sold
- Hit US market in March, 2003
- Sold at:
  - GNC, CVS, RiteAid, Wal-Mart, internet, eBay
- Contains:
  - Caffeine
  - Green tea
  - Three common South American herbs that act as stimulants

http://www.intomyhealth.com/diet-pills/zantrex-3/britney-spears.html

Zantrex Marketing

- Don Atkinson
  - VP of Sales for Basic Research
  - Company that distributes Zantrex-3
- "When I train salespeople, I say to them, 'Do you know what people are calling you for? It isn't the pill. They are calling you for hope. That is really what they want from you.' "
- "I love my job. And do you know why? Because when I get up in the morning I know somebody's life is better because we are here. Somebody today got some hope."

Marketing, Then and Now

Benefits of Supplements

- Vitamin C to prevent scurvy
  - Mid-18th century:
    - Scurvy killed more British sailors than war
- Folic acid to prevent neural tube defects
- Calcium to prevent osteoporosis
- Vitamin B_{12} to prevent dementia
- Research in Alternative Medicine:
  - http://nccam.nih.gov/

History of Supplements

- 1793:
  - Patent legislation that permitted manufacturers to protect their formulations
  - Did not require that they work
- Early 1800s:
  - Number of newspapers in US published increased dramatically
- Early 1900s:
  - Patent-medicine business accounted for more newspaper ads than any other kind of product

Lydia Pinkham's Vegetable Compound

- "A Positive Cure" for "all those Painful Complaints and Weaknesses so common to our female population"
- 1914 AMA analyzed Pinkham's compound
  - 20% pure alcohol
  - 80% pure vegetable extracts
- Many supplements laced with:
  - Cocaine
  - Caffeine
  - Opium
  - Morphine

http://www.lynximages.com/images3/lydia.jpg

History of Regulation

- 1906
  - First federal regulation of drugs
  - Pure Food and Drug Act
- 1938
  - Food, Drug and Cosmetic Act
- 1962
  - Drug amendments to FD&C Act
- 1976
  - Medical Device Amendments to FD&C Act
- 1994:
  - Dietary Supplement Health & Education Act

History of Supplements

- 1906:
  - Pure Food and Drug Act
  - Reaction to "The Jungle" by Upton Sinclair
  - Permitted Bureau of Chemistry to insure that labels contained no false or misleading advertising

http://i.timeinc.net/time/magazine/archive/covers/1934/1101341022_400.jpg

1906

- Pure Food and Drug Act
  - Label could not contain any statement regarding therapeutic effect which is false and fraudulent
- FDA could act only after drugs were marketed
- Was not enough to show that product did not work
- Had to show that seller knew the claims it made were false

History of Supplements

- 1937:
  - Sulfanilimide, antibiotic for streptococcal infections, used safely as a pill for years
  - Most children can't swallow pills
  - One company in Tennessee found they could dissolve drug in ethylene glycol (antifreeze)
  - Tested for flavor, appearance, fragrance, NOT for toxicity
  - Shipped it all over the country
  - Within weeks, scores of children were dead

Sulfanilimide

- 137 children died
  - Severe abdominal pain, nausea, vomiting, convulsions
- "Even the memory of her is mixed with sorrow for we can see her little body tossing to and fro and hear that little voice screaming with pain and it seems as though it would drive me insane."
  - Letter to FDR, from woman describing the death of her child

History of Regulation

- Food, Drug and Cosmetic Act - 1938
  - Gave FDA authority it needed to regulate such products
  - New Drugs:
    - Could not be marketed without first notifying the FDA and allowing agency time to assess safety
    - Beginning of era in which it is illegal to market a new drug without FDA approval
  - Seller's belief regarding product's value was no longer relevant
  - Issue – does the product really work?

History of Supplements

- 1940s-1960s:
  - Line between foods and drugs was fairly clear
  - If manufacturers made a disease related claim for a supplement, FDA would go after them
- 1970s:
  - Government started telling Americans to alter diets if they wanted to have longer, healthier lives
  - Heart disease, diabetes, cancers → eat less salt, fat; add fiber, eat more fruits & vegetables

Kellogg's All Bran

- 1984:
  - Launched campaign with NCI
  - All-Bran cereal illustrated how low-fat, high-fiber diet might reduce risk of certain cancers
  - http://www.kelloggs.com/brand/allbran/

1994: Dietary Supplement Health & Education Act

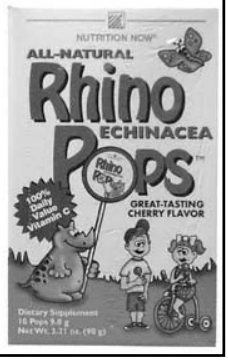
- Congress deregulated supplement industry
- Companies are not required to prove products are effective or even safe before marketing them
- Companies CANNOT:
  - Blatantly lie
  - Claim to have a cure for a specific disease (cancer, diabetes, AIDS)
- Companies CAN say (without evidence):
  - Product is designed to support a healthy heart
    - CardiAll
  - Protect cells from damage
    - Liverite
  - Improve function of compromised immune system
    - Resist
- Almost no standards that regulate how pills are made
- Not tested once they are made

Today

- CANNOT mention disease
- CAN make claims that food can affect structure or function of body
- Examples:
  - CANNOT say that a product reduced cholesterol but CAN say it maintains healthy cholesterol levels
  - CANNOT say echinacea cures disease, but CAN say it has natural antibiotic activities and is considered an excellent herb for infections of all kinds

Echinacea

- One of the most commonly used cold remedies in US
- Clinical Trial:
  - 400 children with common colds over 4 months
  - Compared placebo to echinacea
  - Placebo worked just as well
  - Children taking echinacea were more likely to develop a rash



http://www.kalyx.com/store/images/208093.jpg

Ephedra

- Was most popular supplement in US
- Brought in more than $1B/year
- 10% of supplement industry annual sales
- Risks of ephedra use (when used with caffeine):
  - Increased risk of heart attack, stroke, palpitations, anxiety, psychosis, death
- Steve Bechler
  - 23 year old pitcher for Baltimore Orioles
  - Died February, 2003 of heatstroke following taking an over-the-counter product that contained ephedra
- http://www.npr.org/templates/story/story.php?storyId=1576453
- http://www.npr.org/templates/story/story.php?storyId=11326842

Misfortune, disaster, & tragedy

Lead to reforms in drug and device regulation

FDA

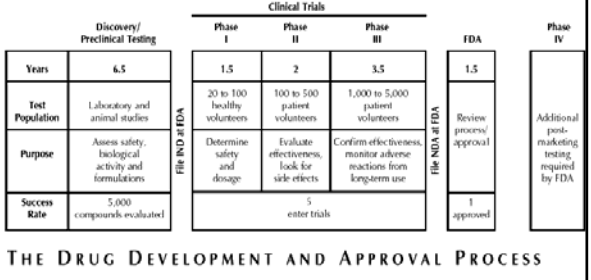
- Regulates products whose annual sales account for ¼ of consumer spending in US
- Responsible for ensuring SAFETY and EFFICACY of CHEMICAL, BIOLOGICAL agents and sophisticated medical DEVICES
- Safe:
  - Probable benefits to health for intended use outweigh any probable risk of harm
- Effective:
  - Device does what it is supposed to do in a reliable fashion

1962

- Drug Amendments to FD&C Act:
  - FDA must review evidence of drug safety and effectiveness
  - Converted pre-market notification system into pre-market approval system
  - Evidence of safety and efficacy must come from well-controlled investigations by qualified experts
- FDA has the authority to prevent harm before it occurs

Drug Approval Process

- Pre-clinical testing (cell, animal) occurs first
  - Assess toxicity
- Investigational New Drug (IND)
- Human clinical trials allowed with IND
  - Phase 1, 2, 3 clinical trials
- Manufacturer files NDA (New Drug Application) for permission to market new drug



THE DRUG DEVELOPMENT AND APPROVAL PROCESS

Phases of Clinical Trials

- Phase 1:
  - Goal: safety of compound
  - Low doses administered to small group of healthy volunteers
  - 20-100 volunteers
- Phase 2:
  - Goal: effectiveness of compound
  - 100-300 patients who suffer from condition
- Phase 3:
  - Final step before seeking FDA approval
  - Randomized clinical trial

Post-Market Surveillance

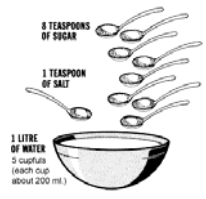
- Phase 4:
  - Study longer term effects of drug exposure
  - Report adverse effects to FDA

Not Many Drugs Make It

- For every 5,000-10,000 drugs that enter pre-clinical testing
- ONE makes it to market
- Average 15 years to develop one drug
- Cost of developing one new drug:
  - $360 million-$800 million

Oral Rehydration Therapy

- Diarrhea – 2nd leading cause of death under 5
- 1.5 million children per year
- Cause of death – dehydration
- Doesn't treat diarrhea

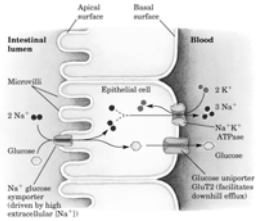


Story of ORT

- Previously treated with IV fluid
  - Expensive, ineffective, dangerous
- 1950's – anecdotal evidence by Dr. Hemendra Chatterjee in India
  - Given no credibility, lack of controlled study or mechanism for efficacy
- Early 1960s' – sodium-glucose cotransport discovery

Sodium-glucose cotransport

- Not affected by cholera or other diarrhea causing diseases
- Works DOWN the concentration gradient



Bangladesh Liberation War

- Proved ORT was effective
- 3.6% death rate compared to 30% death rate with IV fluid

LifeStraw

- Vestegard Frandson
- Personal, portable, electricity free water filter
  - 100 micrometer mesh, 15 micrometer mesh, iodine, activated carbon
- Powered by suction
- Filters up to 700L water, about 1 year supply
- $2
- Drawback – doesn't kill giardia

PUR Purifier of Water

- Procter and Gamble, brain child of Greg Allgood
- $0.10 per packet to treat 10L
- Uses treatment similar to water treatment facilities
- Bonus: cleans and disinfects turbid water