Food and Drug Administration and Drug Development

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Disclosures

- No disclosures to report
- The views articulated are solely my own.

Background and Career

Education

- BS Biology, BS Laboratory Science
- Ph.D. Pharmaceutical Sciences (Pharmacokinetics)

Career

- Pharmacokinetic Reviewer, Division of Biopharmaceutics, CDER, Food and Drug Administration
- Mid 90's departed FDA, transitioned to Regulatory Affairs
- Over my career made several stops along the way small, medium, big-pharma and start-up companies
- Big Pharma Novartis 14 years
- Retired after 35+ years in Pharma
- Regulatory Consultant and Lecturer

Agenda

- Evolution of Drug Regulations
- U.S. Food and Drug Administration
- Drug Development
- Benefit: Risk Evaluation
- Case Study 1: Thalidomide
- Case Study 2: Bridging Strategy

Evolution of Drug Regulations

Beginning → Start → Response

Evolution of Drug Regulation

Prior to 1906	1906	1937	1955
Consumer marketplace for drugs and food entirely unregulated Caveat emptor ("let the buyer beware“)	Upton Sinclair’s “The Jungle” pub Feb 1906 exposed unhealthy practices prevalent in meatpacking industry	June 1937, Massengill made and distributed sulfanilamide dissolved in diethylene glycol to make an elixir for pediatric use. Resulted in >100 fatalities in 15 states due to ethylene glycol toxicity	Thalidomide
	Congress passed Pure Food and Drug Meat Inspection Act 1906. Landmark legislation advanced consumer protection that regulated food and drug industries and created the Bureau of Chemistry, later renamed Food and Drug Administration (FDA) in 1930	1938 Congress passed Federal Food, Drug, and Cosmetic Act (FD&C Act) Expanded FDA's power to oversee drug regulation	

1950
Thalidomide Tragedy

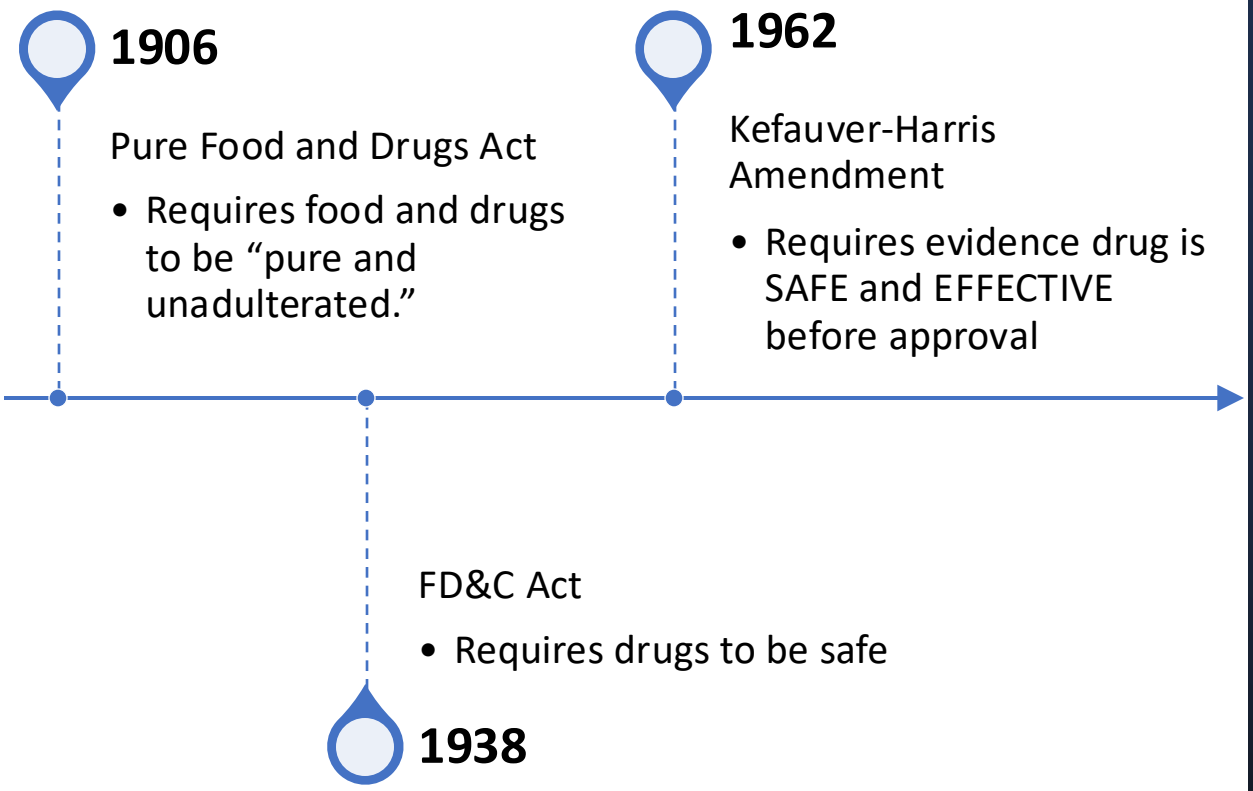
- **The Cause** – Thalidomide prescribe for treating morning sickness in Europe
  - 1955, Richardson-Merrell sought FDA approval of thalidomide as a sedative
  - Dr. Frances Kelsey rejected application due to insufficient safety data
- **The Effect**
  - 1957, thalidomide linked to severe birth defects affecting over 10,000 infants
  - Never approved for sale in the U.S.

Thalidomide: the tragedy of birth defects and the effective treatment of disease - PubMed

The Response

- In 1962, Congress passed Kefauver-Harris amendment to extend the FDC Act of 1938
- Requires manufacturers to
  - Prove with substantial and well-controlled studies that drugs are not only safe but also effective
  - Requires filing of an IND with FDA before initiating clinical trials in humans for review
  - Once proven safe and effective, manufacturers may submit an NDA seeking FDA review and approval to market the drug

Key Milestones in Drug Regulations



"The history of drug regulation is built on tombstones"

Michael Harris

Food and Drug Administration

- Department of Health and Human Service
- **Mission: To protect public health**
- Location: White Oak Campus Silver Spring, MD
- Regulates 25% of US market
  - Drugs, biologics, OTC, tobacco, devices, radiation, cosmetics, **f**oods**,** veterinary products
- Annual budget $6.9 billion (2024)

Translating Act to Action

Act

Legislation written by Congress

Broad outlines general principles and rule of law eg Food, Drug & Cosmetic Act

Code of Federal Regulations

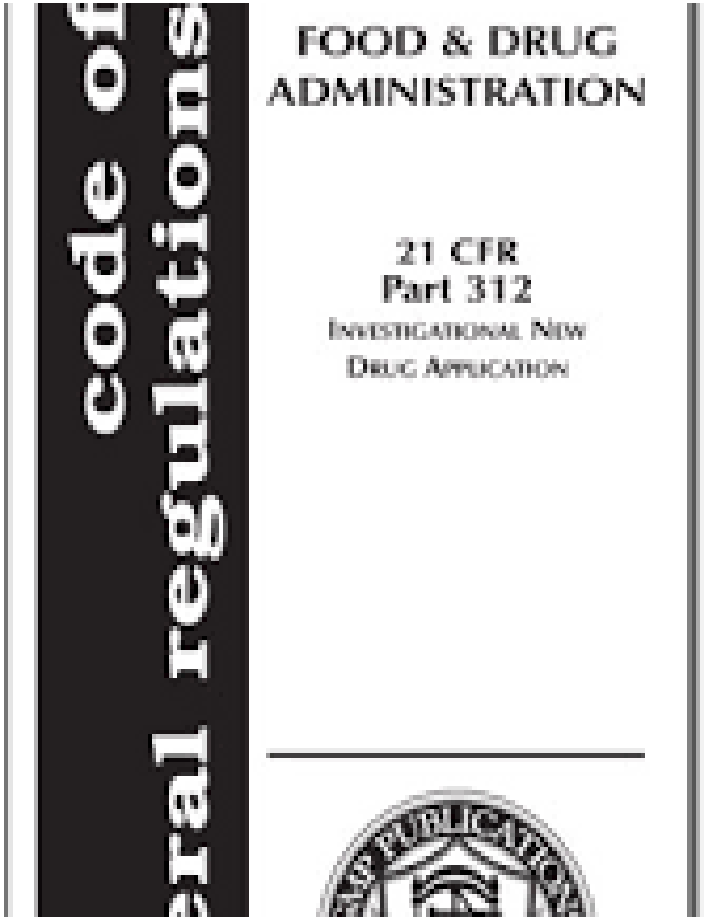
Regulations written by Agency

Specifies **How to Turn Act into Actions by spelling out Requirements to be followed**

Guidance Documents

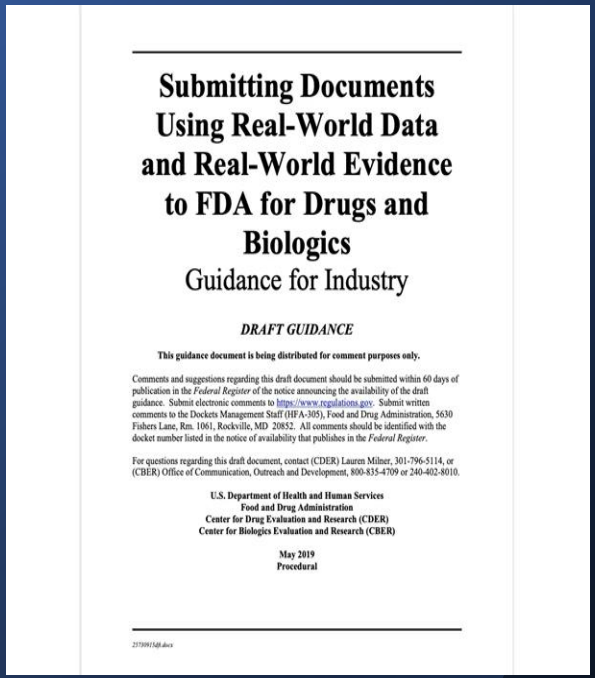
FDA's interpretation or policy on regulatory issues

Food, Drug & Cosmetic Act
21 Code of Federal Regulations (CFR)



- 21 CFR 312—INVESTIGATIONAL NEW DRUG APPLICATION
  - This part contains procedures and requirements governing use of investigational new drugs (IND), including procedures and requirements for the submission to, and review by, the FDA of IND's
- 21 CFR 314 APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG
  - This part sets forth procedures and requirements for the submission to, and review by FDA of applications and abbreviated applications to market a new drug under section 505 of Federal Food, Drug, and Cosmetic Act, as well as amendments, supplements, and postmarketing reports to them

FDA Guidance Documents



Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drugs and Biologics

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Lauren Milner, 301-796-5114, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

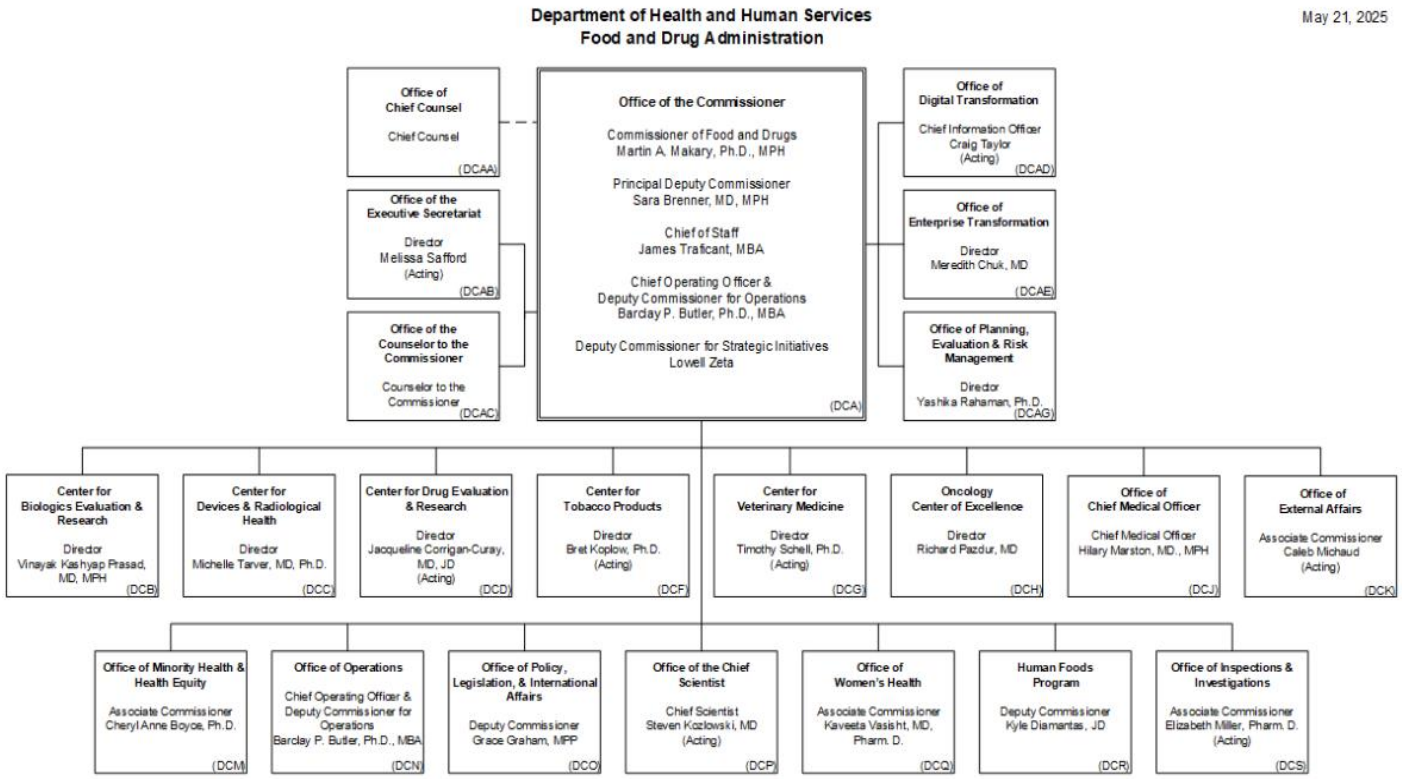
May 2019
Procedural

- FDA's interpretation or policy on regulatory issues.
- Guidance documents reflect Agency's current views and are recommendations unless specific regulations are mentioned.
- Alternative approaches acceptable if meet relevant statutes and regulations.
- Guidances categorized into three areas:
  - Clinical/medical
  - Pharmaceutical quality
  - CMC and procedural

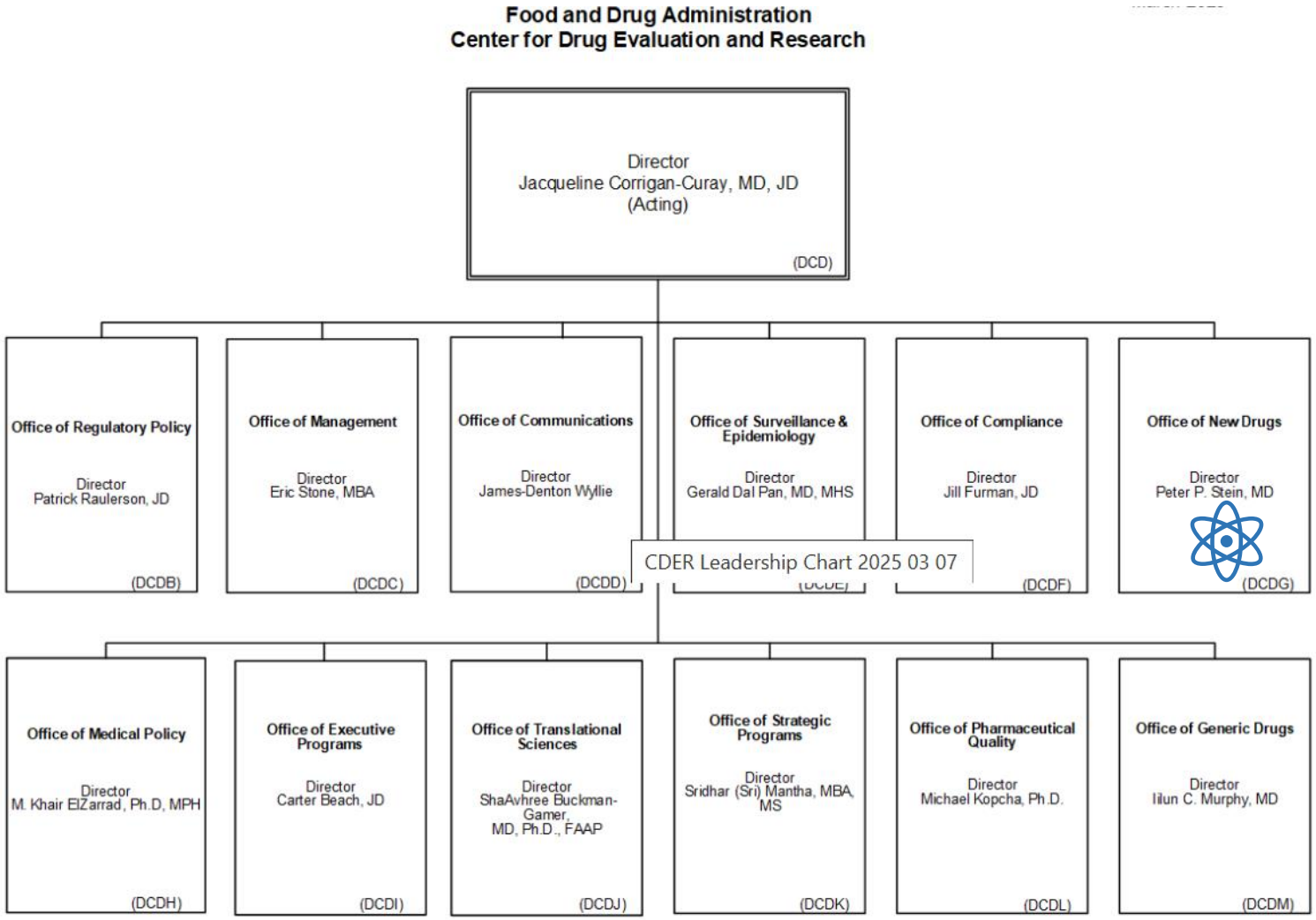
https://www.fda.gov/regulatory-information/search-fda-guidance-documents

FDA Organization Chart

Content current as of:
05/28/2025



Center for Drug Evaluation and Research



Office of New Drugs (OND)

The Office of New Drugs (OND):

- Provides regulatory oversight during drug development.
- Makes decisions regarding marketing approval for new drugs.
- Provides guidance to regulated industry on clinical, scientific, and regulatory matters.
- OND is made up of six review offices (click the graphic for an enlarged PDF).

Office of Antimicrobial Products	Office of Drug Evaluation I	Office of Drug Evaluation II	Office of Drug Evaluation III	Office of Drug Evaluation IV	Office of Hematology Oncology Products
OAP	**ODE I**	**ODE II**	**ODE III**	**ODE IV**	**OHOP**
Division of Anti-Infective Products (DAIP)	Division of Neurology Products (DNP)	Division of Metabolic and Endocrine Products (DMEP)	Division of Gastroenterology and Inborn Errors Products (DGIEP)	Division of Nonprescription Clinical Evaluation (DNCE)	Division of Oncology Products I (DOP1)
Division of Anti-Viral Products (DAVP)	Division of Psychiatry Products (DPP)	Division of Pulmonary, Allergy and Rheumatology Products (DPARP)	Division of Bone, Reproductive and Urologic Products (DBRUP)	Division of Medical Imaging Products (DMIP)	Division of Oncology Products II (DOP2)
Division of Transplant and Ophthalmology Products (DTOP)	Division of Cardiovascular and Renal Products (DCRP)	Division of Anesthesia, Analgesia, and Addiction Products (DAAAP)	Division of Dermatology and Dental Products (DDDP)	Division of Nonprescription Regulation Development (DNRD)	Division of Hematology Products (DHP)
					Division of Hematology Oncology Toxicology (DHOT)

FDA Review Teams

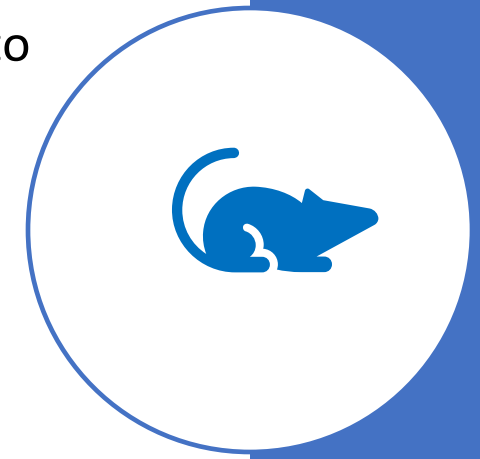
FDA does not perform Clinical Studies; carried out by sponsors who submit applications

- Structure of FDA Review Teams
  - Project Managers
  - Medical Reviewers
  - Biostatisticians
  - Clinical Pharmacology and Pk Reviewers
  - Chemistry, Manufacturing, and Controls (CMC) Experts
  - Toxicology Reviewers
  - Device Reviewers
  - Interdisciplinary Review Teams for specialized consultations
  - Good Practice (GXP) inspectors for manufacturing and research sites.
- Key Review Team Responsibilities:
  - Review applications
  - Evaluate study findings and identify potential data issues, including design flaws or statistical limitations
  - Audit manufacturing sites to ensure GMP
  - Assess balance of benefits and risks

Drug Development
Start to Finish

Pre-Clinical Development

- Good Laboratory Practice (GLP)
- Drug Discovery
  - Investigate and identify potential receptors/targets
  - Conduct in vitro and in vivo experiments to determine cause and effect in animal models
- Chemistry
  - Synthesize molecules as antagonist or agonist to target receptor
- Toxicology
  - Conduct IND enabling tox studies (2 species), ADME, safety studies (heart, kidneys, liver), toxicokinetic studies



Chemistry Manufacturing and Control

- Good Manufacturing Practice (GMP) 21 CFR 211
- Provide CMC information required to assure drug substance (DS) and drug product (DP)
  - Potency
  - Identity
  - Quality
  - Purity
  - Strength

Clinical Development

- IND filed, FDA 30-day review, no hold, initiate clinical development
  - Good Clinical Practice (GCP)
  - Phase 1 – healthy volunteers, single dose, multiple dose studies, to determine the PK profile of the drug, safety
  - Phase 2 – patients with the indication, to determine safe and effective dose, safety
  - Phase 3 – two duplicate, powered studies, to confirm efficacy and safety, safety

Sponsor's Drug Development Project Team

- Regulatory Affairs + Reg Ops
  - Liaise with FDA
  - Prepare submissions
  - Leads teams in preparation of Briefing Books
  - Leads team in preparing for meetings with FDA
- Statisticians
- Project managers
- Clinical Operations
- Pharmacologist
- Toxicologist
- Chemist
- MDs

Drug Development: Step 1 to 5

STEP 1 : Basic Science
Academic disciplines that derive new knowledge from scientific experiments,

STEP 2 : **Applied Science**
Takes the findings and applies the knowledge to develop practical applications ie NEW

STEP 3 : **Translational Science:** Conducts investigation with NEW DRUG to determine if hypothesis is true or not If true

STEP 4 : **Clinical Research**: NEW DRUG tested in patients by Phase

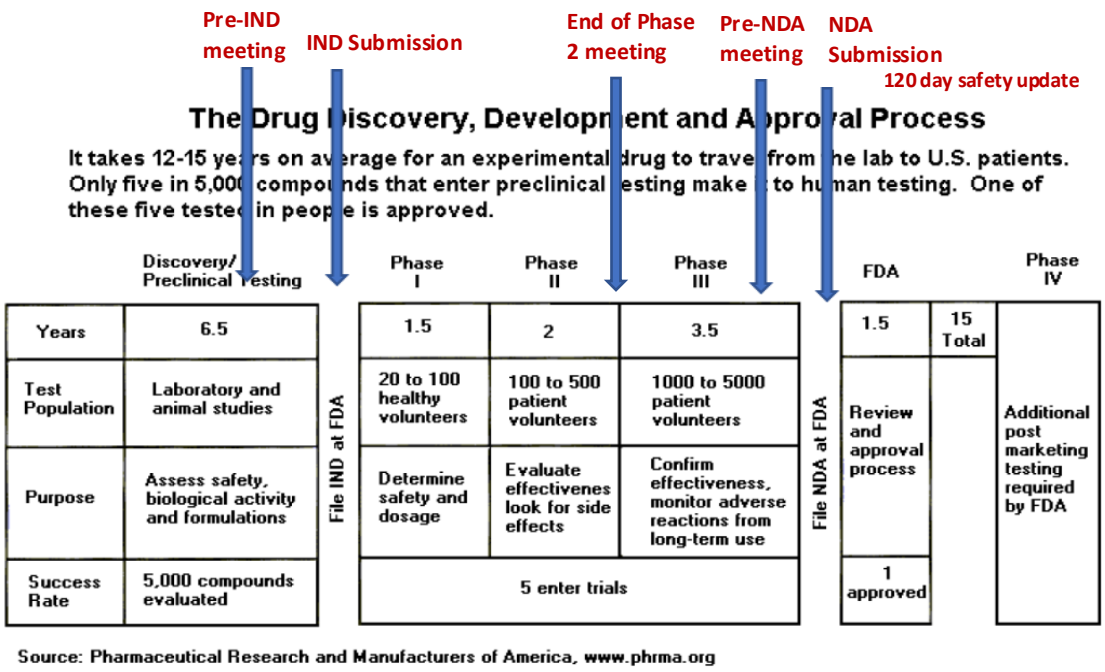
PHASE 1	PHASE 2	PHASE 3
Purpose: Pharmacokinetics • Safety and dose PK determination of NEW DRUG • Study Participants 20–100 HV or people with disease/ condition • Length of Study Several months • Approximately 70% of drugs move to the next phase	Purpose: Dose Ranging • Efficacy and side effects of low, medium, high dose range of NEW DRUG • Study Participants Up to several hundred people with disease/ condition • Length of Study Several months to 2 years • Approximately 33% of drugs move to the next phase	Purpose: 2 Pivotal trials • Efficacy and Safety of NEW DRUG • Study Participants 300–3,000 volunteers who have disease or condition • Length of Study 1 to 4 years • Approximately 25– 30% of drugs move to the next phase

STEP 4 : NEW DRUG NDA SUBMITTED: FDA review teams examine submitted NEW DRUG data and decide to approve or not to approve new drug (12-month review)

STEP 5 : IF APPROVED
- FDA and drug sponsor continues to monitor NEW DRUG safety once available in the market for use by the public.
- Additional Phase 4 studies may be performed after the NEW DRUG is approved

Drug Discovery to Approval
Average Duration: 12-15 years

Milestones Patent filed | IND filed 30 Day review | NDA submitted - 12 months review



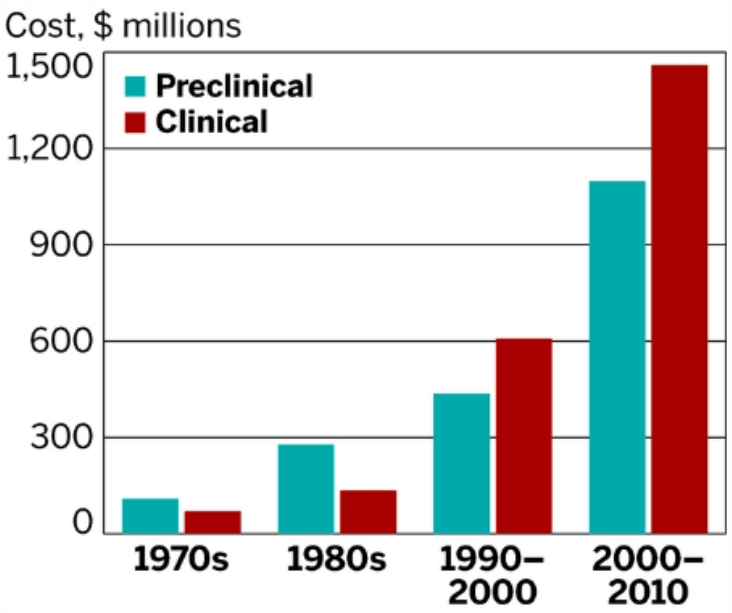
Source: Pharmaceutical Research and Manufacturers of America, www.phrma.org

Post Approval Activities

- Advertising and promotional
- Distribution
- Detailing
- Reimbursement
- Safety reporting
- Phase IV studies
- Annual Reports

Clock is ticking Patent term 20 years which starts when patent is filed

Notable rise in drug development costs



The cost of developing a new drug has skyrocketed since the 1970s. Source: Tufts Center for the Study of Drug Development.

- Tufts Center for Study of Drug Development (Tufts CSDD), independent, academic, non-profit research center
- Cost approaching $3 billion (Rick Mullin November 20, 2014)

Critical document
Study Protocols

Document outlines study's rationale, design, proposed methodologies, inclusion and exclusion criteria, ethical considerations, and specifies *a prior* criteria for achieving a positive study outcome

Intended for trial investigators and staff to follow in conducting the trial in terms of inclusion/exclusion, study assessments and timing

To be prepared by Clinical with epert input, finalized, and submitted to the IND before commencement of study.

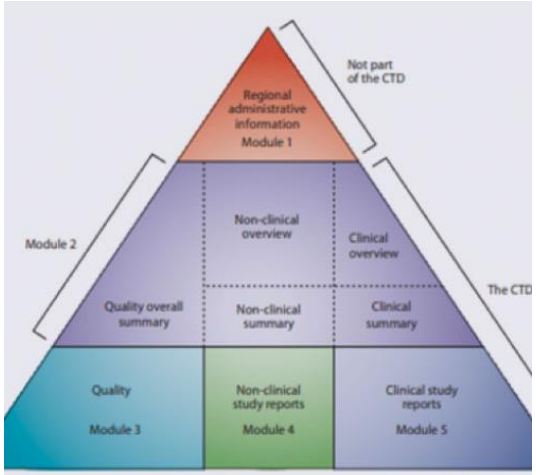
Required for Pre-Clinical, Phase 1, 2, 3 and 4 clinical trials

New Drug Application

- Submission to FDA of all data, study reports, CMC, and analysis conducted with investigational product
- Prepared electronically by Sponsor's Regulatory Operations via FDA protal
- 12-month review
- During review period
  - FDA Reviewers can ask Questions, for reanalysis, for additional data
  - At the end of the review, labeling negotiations over the package insert

IND and NDA e-CTD Format

- Composed of 5 modules
  - Module 1 : Region-specific information
  - Module 2: Summary tables
    - CMC, PC, Clinical
  - Module 3: CMC data
    - DS
    - DP
  - Module 4: Nonclinical study reports
  - Module 5: Clinical study reports



TD triangle. The Common Technical Document is organized into five modules. Module 1 is specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

After NDA submitted to FDA

FDA's Review Focus

- Chemistry Manufacturing and Controls (CMC) (Module 3)
  - Drug substance (3S)
  - Drug product (3P)
  - GMP
- Clinical (Module 5)
  - Review of clinical study reports
  - Benefit : Risk
  - GCP
  - Statistical evaluation of study results

PART 211—Current Good Manufacturing

- Part 211 current good manufacturing practice (GMP) for preparation of drug products
- FDA reviews following Critical Quality Attributes (CQA) data to ensure drug substance and drug product are what they claim to be

Strength	Amount of active pharmaceutical ingredient (API) in a dosage form
Identity	Confirms drug contains the API that it's supposed to (analytical IR, Mass Spect, HPLC)
Potency	Relative strength indicating how much of a drug is needed to produce a certain effect. More potent drug requires less to achieve same therapeutic effect
Purity	Freedom of drug from impurities
Quality	Can be made consistently

Benefit : Risk Assessment

FDA's Clinical Evaluation of Risk : Benefit
Questions to put New Drug into context

How serious is disease/condition to be treated by the NEW DRUG?	**<u>Serious, life threatening, or unmet medical need?</u>**
What are benefit(s) or advantages of compared to currently approved therapies?	What is NEW DRUG value proposition compared to approved drug(s)? Is its efficacy superior? Better safety? More convenient?
If there is potential harm (risk), how big is the harm relative to disease?	Severe side effects of NEW DRUG for cancer is acceptable (nauseous, hair loss, bone marrow toxicity) but not for NEW DRUG for nonlife threatening indications such as allergic rhinitis
Are there safer alternatives already approved?	*If there are approved drugs that are safer or more effective, then if NEW DRUG has weaker efficacy with questionable safety, then may be strongest argument against approval*

Case Study Thalidomide
Assessing Benefit: Risk based on Indication

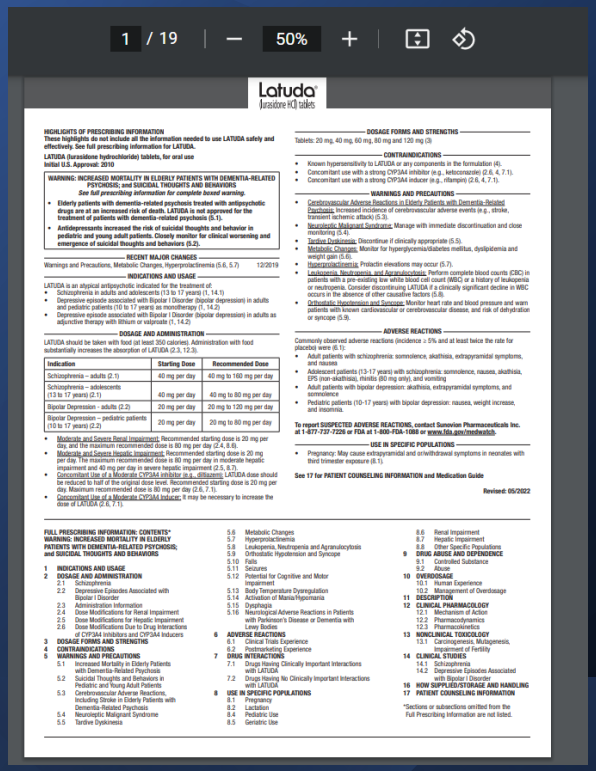
Question	Morning sickness during pregnancy	Multiple myeloma
How serious is illness/condition/ syndrome being treated ie life threatening, unmet?	Unmet Not serious Not life threatening	Unmet Serious Life threatening
Patient population	Pregnant women otherwise healthy	Multiple myeloma patients not healthy
Risk: How big is the harm of an AEs/SAEs?	Fetal toxicity Neuropathy Deep vein thrombosis Pulmonary embolism	Fetal toxicity Neuropathy Deep vein thrombosis Pulmonary embolism
Benefit: What are the benefits?	Marginal reduction in nausea and vomiting	Extends life
Safer options available?	Diet	No
Approved or not approved?	**No**	**Yes**

Evaluating Risk : Benefit Evaluation After Ph2

Efficacy : Drug vs Control $p < 0.05$ Safety: Drug ≥ Control Probability of Approval Very good 	Efficacy : Drug vs Control $p > 0.05$ Safety : Drug ≥ Control Probability of Approval 0 
Efficacy : Drug vs Control $p < 0.05$ Safety: Drug < Control Probability of Approval depends on context of drug use  • Unmet Medical Need • Life Threatening • Magnitude of effect • Can Risk Be Managed • Can Drug Be Stopped and Safety Reversed	Efficacy : Drug vs Control $p > 0.05$ Safety : Drug < Control Probability of Approval 0 

- 25% probability to end up in green – POA approaching 100%
- 25% probability to end up in yellow – POA depends on if the Benefit outweighs the Risk?
- 50% probability to end up in red – POA 0%

Package Insert



- Once FDA Review of NDA is completed
- Drug is approvable
- FDA Focuses on Package Insert (PI)
  - Contains summary of essential scientific information needed for safe and effective use of the New Drug based on information submitted and reviewed
  - Is to be informative, accurate and not promotional
  - Living document that is updated when new information such as safety or new indications becomes available

Case Study
Bridging Strategy

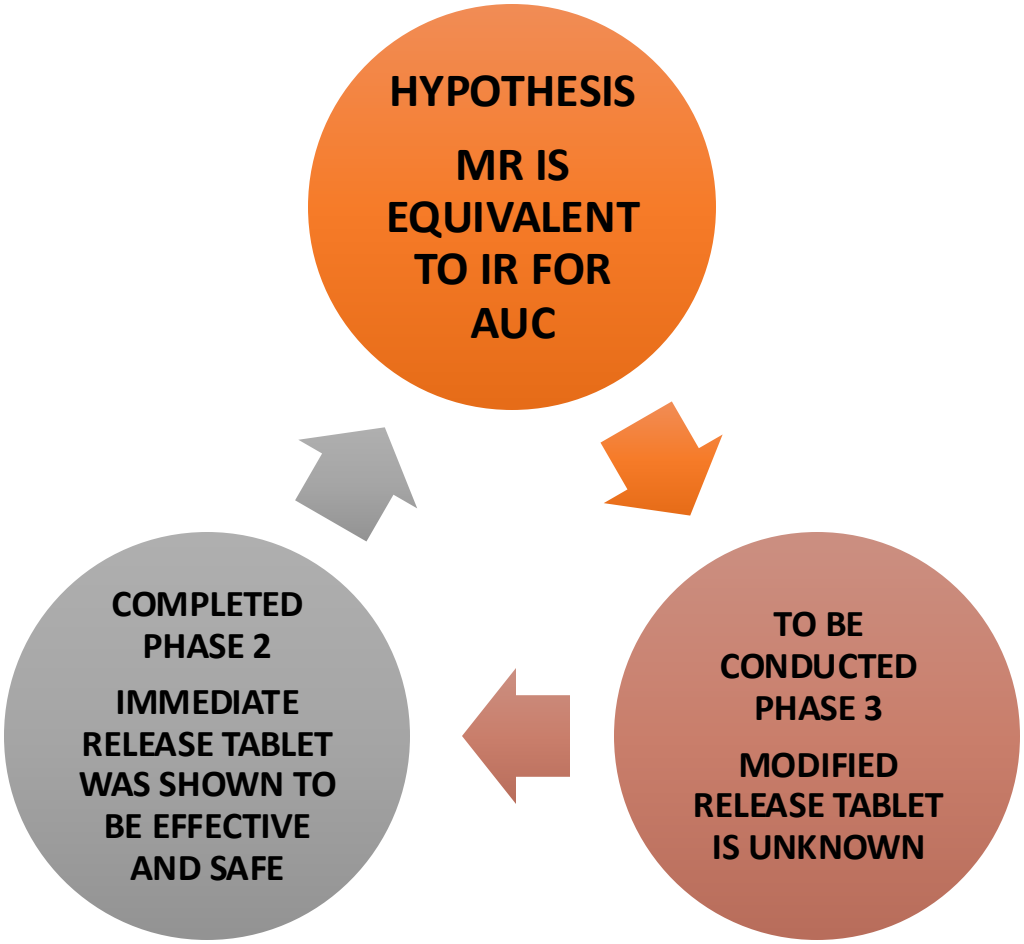
Case Study

- An experimental DRUG is an immediate release (IR) dosage form was administered BID in the Phase 2 dose ranging study.
- The Phase 2 results showed the IR drug was effective with acceptable safety profile.
- Following the study, marketing indicated that market research indicated that to be competitive with the approved competitor, QD administration was needed.
- Regulatory was requested to devise a winning regulatory strategy to support switch from BID IR formulation to QD modified release (MR) tablet which is planned to be used in Phase 3.

Questions

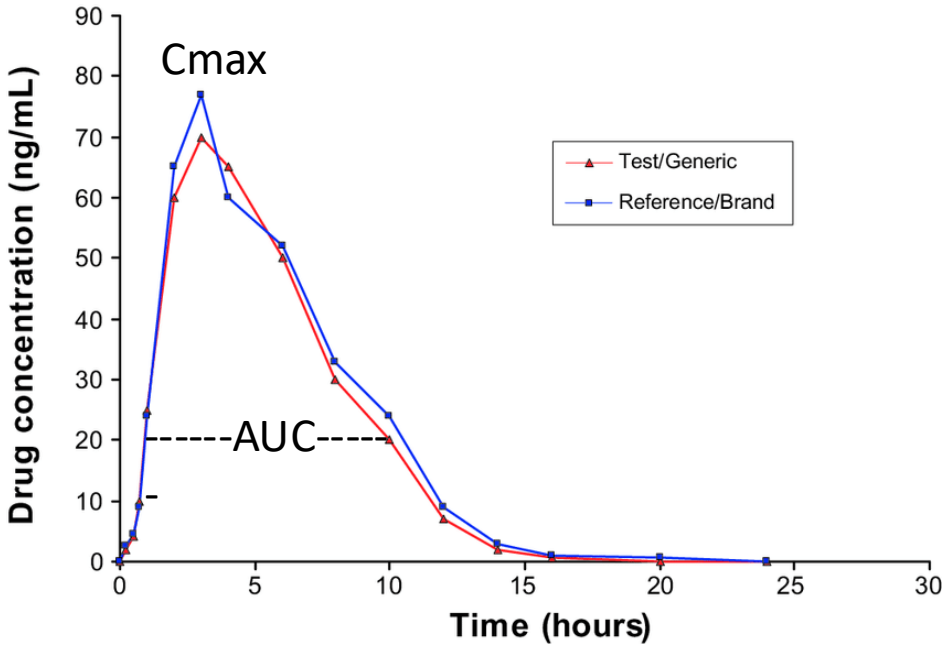
1. What approach should be used to determine if the MR tablet can be used in Phase 3?
2. What studies would you recommend be conducted with the MR tablet to determine if the MR can replace the IR for use in Phase 3 pivotal studies?

Scenario


HYPOTHESIS
MR IS EQUIVALENT TO IR FOR AUC
TO BE CONDUCTED PHASE 3
MODIFIED RELEASE TABLET IS UNKNOWN
COMPLETED PHASE 2
IMMEDIATE RELEASE TABLET WAS SHOWN TO BE EFFECTIVE AND SAFE

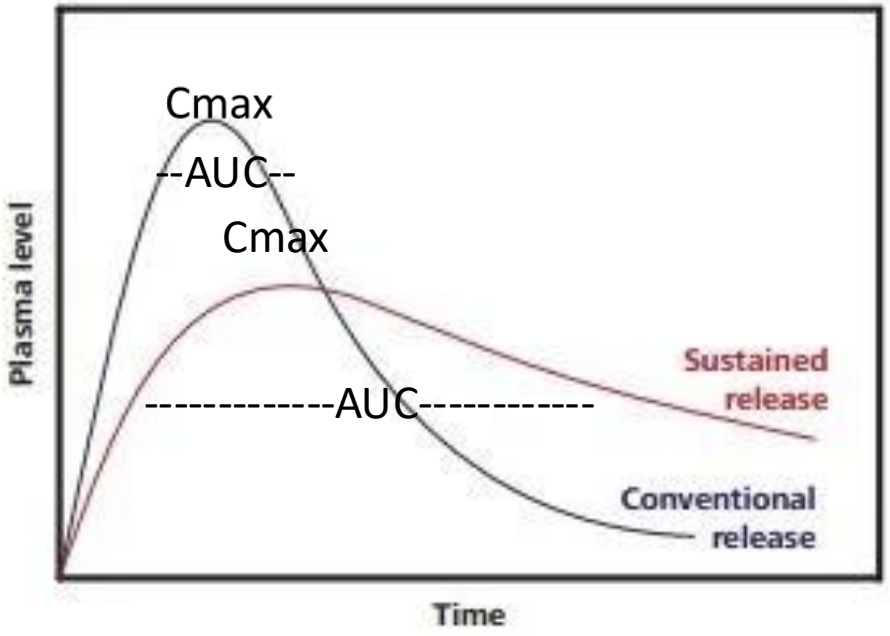
Pharmacokinetics (PK) 101
AUC and Cmax

- Area under the curve (AUC)
  - measures extent of drug absorption dosage form over time
- Maximum concentration (Cmax)
  - measures rate of absorption as to how fast drug is absorbed from GI tract into blood



MR PK compared to IR PK

- Modified release (MR) formulation
  - Designed to prolong release of drug from dosage form
  - MR Cmax < IR Cmax
  - AUC expected within 80-125% CI
- High fat meals may affect MR formulation drug release (Food effect)
- Delay in MR tablets from GI tract may cause dose dumping



IR to MR Change Assumptions

- Tech operations provides MR formulation that has passed Stability (Guidance for Industry Q1A(R2) Stability Testing of New Drug Substances and Products November 2003)
- In vitro dissolution testing for MR release (Guidance for Industry Extended-Release Oral Dosage Forms: Development, Evaluation, and Application of In Vitro/In Vivo Correlations September 1997)
- Linear pharmacokinetics

Options

Option 1 – Repeat Phase 2	Option 2 – Bridging strategy
Repeat phase 2 with MR formulation Advantage • Definitive outcome if it works Disadvantage • Significant delay with repeating phase 2 study	Compare IR to MR formulation Advantage • Delay is considerably less than repeating a phase 2 study Disadvantage • Outcome maybe give a false positive if not tested rigorously

Option 2 Bridging Strategy

BE Study	Food Effect Study	Multiple Dose Study
• Two-arm, single dose, randomized study comparing MR formulation (Test) against IR phase 2 formulation (reference) • Objective: to determine the equivalence of MR to IR for AUC • healthy volunteers • Draw timed blood samples from 0 to 24 hrs • Two one-sided t-test • 90% Confidence interval between 80 - 125% for Cmax and auc	• Two-arm, single dose, randomized study comparing MR formulation fasted (reference) against MR fed with high fat meal (test) • Objective: to determine if high fat meal causes dose dumping • healthy volunteers • Draw timed blood samples from 0 to 24 hrs • Two one-sided t-test • 90% Confidence interval between 80 - 125% for Cmax and AUC	• Two-arm, randomized, multiple dose, study comparing MR formulation 7 days QD dosing • Objective: to determine if pk changes after multiple dosing • healthy volunteers • Draw timed blood samples from 0 to 24 hrs on day 1, Cmins, and 0-24 hrs on day 6 • Two one-sided t-test, 90% • Confidence interval between 80 - 125% for day 1 Cmax and AUC and day 6 AUC and Cmax

Option 2 Bridging Strategy Results

BE Study	Food Effect Study	Multiple Dose Study

• AUC within 80-125% ci
• CMax not within 80-125% Ci
• Conclusion
  • Equivalent for AUC
  • Not Cmax (by design)
	• AUC food and AUC fed within 80-125% CI
	• Cmax food and Cmax fed within 80-125% Ci
	• Conclusion
	  • No food effect
	  • Can be administered with food
		• Day 1 Auc 0-24 to day 6 AUC 0-24 within 80-125% CI
		• Day 1 Cmax to day 6 auc within 80-125% Ci
		• Conclusion
		  • No dose dumping
		  • No delayed release with qd dosing for 7 days

Conclusion:

- MR formulation equivalent to IR formulation, not affected by food and does not dose dump after multiple dosing
- MR can be used with confidence in Phase 3 studies.

Option 2
Final Thoughts on Bridging Strategy

- Ideal to avoid significant formulation changes after Phase 2
- Check FDA website for guidance documents
  - Guidance for Industry SUPAC-MR: Modified Release Solid Oral Dosage Forms Scale-Up and Postapproval Changes: Chemistry, Manufacturing, and Controls; (September 1997 CMC 8)
- Technical operations needs to provide necessary data to support MR formulation
- CMC Amendment and study protocols to be submitted to the IND
- Expect development delay > 12 months
- Bridging strategy not “one size fits all”
    - Solid dosage forms
    - Drugs with linear kinetics
    - Not biologics (mAB) or cell therapies
- Ensure if bridging strategy fails, then IR BID dosing can be ready for Phase 3


Thank you

Fair Balance

Positive and Negatives

- **Positive**: New treatments are now available for previously untreatable disorders.
- **Negative**: Costs of new medications are increasing significantly.

- With rising healthcare expenses, society must consider:
  - Who will cover the costs of these innovative treatments?
  - Who will have access to them?

Regulatory's recommendation

- What strategy would you recommend to bridge the MR formulation to the ir formulation?

  If tech ops provides in vitro results that show MR is viable then recommend Bridging strategy

- What studies would you recommend to the project team be conducted with the mr tablet prior to initiating the phase 3 pivotal studies?

  Next slide

- What do you say to skeptics?

  Suggest that the bridging strategy proposal can be submitted to the fda for review and comment before initiating the work, however, expect at least a 6-month delay

Options

Options	Opposed by
Option #1 Inflation Reduction Act permits Medicare, for first time, to negotiate prices of certain high-cost drugs that lack competition. Goes into effect in 2026	PhRMA
Option #2 Universal Health Insurance single payer in which costs are shared by society	Private Health Insurance
Option #3 Outcomes-based pricing which refunds some or all of treatment's cost if results don't last	PhRMA
Outcome #4 Rationing and/or only those with wealth have access	Patients/Parents/Society

Back up slides

Dan's thy shall

1. Remember Clinical studies are scientific experiments
2. Follow the data and remember FDA's motto "In God we trust, but others need to show data"
3. Listen to Statisticians who are critical in designing the clinical study
4. Remember KISS Principle – Keep clinical study design Simple as complicated study designs impacts time and costs
5. Remember before initiating the next trial, learn from the last trial, pressure test I/E requirements and study related assessments with potential investigators and trial participants
6. Remember pharmacokinetic profile of the drug is foundational to understanding the drug
7. Don't forget CMC and ensure CMC is in sync with the Phase of development
8. Remember when considering PE ensure it is appropriate for the indication and has agreement with FDA

Dan's thy shall
(Part 2)

9. Avoid amending ongoing trials which increases complexity and costs
10. Use milestone meetings with FDA wisely to obtain input from the key customer
11. Remember oversight of the clinical site is critical
12. Efficacy is measurable but Safety is in the "eyes of the beholder"
13. Remember data speaks for itself
14. It is not a "true" negotiations as FDA as all the power in granting the approval
15. Remember the awesome responsibility we have in asking patients to enroll in a trial of an unproven drug
16. Be totally transparent with the FDA
17. Be totally transparent with the FDA
18. Be totally transparent with the FDA

Evolution of medicine

Galen AD 129

Natural derived drug products Digitalis, quinine, penicillin, rapamycin, opiates, and vinca alkaloids

1950s

Synthetically derived drug

1990s

Biologics

Infliximab (mAB) approved 1998

21st century

Luxturna first approved gene therapy (2017) able to reverse some degree of blindness due to retinitis pigmentosa

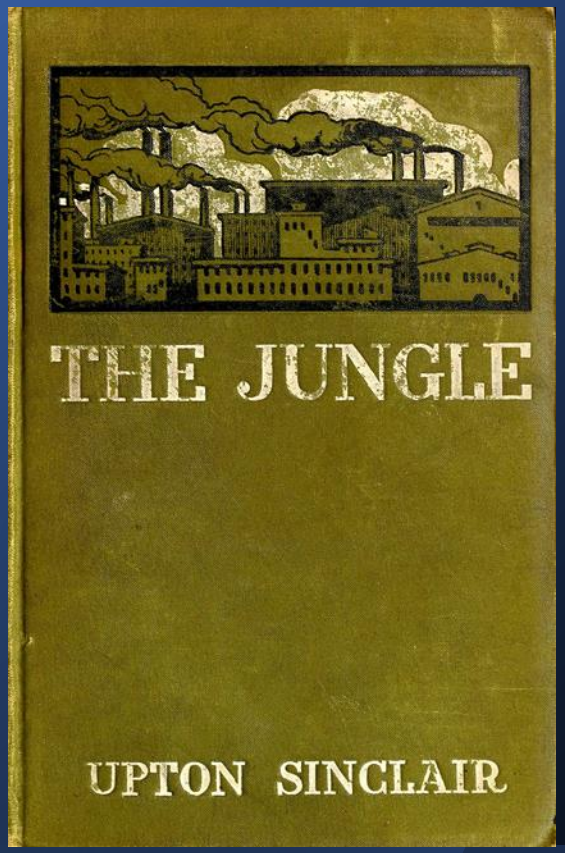
Kymriah (Novartis) (2022) first approved CAR-T cell therapy for adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy

What captures public attention is often not the transformative effects but the enormous price tags.

When gene therapies prove to be life-transforming — even lifesaving — that leads to a very high dollar amount. “You’re sort of deciding, ‘What’s the value of a life?’” says Young.

Beginning
Prior to 1906

- Consumer marketplace entirely unregulated
- *Caveat emptor* ("let the buyer beware“)
- Liniments Cure Alls
  - "Snake oils"
  - Asserted to treat and heal variety of conditions and illnesses
  - Absence of prior evaluation concerning product's safety or effectiveness
  - No restrictions on use enforced
  - Frequently ineffective and/or potentially harmful



The Start 1906

- **The Cause** – "The Jungle" pub Feb 1906
  - Upton Sinclair's exposed unhealthy practices prevalent in meatpacking industry
- **The Effect** – Caused considerable public uproar
- **The Response** – Congress passed Pure Food and Drug Meat Inspection Act 1906
  - Landmark legislation that advanced consumer protection aimed at regulating food and drug industries
  - Required truthful labeling of food and drugs, mandated meat inspections, and enforced sanitary conditions in meatpacking facilities.
  - Created Oversight and Enforcement
    - Bureau of Chemistry within Department of Agriculture to oversee compliance, later renamed Food and Drug Administration (FDA) in 1930

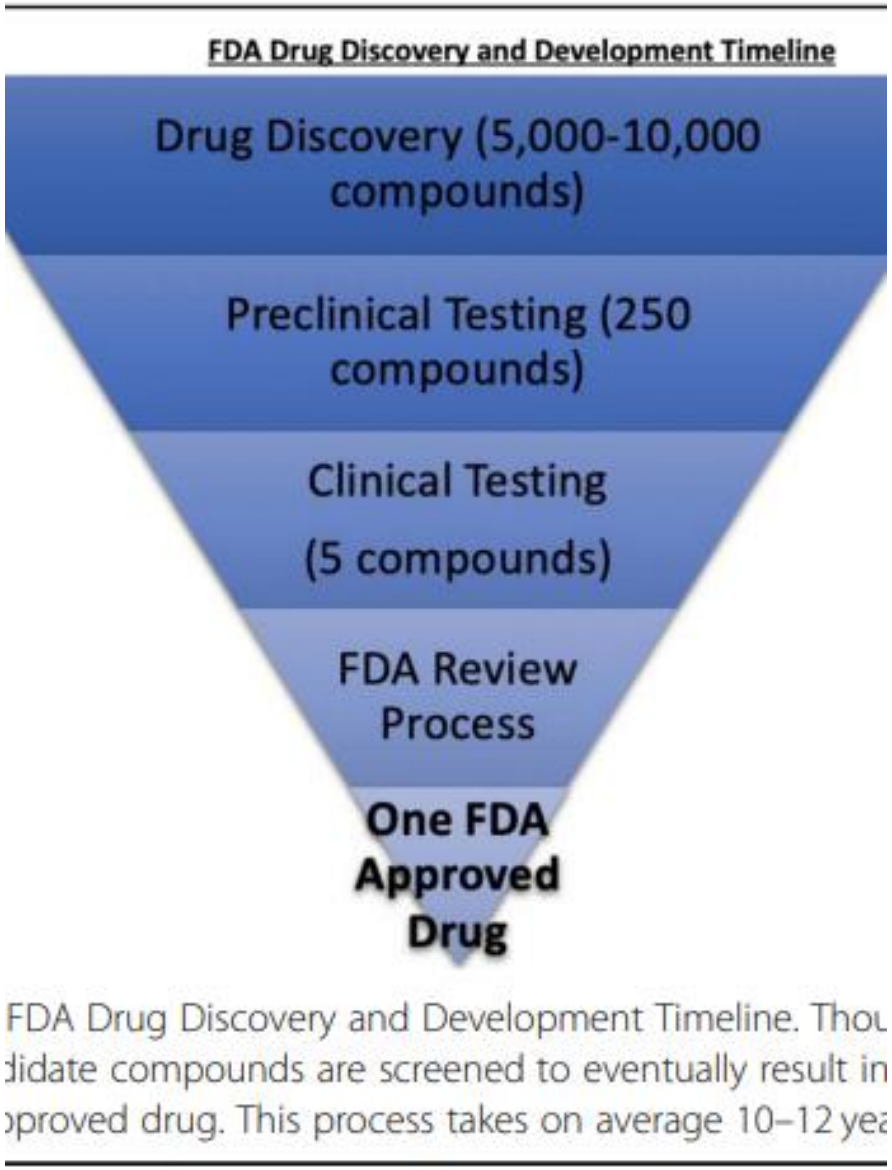
The Jungle - Wikipedia

Bottles of elixir sulfanilamide

1936
Elixir Sulfanilamide Disaster

- **The Cause** - Sulfanilamide (Massengill)
  - Antibiotic Prescribed for treatment of streptococcal infections.
  - June 1937, dissolved in diethylene glycol to create an elixir for pediatric use
  - Rapidly distributed across the country
- **The Effect**
  - By fall 1937, >100 fatalities in 15 states reported due to ethylene glycol toxicity
- **The Response**
  - **1938** Congress passed Federal Food, Drug, and Cosmetic Act (FD&C Act),
  - Expanded FDA's power to oversee drug regulation.

The-Sulfanilamide-Disaster.pdf



What are chances of an Investigational Product progressing from Discovery to Approval?

Cassidy et al. Infectious Agents and Cancer (2020) 15:73

As science evolves, think what's possible

What has partnership of Scientists, Pharma, and FDA Accomplished?

- Novel Receptors identified
- Deadly infections treated
- Childhood diseases eradicated by vaccination
- Chronic conditions such as diabetes, hypertension, schizophrenia managed
- Diseased organs can be replaced and maintained with immunosuppressants
- Knees and hips replaced with artificial devices
- Inside of body imaged with CT, MRI
- Cancer treatments (poisons) replaced with more targeted, less debilitating therapies

OUTCOME Average life span and Quality of Life (***QoL)*** increased significantly over the decades