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UCDAVIS HEALTH | SCHOOL OF MEDICINE

The FDA, BARDA and the Animal Rule

Disclosures of Conflicts of Interest

Dr. Wulff is an inventor on several University of California patents claiming ion channel modulators for the treatment of autoimmune diseases, epilepsy and pain.

She is consulting on ion channel drug discovery and the pharmacology of voltage-gated and calcium-activated potassium channels. She is receiving consulting fees from Saniona (Denmark), DE Shaw, Muna Therapeutics and TetraGenetics.

Dr. Wulff is the Chief Field Editor for Frontiers in Pharmacology.

FDA (*Food and Drug Administration*)

- Federal agency that regulates food, drugs, medical devices, vaccines, blood products and cosmetics in the United States
- power to approve, restrict the use and withdraw drugs from human or veterinary use
- oversees facilities and adherence to GLP/GMP guidelines, factory inspections

GLP = Good Laboratory Practices; GMP = Good Manufacturing Practices *(or Great masses of paper?)*

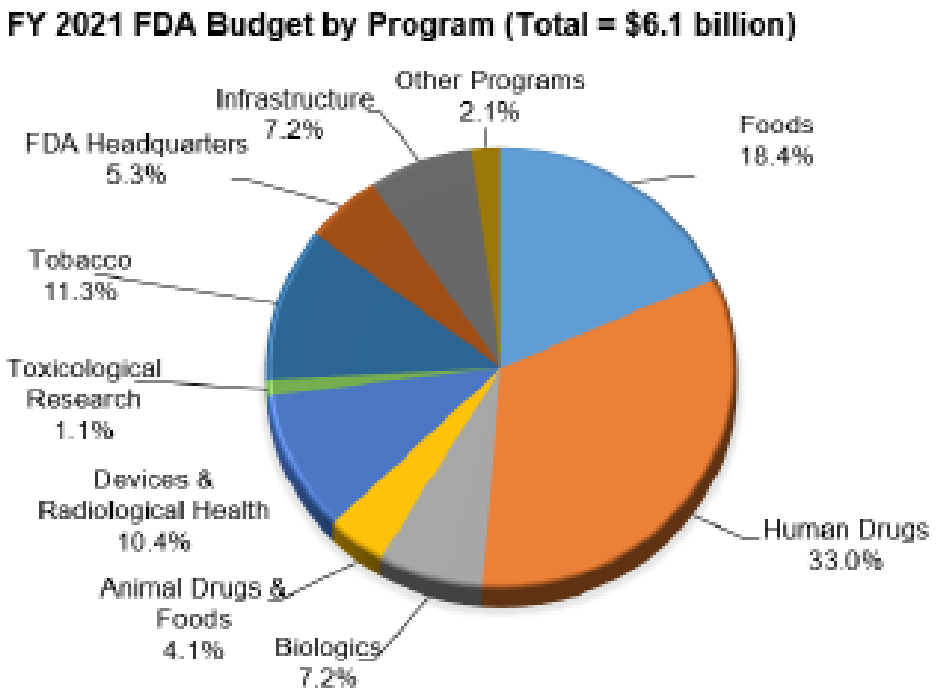
→ ***Pre-clinical and Clinical Trials System***

FDA White Oak Campus

Silver Spring, Maryland

FDA Budget

FY 2021: $6.1 billion
Congressional appropriation: $3.3 billion
Regulated industries (user fees): $2.8 billion



- The FDA oversees $2.7 trillion in consumption of food, medical products and tobacco
- The FDA regulates 35,000 produce farms, 300,000 restaurants and 10,500 vending machine operations
- The FDA oversees 100,000 tobacco products
- There are 20,000 approved prescription drug products for human use and 1,600 drugs for animals
- 78% of APIs (= active pharmaceutical ingredients) manufacturers are located outside of the US
- The FDA oversees 1,600 medical device categories
- The FDA employs close to 20,000 people

FDA (*Food and Drug Administration*)

Drug manufacture and drug approval are among the most regulated processes on the planet.

But there is a reason for this. Let's look at how we got there.

"Oh great. Now the FDA is regulating safety coated caplets of eyes of newt."

CartoonStock.com

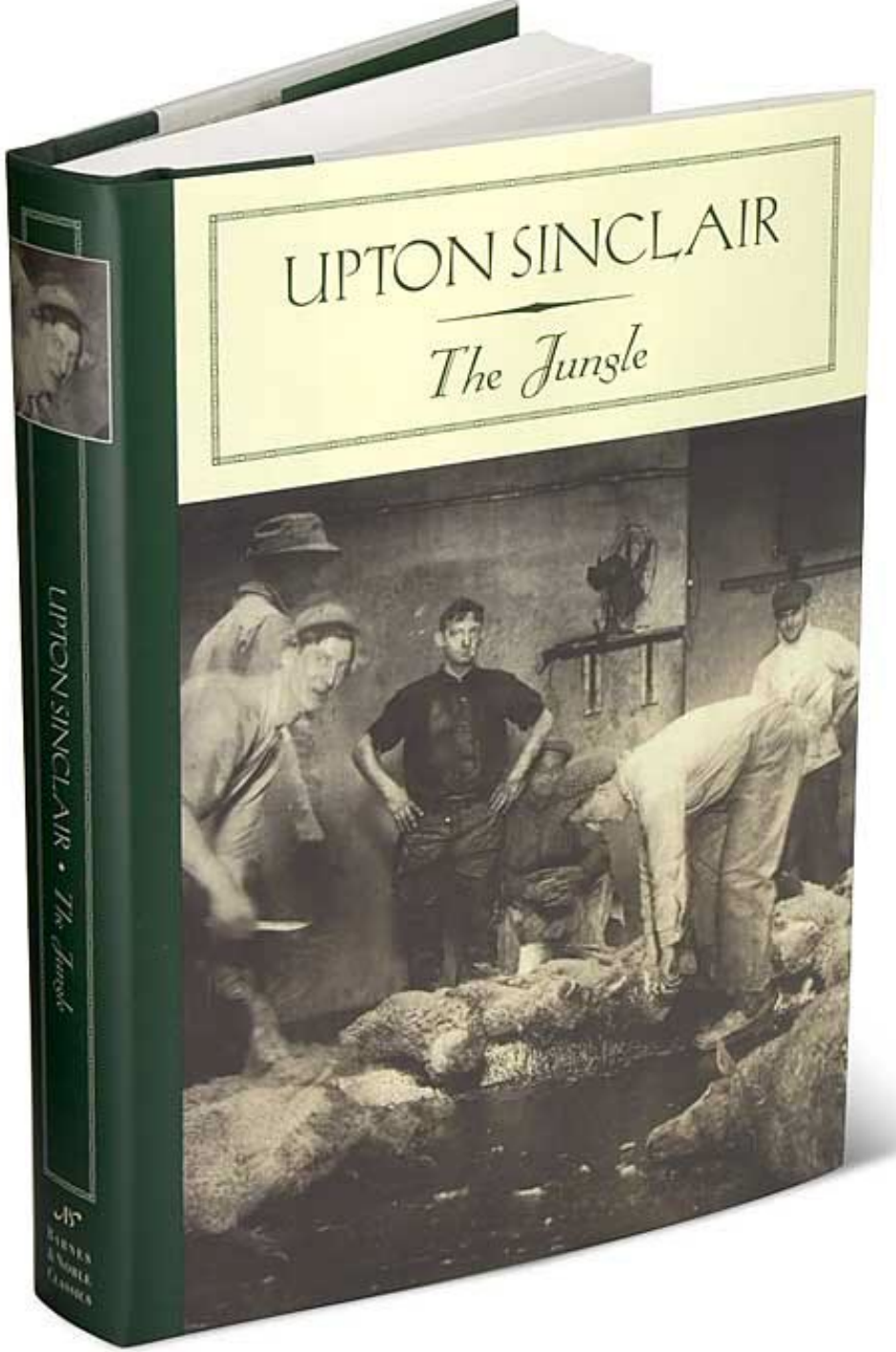
The Poison Squad tested Preservatives in 1902

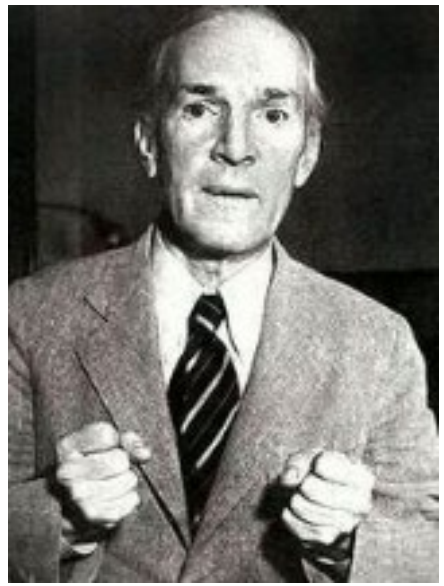
In 1902 Harvey W. Wiley was trying to build support for a national food and drug law and initiated the "Poison Squad" to test the effect of preservatives on human health.

→ Healthy volunteers (all men, mostly chemists) ate capsules containing borax, salicylic acid, formaldehyde, saccharin, sodium benzoate and copper salts with their meals

→ Americans became interested in food safety

→ Formaldehyde was banned as a preservative





- Published 1906
- Originally intended to expose the exploitation workers
- Sinclair described workers falling into rendering tanks and being ground, along with animal parts, into “Durham's Pure Leaf Lard“
- Public shocked
- Foreign sales of American meat fell by 50%.

Drugs and “Patent” Medicines


Am. J. Ph.] 7 [December, 1901

BAYER Pharmaceutical Products

HEROIN—HYDROCHLORIDE

is pre-eminently adapted for the manufacture of cough elixirs, cough balsams, cough drops, cough lozenges, and cough medicines of any kind. Price in 1 oz. packages, $4.85 per ounce; less in larger quantities. The efficient dose being very small (1-48 to 1-24 gr.), it is

The Cheapest Specific for the Relief of Coughs

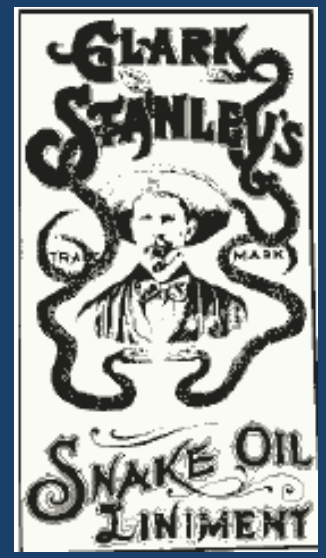
(In bronchitis, phthisis, whooping cough, etc., etc.)

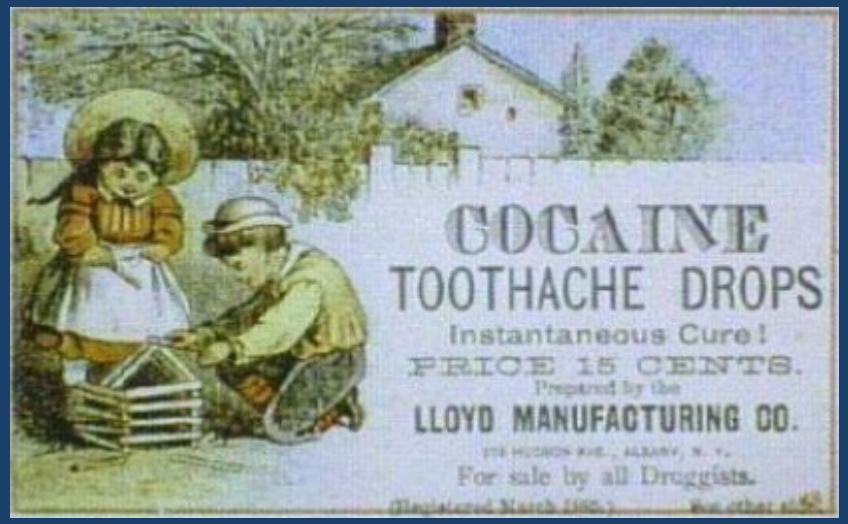
WRITE FOR LITERATURE TO

FARBENFABRIKEN OF ELBERFELD COMPANY

SELLING AGENTS

P. O. Box 2160 40 Stone Street, NEW YORK





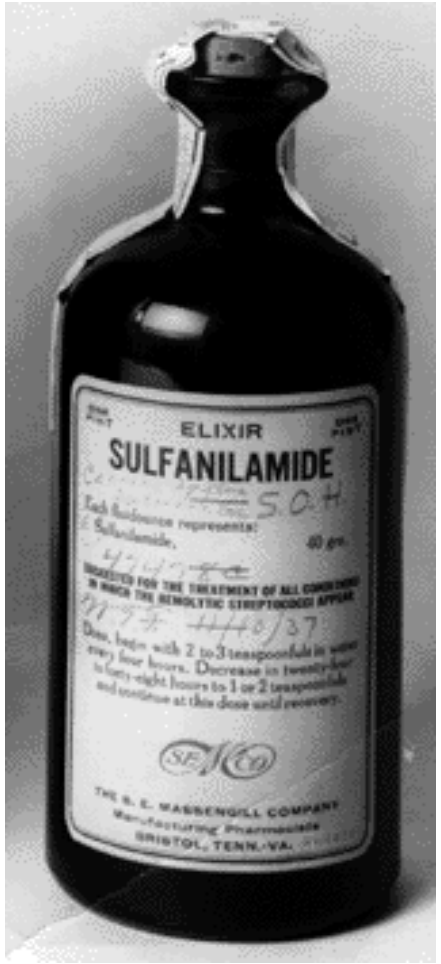
65 mg morphine per ounce

1906 Pure Food and Drugs Act

- Created the FDA (Roosevelt a strong supporter)
- Prohibited “Adulteration” and “Misbranding” of food
- Required labels that described content and declared alcohol and heroine!!
- Introduced first drug standards
- Meat Inspection Act

A Turning Point

- Elixir Sulfanilamide in 1937
  - First Sulfonamide sold for the treatment of infections
  - Contained diethylene glycol as solvent and raspberry flavor to make it “sweet” for children
  - More than 100 children died from kidney failure leading to a public outcry



Federal Food, Drug, and Cosmetic Act 1938

- Pre-market **safety** approval of all new drugs
- Prohibited false therapeutic claims for drugs
- Drugs labeled with adequate directions for safe use
- Food standards “in the interests of consumers”
- Cosmetics and medical devices come under FDA jurisdiction

This says nothing about efficacy yet.

Amendments – 1950s

- Durham-Humphrey Amendment of 1951 required human drugs which cannot be safely used without medical supervision must be dispensed only on the prescription of a licensed practitioner, and must bear the **Rx** legend

Drug Abuse

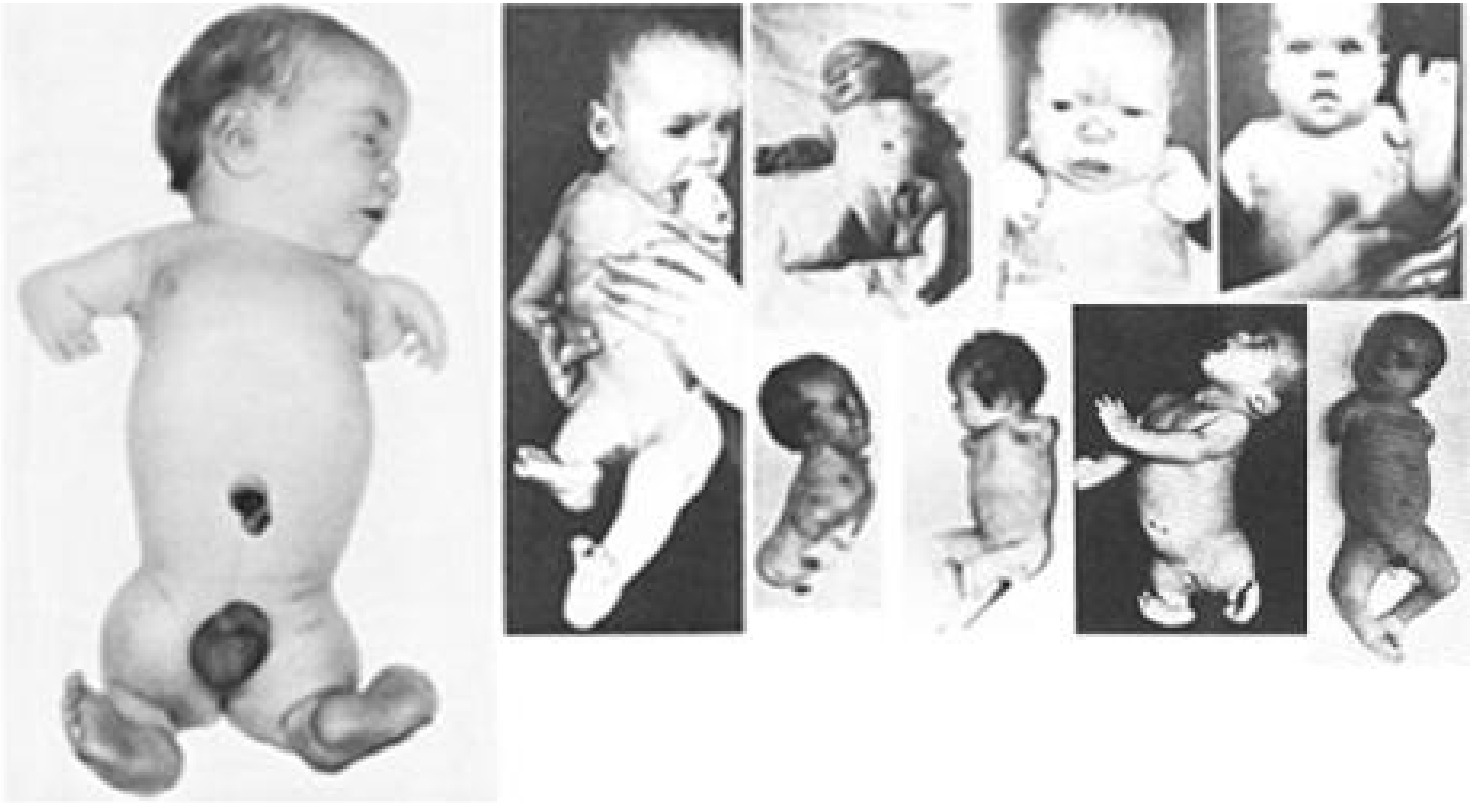
- From the 1940s to the 1960s, the abuse of amphetamines and barbiturates required more regulatory effort by FDA than all other drug problems combined

- 1965 Drug Abuse Control Amendments curbed abuse and introduced concept of:

  "Controlled Substance"

Thalidomide, the Biggest Drug Disaster ever

- marketed in 1960 as Kevadon or Contergan as a sleep-inducing drug and to prevent early morning sickness during pregnancy



→ caused ~10,000 birth defects before taken off the market

A Disaster Averted: Thalidomide

- Sedative sold over-the-counter in Europe
  - Treated morning sickness during pregnancy
  - Produced birth defects in European babies
- FDA received application for marketing in the US
  - Reviewer Frances Kelsey had concerns
  - Delay in approval prevented its being sold in US

Amendments – 1960s

- Kefauver-Harris Amendments - *the most significant changes in the Food, Drug and Cosmetic Act*
  - Required premarket **efficacy and safety** testing
  - Toxicity in at least two species (rodent + dog or primate)
  - Good manufacturing practices
  - Prescription drug advertising regulated
  - Required IRB boards, informed consent
  - Privacy protection for patients
  - Retrospective review of drugs approved before 1960: many ineffective drugs taken off the market

Drug Development

Epidemiology/Analysis of Clinical Trials

For this lecture:

Yes, Dan, PK is descriptive.
Even in humans!!!!

Phase I: Is it safe?

PK and safety in healthy volunteers; sometimes patients but never statistically powered

Phase II: Does it work?

Dose finding and efficacy testing in patients; can be blinded but typically not powered for statistical significance (50-400 patients)

Phase III: Does it really, really work??

This is the real deal: Double blind, placebo controlled and statistically powered; 500 to thousands of patients; FDA requires 2 trials

Orphan Drug Act 1983

- For rare diseases with < 200,000 patients in the US the FDA offers grants, protocol assistance and tax credits

  - Rare cancers
  - Hemophilia
  - Cystic fibrosis
  - Sickle cell anemia
  - Ataxias

Has been very successful: More than 400 drugs for rare and orphan diseases have been developed and approved.

Review Time and Fast-Track

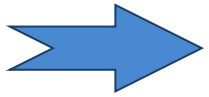
By the late 1980s the average FDA review time for an NDA was close to 3 years !!

- **Drug companies exerted pressure.**
- **Patients and physicians criticized the FDA, severe pressure from AIDS activists since patients needed access to HIV drugs.**

→ "new treatment" IND regulations allow patients with life-threatening diseases to receive drugs that were effective in Phase-3 before general marketing

→ expedited review for life threatening diseases (AIDS, Cancer, Multiple Sclerosis, COVID-19)

→ 1996 Prescription Drug User Fee act allows the FDA to collect a fee from Pharmaceutical Companies to help finance review ($2.8 billion in 2021)



Review time now down to ~1 year
"Fast-track" for urgently needed drugs

Trade in vouchers between companies

And with COVID you have all seen EUAs

➢ An **Emergency Use Authorization (EUA)** is a mechanism to facilitate the availability and use of medical counter-measures, including vaccines, during public health emergencies.

➢ Under an EUA, FDA may allow the use of unapproved medical products, to diagnose, treat, or prevent serious or life-threatening diseases or conditions when there are no adequate, approved, and available alternatives.
If you are interested in the details check this:
Emergency Use Authorization for Vaccines Explained | FDA

Initially all COVID vaccines were being used following an EUA request based on Phase-1 and Phase-2 safety and Phase-3 efficacy without much long-term safety data (lots of follow-up trials going on).

Post-authorization vaccine safety monitoring is a federal government responsibility shared by the FDA and the Centers for Disease Control and Prevention (CDC).

How do you get a drug to market?

Rigorous proof of concept rodent data

Most Pharma companies want at least first in human; ideally Phase-2 data

BARDA wants “technical readiness Level 4”

The Valley of the Shadow of Death (Psalm 23)

IND Contents

- Form FDA 1571
- Table of Contents
- Introductory statement
- General investigational plan *you need to have to have an indication*
- Investigator's brochure *you need to have designed early clinical trials*
- Protocols (study, investigator, facilities, IRB)
- Chemistry, manufacturing, control data (and environmental impact statement) *GMP material required*
- **Pharmacology and toxicology data**
- Previous human experience with the investigational candidate or related compounds, if there is any
- Additional information

Nonclinical Pharmacology in IND/NDA

- **Primary pharmacology** - MOA, animal models
- **Pharmacokinetics (ADME)**
  - Validation of bioanalytical method in plasma
  - Absorption, distribution, metabolism, excretion

Dan, this PK is again descriptive.
No stats!!!

- **General toxicology**
  - Single dose (mouse, rat, rabbit, dog, non-human primate)
  - Repeat dose (mouse, rat, rabbit, dog, non-human primate)

The FDA really wants to know what the Therapeutic Window is and what the side effects are!!

- **Genotoxicity**
- **Carcinogenicity**
- **Reproductive and developmental toxicity**
- **Juvenile toxicity**

Depends in the indication

- **Safety pharmacology** -
  - General physical condition and behavior in rats (Irwin Test)
  - hERG (stably transfected HEK293 cells)
  - Heart rate, blood pressure, EKG in conscious dogs
  - Body temperature in rats
  - Respiratory function in rats

The FDA really wants to know what the side effects are!!

Phases of Clinical Trials

- **Phase 1:** Effects of the drug as a function of dosage established in a small number (25–50) of healthy volunteers to find maximum tolerated dose (MTD); PK measurements; food-interaction; drug-interaction
- **Phase 2:** Studied in patients with target disease to determine safety, tolerability and efficacy (20–300 patients); **may not use final formulation**
  - 2A: Pilot or feasibility study; dose ranging
  - 2B: Well controlled studies on several hundred patients

If a drug is spectacular the FDA sometimes approves after Phase 2

- **Phase 3:** Pivotal trials to meet safety and efficacy standards of FDA; large number (hundreds to thousands) of patients; **establish final formulation, marketing claims and product stability, and packaging and storage conditions**. FDA generally requires two for registration.
- **Phase 4:** Post-marketing

Single Ascending Dose

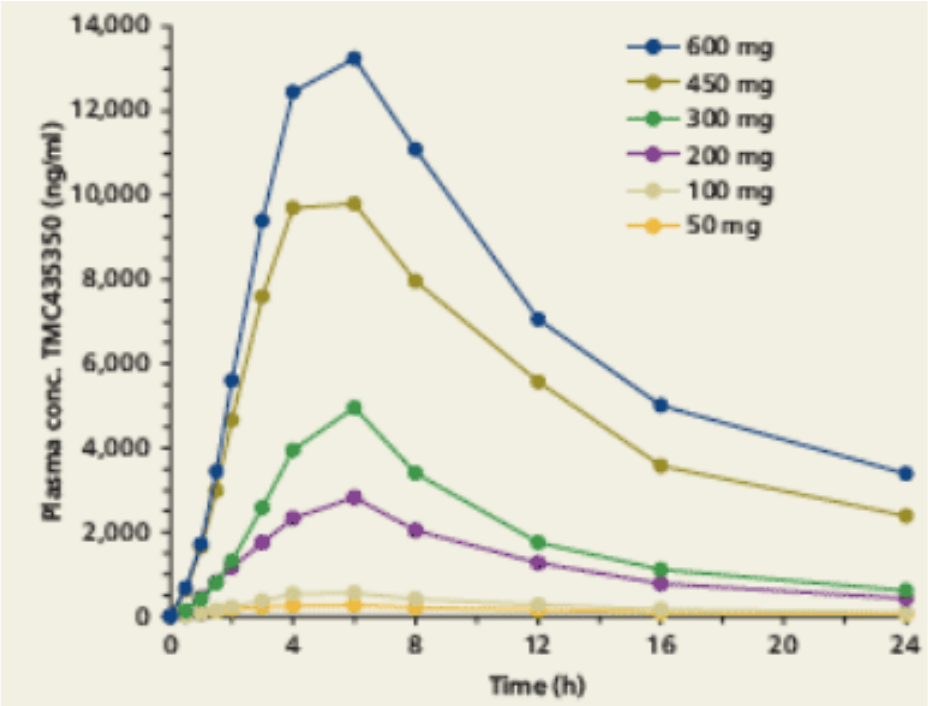


Table 2: Mean (± standard deviation, n=6) PK parameters after single doses of TMC435350.

	50 mg	100 mg	200 mg	300 mg	450 mg	600 mg
t_{max}, hour*	5.0 (3.0 - 6.0)	5.0 (4.0 - 6.0)	6.0 (4.0 - 6.0)	6.0 (4.0 - 6.0)	6.0 (4.0 - 6.0)	6.0 (4.0 - 6.0)
C_{max}, µg/ml	0.29 ± 0.10	0.58 ± 0.09	2.96 ± 1.02	5.09 ± 0.79	10.46 ± 2.46	13.55 ± 1.79
AUC_{24hr}, µg.h/ml	3.35 ± 1.36	6.28 ± 1.09	30.05 ± 10.02	46.38 ± 11.62	125.00 ± 31.82	166.70 ± 23.65
AUC_{last}, µg.h/ml	4.21 ± 2.14	7.55 ± 1.63	37.55 ± 14.82	54.72 ± 15.89	175.50 ± 69.21	225.00 ± 42.67
$t_{1/2}$, hour	9.9 ± 2.7	9.5 ± 1.4	10.9 ± 2.8	9.9 ± 1.6	13.4 ± 4.2	11.7 ± 2.0

Dan, please note again that this is descriptive. No statistics. You really just want to get the numbers!!!

How do you get a drug to market?

Or to the point where large Pharma licenses or buys it?

Being acquired is the goal of 90% of all Biotechs.

- Start your own biotech and raise venture capital and/or apply for NIH grants (SBIR or Blueprint)
- NIH programs: IGNITE and HEAL
- BARDA for countermeasures (at least theoretically)

The Animal Rule

The FDA Animal Rule

ASM Biodefense and Emerging Diseases Meeting
February 10, 2016

Dr. Tracy MacGill
Office of Counterterrorism and Emerging Threats
Office of the Chief Scientist
Office of the Commissioner
U.S. FDA

I found this slide deck in one of my old CounterACT folders and shamelessly plagiarized for a good cause

Challenges in MCM Development

MCM = Medical Counter Measurement

- Section 505 (d) of the Federal Food, Drug, and Cosmetic Act (FD&C) requires a drug to be safe under conditions of use, and effective as demonstrated by "substantial evidence"
- "Substantial evidence" means adequate and controlled investigations, including well-controlled clinical trials
- Natural or accidental exposures to threat agents are rare
- It would be unethical to intentionally expose human volunteers to potential threat agents

The Animal Rule

- "New Drug and Biological Drug Products; Evidence Needed to Demonstrate Effectiveness of New Drugs When Human Efficacy Studies Are Not Ethical or Feasible"
  - 21 CFR 314 Subpart I (drugs) and 21 CFR part 601 Subpart H (biologics)
  - May 31, 2002 (67 FR 37988)
- Allows for the use of adequate and well-controlled animal studies as evidence of effectiveness for approval

- Study considerations
  - Conducted in a manner that ensures **data quality** (accordance with protocol, SOPs, and research standards) and **integrity** (assurance raw data and documentation)
  - Good Laboratory Practice (GLP) for Nonclinical Laboratory Studies is an established and relevant system
- Must be in compliance with applicable laws and regulations governing the care and use of laboratory animals

The Animal Rule

- Safety must still be established through the traditional pathway
  - Non-clinical studies (animals)
  - Clinical studies (human volunteers)

The Animal Rule: Requirements

1) The pathophysiological mechanism of the toxicity of the agent, and the mechanism by which the product prevents or substantially reduces that toxicity, must be reasonably well-understood
2) The effect is demonstrated in more than one animal species expected to react with a response predictive for humans

-Unless the effect is demonstrated in a single animal species that represents a sufficiently well-characterized animal model for predicting the response in humans

The Animal Rule

The Animal Rule Requirements (2)

3) The animal study endpoint is clearly related to the desired benefit in humans
   - Enhancement of survival
   - Prevention of major morbidity
4) Data allow selection of an effective dose in humans
   - Kinetic and pharmacodynamic or immune correlate data/information

The Animal Rule

Caveats

- The Animal Rule does not apply if licensure is possible based on other routes
- Use of Animal Rule does not preclude the requirement for human safety studies
- Subject to additional postmarketing data collection on safety and efficacy
- In assessing the adequacy of animal data, the FDA may take into account other available data, including human data

Products Approved under the Animal Rule

- 2003 Pyridostigmine bromide
  - for use as a pretreatment for exposure to the chemical nerve agent Soman
  - Non-human primates, guinea pigs, and rodents
- 2006 Cyanokit (hyrdoxycabalomin)
  - for treatment of known or suspected cyanide poisoning
  - Dogs
- 2012 Levaquin (levofloxacin)
  - for prophylaxis and treatment of plague
  - Non-human primates
- 2012 Raxibacumab
  - for treatment of inhalational anthrax in combo with antibacterial drugs
  - Non-human primates and rabbits

Products Approved under the Animal Rule

- 2013 Botulism Antitoxin Heptavalent (A, B, C, D, E, F, G)-(Equine)
  - for treatment of patients showing signs of botulism following documented or suspected exposure to botulinum neurotoxin
  - Non-human primates and guinea pigs
- 2015 Ciprofloxacin
  - for the prophylaxis and treatment of plague
  - Non-human primates
- 2015 Moxifloxacin (Avelox)
  - for the prophylaxis and treatment of plague
  - Non-human primates

2001

- 2015 Anthrax Immune Globulin Intravenous (Anthrasil)
  - for the treatment of inhalational anthrax in adult and pediatric patients in combination with appropriate antibacterial drugs
  - Non-human primates and rabbits
- 2015 Filgrastim (Neupogen)
  - to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)
  - Non-human primates
- 2015 Pegfilgrastim (Neulasta)
  - to treat adult and pediatric patients at risk of developing myelosuppression
  - Non-human primates
- 2015 Anthrax Vaccine Absorbed (BioThrax)
  - for use after known or suspected anthrax exposure
  - Non-human primates and rabbits

Products Approved under the Animal Rule

Most recent approvals:

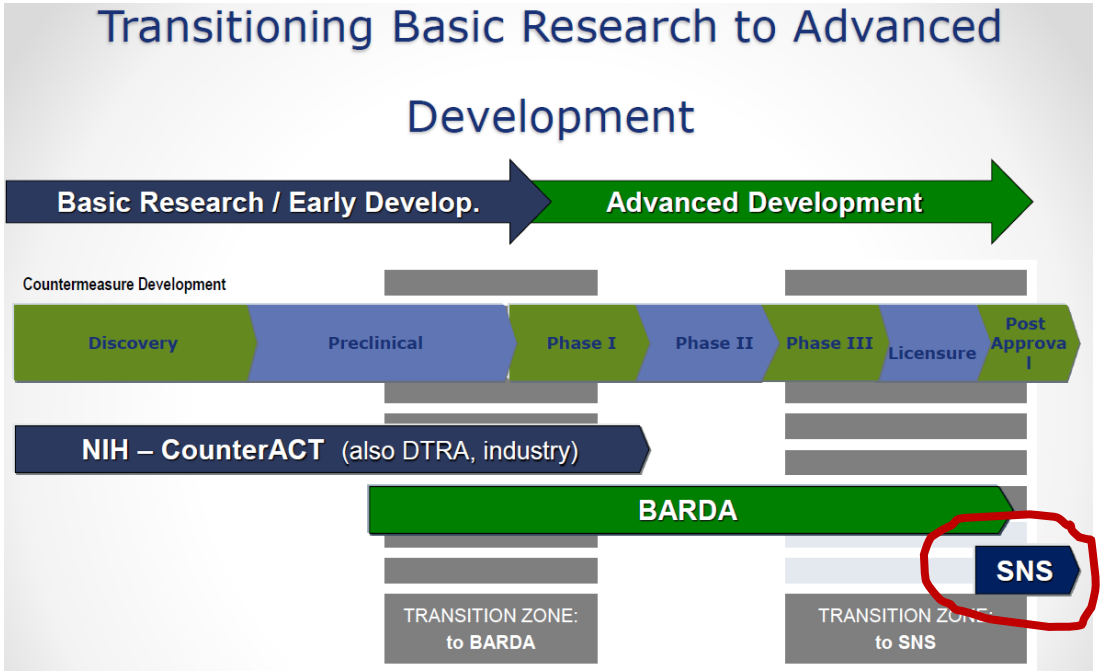
- **TEMBEXA** brincidofovir for smallpox in pediatric patients 6/4/2021
- **TPOXX** tecovirimat capsules and injection solution for smallpox in pediatric patients 5/18/22

This is from a talk from Judy Laney in 2016 telling us that if we provided proof of concept BARDA would do the rest and that we would be using the Animal Rule

Product Development Model

- Early Development (CounterACT)
  - Emphasis on Proof of Concept
  - Integration of platforms, CROs, CMOs
  - Relies on tech-transfers, data and model sharing
  - Rapid Go/No Go Decisions

- Advanced Development (BARDA)
  - Emphasis on licensure and availability
  - Scale-up, validation of manufacturing
  - Phase II/III, pivotal animal studies
  - Life cycle and sustainment important

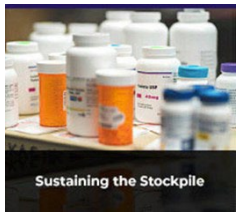


Strategic National Stockpile

The Strategic National Stockpile (SNS)

For more details see: https://www.phe.gov/about/sns/Pages/default.aspx

A health threat can appear at any moment, and the United States must be ready to respond. **The Strategic National Stockpile (SNS) is part of the federal medical response infrastructure and can supplement medical countermeasures needed by states, tribal nations, territories and the largest metropolitan areas during public health emergencies.** The supplies, medicines, and devices for lifesaving care contained in the stockpile can be used as a short-term, stopgap buffer when the immediate supply of these materials may not be available or sufficient.



Strategic National Stockpile (SNS) has large quantities of medicine and medical supplies to protect the American public if there is a public health emergency (**terrorist attack, outbreak, earthquake, hurricane**) severe enough to cause local supplies to run out.

Once Federal and local authorities agree that the SNS is needed, medicines will be delivered to any state in the U.S. in time for them to be effective. Each state has plans to receive and distribute SNS medicine and medical supplies to local communities as quickly as possible.

CHEMPACK

SNS has a 12-hour response time → too long for chemical threat: Therefore CHEMPACK program

CHEMPACKs are containers of nerve agent antidotes placed in secure locations in local jurisdictions around the country to allow rapid response to a chemical incident. These medications treat the symptoms of nerve agent exposure and can be used *even when the actual agent is unknown*.

- Because these antidotes must be administered quickly, the CHEMPACK team maintains 1,960 containers strategically placed in more than 1,340 locations in the United States.
- More than 90 percent of the U.S. population is within 1 hour of a CHEMPACK location.
- Most are located in hospitals or fire stations selected by local authorities to support a rapid hazmat response and can be accessed quickly if hospitals or first responders need them.

CHEMPACK

Atropine and 2-PAM

- Autoinjectors updated
- Diazepam replaced by MDZ

CHEMPACK Container Contents			
Product	Unit Pack	Cases per EMS Container	Cases per Hospital Container
Mark 1 auto-injector	240	5	2
Atropine Sulfate 0.4mg/ml 20ml	100	1	9
Pralidoxime 1gm inj 20ml	276	1	10
Atropen 0.5 mg	144	1	1
Atropen 1.0 mg	144	1	1
Diazepam 5mg/ml auto-injector	150	2	1
Diazepam 5mg/ml vial, 10ml	50	1	13
Sterile water for injection 20cc Vials	100	2	28
Approximate treatment capacity (depending on severity of event)		454	1,000

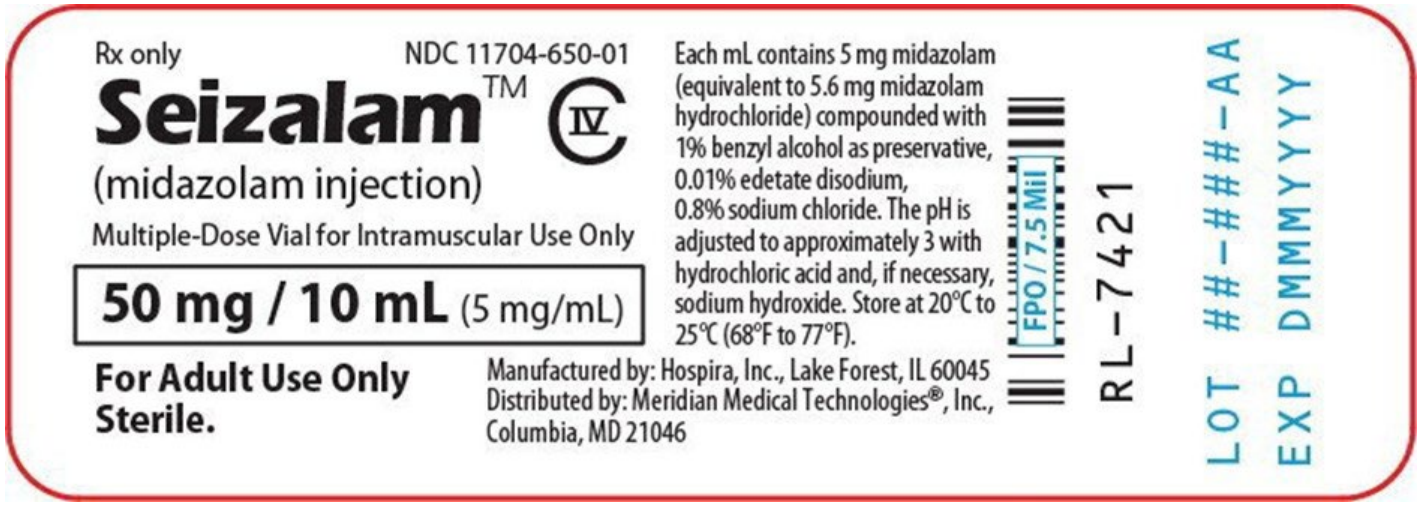
CHEMPACK is supposed to rotate products every 18 month;
shelf-life can be extended to 6 years based on stability testing in collaboration with manufacturer

CHEMPACK

Mark 1 autoinjector replaced by **DuoDote.**

<u>Indication:</u> Nerve agent exposure and OP insecticide poisoning

CHEMPACK



BARDA and Crossject partner under Project BioShield to provide novel needle-free ZENEO Midazolam autoinjectors for national preparedness.

I don't know what the state of this replacement is

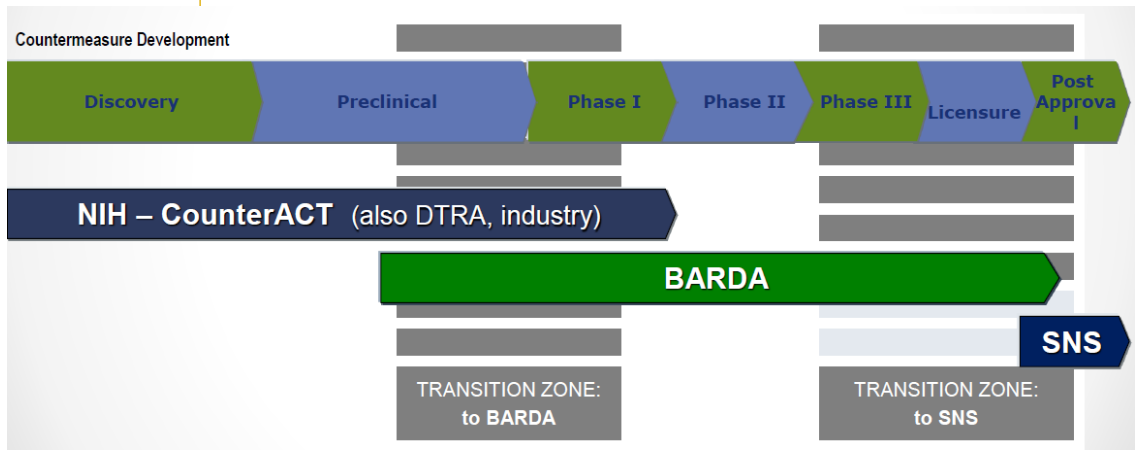
CounterACT Program

The CounterACT program supports basic and translational research aimed at the identification of better therapeutic medical countermeasures against chemical threat agents and facilitates their movement through the drug development and regulatory processes in collaboration with other federal departments, agencies, and initiatives, such as the **Biomedical Advanced Research and Development Authority** (HHS BARDA) and the **FDA Medical Countermeasures Initiative** (MCMi).

The **CounterACT program is funded by a special annual Congressional supplemental appropriation** to the NIH budget through the Office of the Director (NIH OD) and operates under the oversight of the Office of Biodefense Research and Surety (OBRS). This is a trans-NIH effort, involving partnerships with the NEI, NIAID, NIAMS, NICHD, NIEHS, NIDA, NIGMS and NINDS to execute the overall NIH Medical Research Program Directed Against Chemical Threats.

→ ***Milestone driven***

BARDA 2016



Near Term Focus Areas in 2016

And there was the first mention of a commercial indication……

Near Term Focus Areas

- Pulmonary Injury from Chlorine and Vesicants
  - Commercial Indications: Pulmonary Edema, Inflammation, Fibrosis, COPD
- Anti-seizure drugs for nerve agent victims whose seizures are refractory to treatment with benzodiazepines
  - Commercial Indications: Refractory seizure, status epilepticus, epilepsy
- Cyanide Treatments- Improved Ease of Use

CounterACT EAC Meeting 2020

CounterACT FOA Requirements

		Achieved	In Progress
1	A lead compound with well understood ADME and established affinity, potency and selectivity.	✔	
2	Efficacy in an appropriate animal model relevant to the proposed concept of use in humans.	✔	
3	Initial pharmacology and toxicology studies.		✔
4	Stable synthesis of the lead compound.	✔	
5	Preliminary regulatory strategy, e.g., a viable Target Product Profile, regulatory expertise, communication with FDA.		✔
6	Commercialization plan for other indications, if applicable.	✔	
7	Intellectual property rights/freedom to operate.	✔	

We were close to meeting the CounterACT FOA and the BARDA TLR4 Readiness requirements with Allopregnanolone

BARDA Recommendations

		Achieved	In Progress
1	Technology Readiness Level TRL 4.	✔	
2	Integrates with BARDA priorities: Area of Interest #5, Chemical Threat Medical Countermeasures.	✔	
3	Provide data to support the proposal.	✔	
4	Proof of concept data in translational models.	✔	
5	Have a path to regulatory approval.		✔

CounterACT EAC Meeting 2020

Product Targets	Minimum Acceptable Result	Ideal Result
Primary Product Indication	Termination of benzodiazepine-refractory nerve agent status epilepticus	Termination of benzodiazepine-refractory nerve agent status epilepticus
Patient Population	Adults with nerve agent-induced seizures in which seizures continue for 10 min after treatment with 10 mg of diazepam or midazolam	Adults, infants, children, adolescent, pregnant women, and elderly with nerve agent-induced seizures in which seizures continue for 10 min after treatment with 10 mg of diazepam or midazolam or an age and weight appropriate dose
Treatment Duration	Acute	Acute
Delivery Mode	IV or Intraosseous	IM
Dosage Form	Solution in pre-filled syringe	Solution in autoinjector
Regimen	Bolus	Bolus
Efficacy	Termination of behavioral and EEG seizures within 30 min and failure of seizure recurrence for 120 min in 60% of those treated	Termination of behavioral and EEG seizures within 30 min and failure of seizure recurrence for 120 min in 90% of those treated; survival in ≥90%; ≥90% mitigation of nerve-agent and seizure-induced brain damage
Risk/Side Effect	Devoid of respiratory depression (SpO_2 < 90% for >10 min) or a >10% reduction in SpO_2 if the victim's pretreatment SpO_2 is <90% or hypotension (systolic BP < 90 for >10 min) and no clinically significant severe adverse effects when administered 10 min after a 10 mg dose of midazolam or diazepam	Devoid of respiratory depression (SpO_2 < 90% for >10 min) or a >10% reduction in SpO_2 if the victim's pretreatment SpO_2 is <90% or hypotension (systolic BP < 90 for >10 min) and no clinically significant adverse effects when administered in conjunction with a 10 mg dose of midazolam or diazepam
Therapeutic Modality	Small molecule	Small molecule

Target Product Profile for Allopregnanolone

BARDA 2022

Biomedical Advanced Research and Development Authority

BARDA's Strategic Plan 2022-2026

Fortifying the Nation's Health Security

Partnerships are a big area of emphasis

Objective 3.1: Advance new, adaptable partnership models

Objective 3.2: Foster existing and establish new partnerships

Objective 3.3: Enhance sustainability by supporting development and repurposing of products and technologies with commercial value

Objective 3.4: Expand partnerships with socially and economically disadvantaged businesses

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Enhancing the Nation's PUBLIC HEALTH SECURITY and emergency preparedness by facilitating communication on innovative products and solutions between federal agencies and public stakeholders *NOT advanced development like in 2016???*

64 FDA Approvals, Licensures and Clearances for BARDA supported Products

64 Simplexa™ COVID-19 Direct

63 TPOXX (tecovirimat) injection, for intravenous use

62 Spikevax (COVID-19 Vaccine, mRNA)

61  StrataGraft

60 TEMBEXA

59 Lumify Ultrasound

58  Nplate (romiplostim)

57 Ebanga (Ansuvimab/mAb114) treatment for Ebola virus diease (EVD)

56  Inmazeb® First Treatment for Zaire ebolavirus (Ebola virus) infection in adult & pediatric patients

55  Zika Antibody Response Detection - DPP® Zika IgM System

44  FluChip-8G Influenza A+B Assay

43 QMS Plazomicin Immunoassay

42  RECELL

41 Seizalam

40 Flucelvax Process 3.0

29 Q-Pan H5N1 AS03-Adjuvanted Pandemic Influenza Virus Vaccine for Pediatrics

28  Flucelvax Quadrivalent Influenza Virus Vaccine (Pediatric Indication)

27 Flucelvax Quadrivalent Influenza Virus Vaccine

26  Anthim

25  Fluad® (with MF59® adjuvant) Influenza vaccine for seniors

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- Website also lists 102 COVID products supported
- COVID 19 contract awards in as little as 9 days
- **1335+ TechWatch** meetings with innovative companies!!!!!

There is NO free money for drug development.

We will need a civilian indication and a partner if we want to develop any of our potential therapeutics!!!!!