

# History of cGMP's & FDA

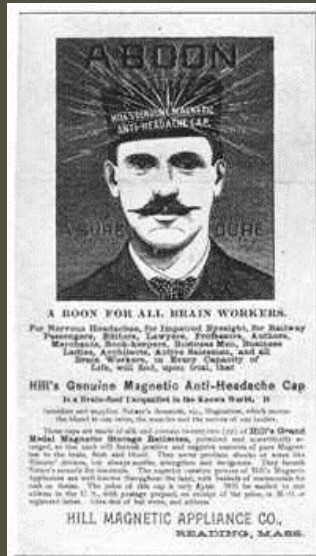
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ASQ – June 1, 2005

# Not a second thought



# What Ails Ya ?



- **Latham's Cathartic Extract:** Sick, headache, Impurities in the blood? Constipation? Here's your cure!
- **Peruvian Syrup:** Cures Dropsy, Dyspepsia, Debility and Humors. Quite the comprehensive medicine!
- **Electro-Voltaic Belt:** to men afflicted with nervous debility, loss of vitality and all kindred troubles. Also for Rheumatism, neuralgia, paralysis, and many other diseases.



- **Munyon's Paw-Paw Pills:** "They coax the liver into activity, they invigorate instead of weaken, & they enrich the blood instead of impoverishing it".
  - (Corrects constipation.)

# 1883 -Dr. Wiley comes to Washington

- Food / Drug rules regulated by states
- Adulteration & misbranding increased by late 1800's
- Wiley expanded research in this area
- Concerned over chemical preservatives in food



“I believe in ‘trying it on the dog’ ”

- Harvey W. Wiley



The Poison Squad dining room

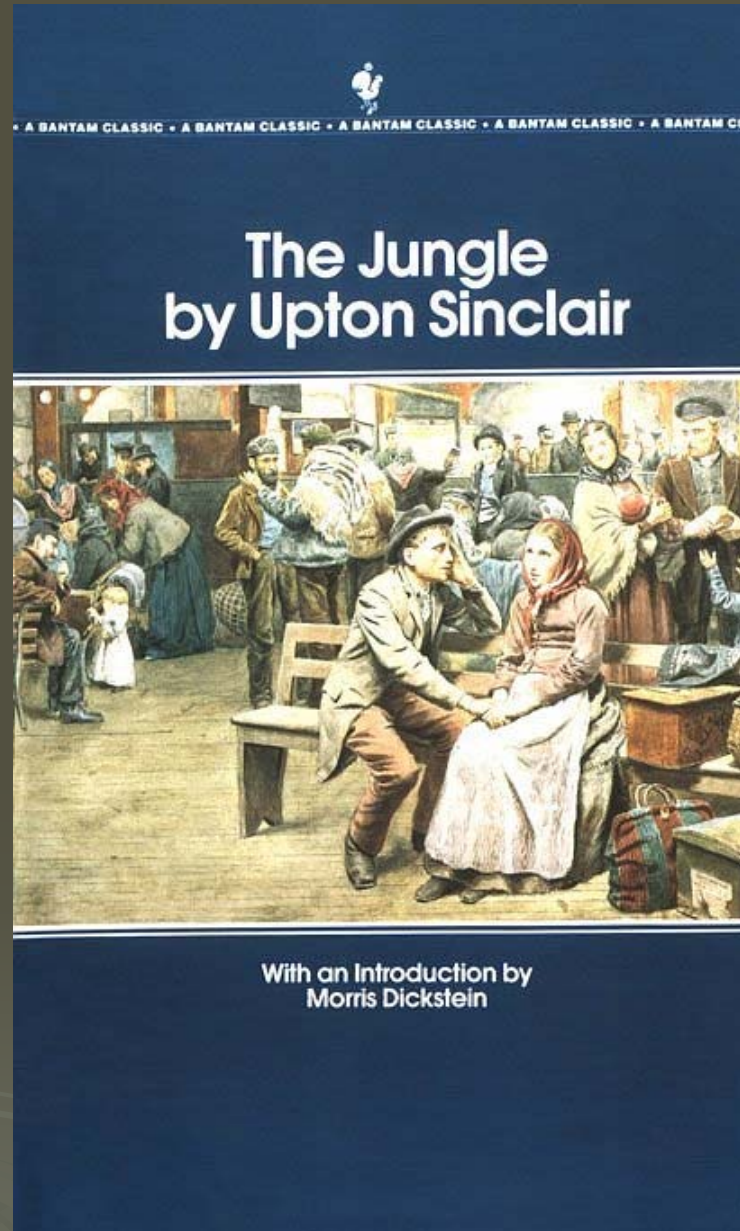
**Christmas Dinner**

*Apple Sauce  
Borax  
Soup  
Chipped Beef with Creamed Gravy  
or  
Turkey  
Borax  
Choice of Sweet or White Potato  
Canned String Beans  
Borax  
Cranberry Sauce, Pickles, Celery  
Rice Pudding  
Milk, Coffee or Tea  
A Little More Borax*



1906

Publication of  
The Jungle  
by Upton Sinclair.



# Get a Bill Passed – NOW!!



# 1906 – Pure Food and Drug Act

- Forbade commerce of adulterated / misbranded food & drugs
- Seized & condemned offending products
- Offending persons could be fined & jailed
- Accurate label statements
- Alcohol / Narcotic presence must be stated on the label



# 1937 - Sulfanilamide

- 7 to 21 days of symptoms
  - stoppage of urine,
  - severe abdominal pain,
  - nausea,
  - vomiting,
  - stupor, and convulsions.
  - intense pain.
  - No known antidote or treatment for diethylene glycol poisoning.



# 1937 - Sulfanilamide

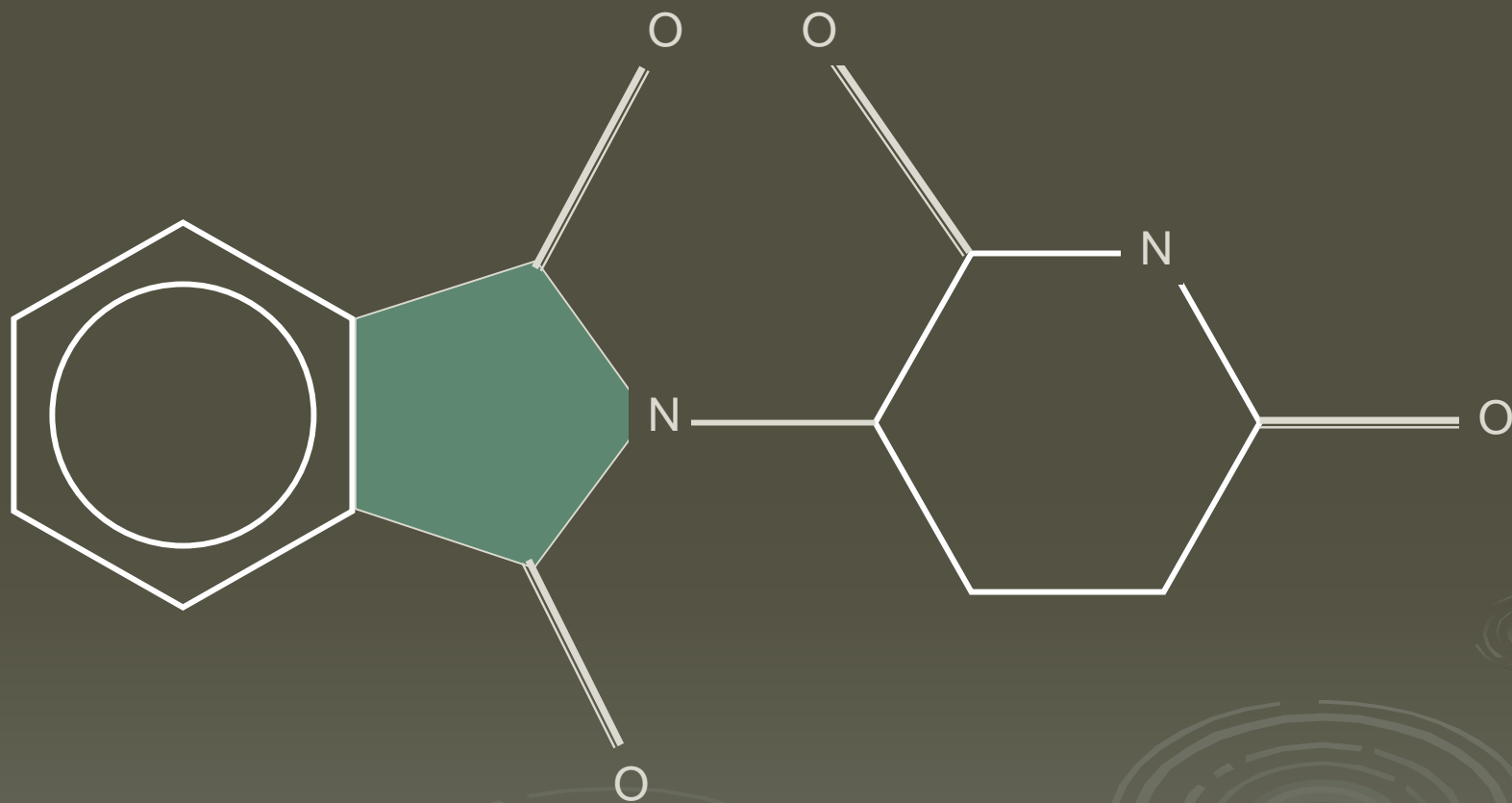
- 108 deaths
- Company was charged with misbranding.



# 1938 – Food, Drug and Cosmetic Act

- New drug application (NDA) required showing drug safety.
- Safe tolerances set for unavoidable poisonous substances
- Directions for use and warnings about possible misuse also required unless the drug was sold by prescription
- Authorized factory inspections

# Thalidomide



# Kefauver-Harris Amendments

- Drug manufacturers must provide information on a drug's effectiveness as well as its safety
- Mandated record keeping
- 60-day review period eradicated
- Permitted FDA to withdraw approval
- Teratogenic testing required
- Clinical trial patient consent



*Dr. Kelsey receiving the Distinguished Federal Civilian Service Award from President John F. Kennedy – Aug 7, 1962*



# Milestones

- **1962** - cGMP's Established in CFR for Drug Manufacture.
- **1978** - Major revisions to the cGMP's dealing with personnel & facilities, as well as products and processes.
- **1995** – Proposed updates to cGMP's - stalled
- **1997** – FDA Modernization Act – globalized industry requires consistent and efficient regulatory requirements

# cGMP's

- Write procedures and work instructions
- Follow procedures and instructions
- Document your work
- Validate / Qualify processes and equipment
- Design proper facilities & equipment
- Maintain and cleanse facilities, equipment & self
- Define, develop & demonstrate job competence
- Protect against contamination
- Control components & product related processes
- Conduct planned & periodic audits

# Quality Systems Approach

- Six System Inspection Approach
  - **Quality System**
  - Facilities & Equipment Systems
  - Production System
  - Materials System
  - Packaging & Labeling System
  - Laboratory Controls System

# 2004 – Risk-Based Approach

- High Risk Products & Processes
  - Sterile drugs, aseptic filtration, prescription drugs
- High Risk Facilities
  - New facilities, First application, Warning letter recipients, Sterile product manufacturers, Recalls
- Encourage technological Advances
- Train FDA on regulating technological advancement

*“Can we learn from this lesson, or can mankind educate itself only by disaster and tragedy?”*

- Sen. Paul Douglas, on the acceptance of the Senate's 1962 drug bill





# Sources

- [www.fda.gov](http://www.fda.gov)
- <http://www.kevincmurphy.com/harveywiley.htm>
- <http://www.annals.org>
- <http://leda.law.harvard.edu>

Thank You !

