



Drug Development and Review Process

Objectives



Go over the processes involved in drug discovery and development



Explain the role of the Food and Drug Administration (FDA) in the drug development and review process in the United States



Describe the phases involved in FDA drug approval

Research and Development Process (R&D)



Development of new drugs is a complex and costly process



It takes an average of 12 years and about \$350 million to get a new drug from the laboratory to the pharmacy shelf



R&D involves discovery (preclinical studies) and development (clinical studies)



Only one in 1000 compounds which begin laboratory testing will make it to human testing

Role of FDA

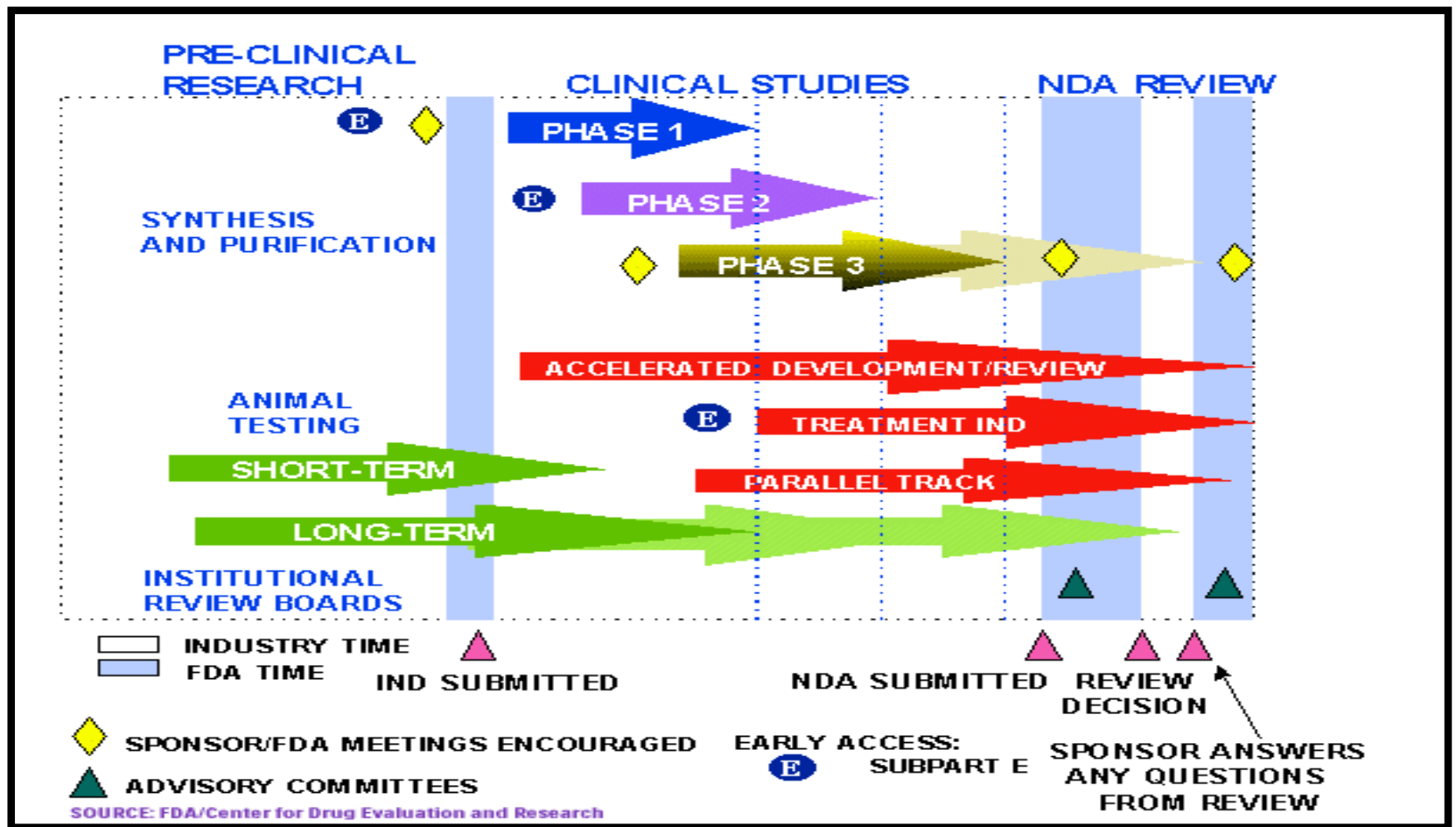


The Food and Drug Administration (FDA) is required to review and approve all new drugs in the United States



The FDA reviews and evaluates new drugs based on the evidence presented from the clinical research studies performed by the drug sponsor-typically a pharmaceutical company

Summary of Drug Development and Evaluation



Preclinical Studies



- Purpose:
 - Reasonably safe for initial use in humans?
 - Sufficiently effective against a disease target in chemical assay tests or animal models?
- Synthesis and purification of the new drug
- Pharmacology of the new drug in animal models:
 - Pharmacokinetics: absorption, distribution, metabolism, excretion, half-life
 - Pharmacodynamics: mechanism of action and estimates of therapeutic effects
 - Toxicology including carcinogenicity, mutagenicity, and teratogenicity

Investigational New Drug



Investigational New Drug (IND):
Application for permission to
administer a new drug to humans

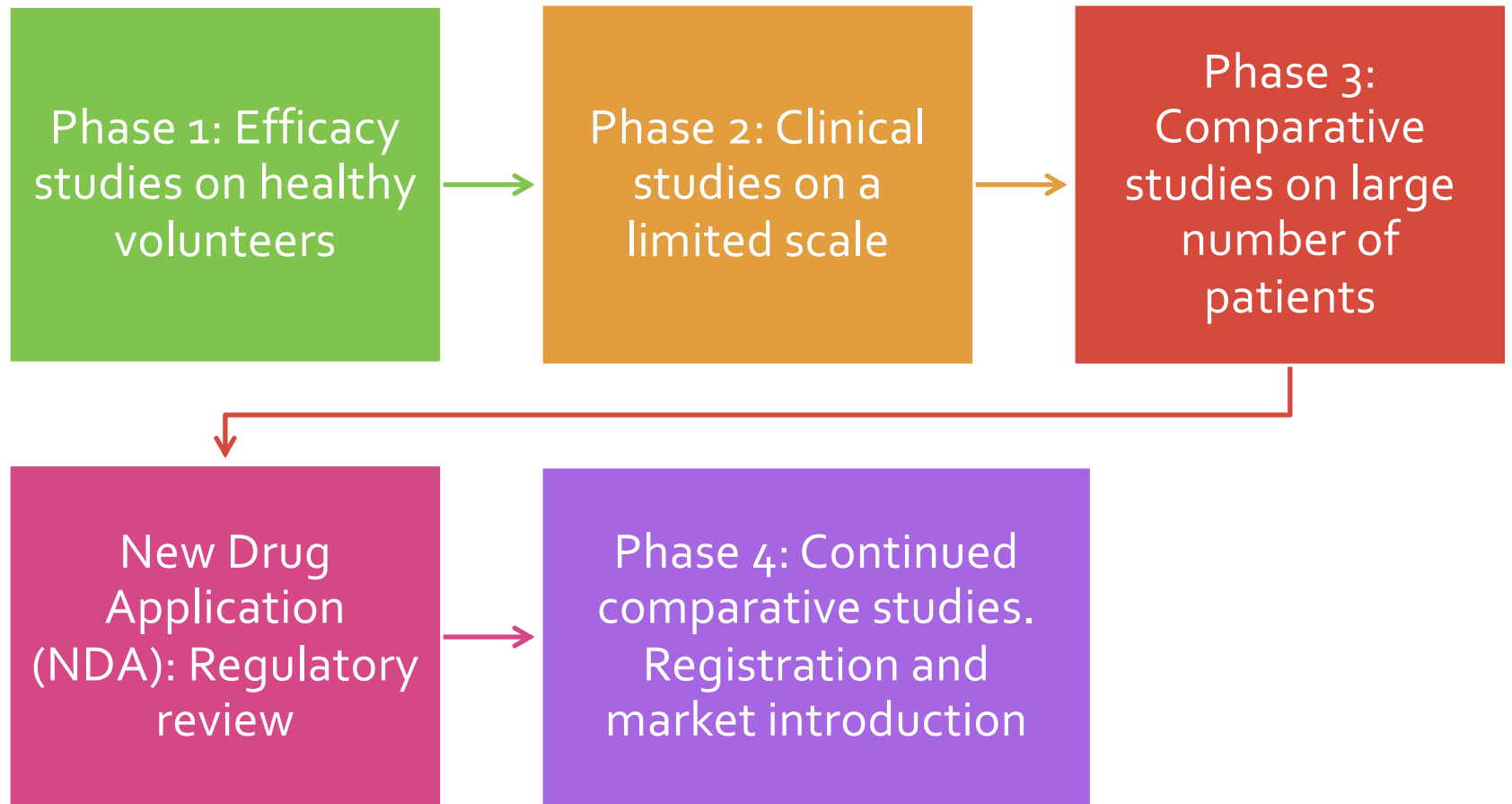


**Outlines the proposal to use the new
drug for human testing in clinical trials**



**Studies in humans can only begin after
IND is reviewed and approved by the
FDA and an Institutional Review Board
(IRB)**

Phases of Clinical Studies





Phase 1

- Typically involves 20-80 healthy volunteers (no women of childbearing potential)
- Emphasis is on drug safety
- Goal is to identify major side effects, metabolism and routes of excretion
- Lasts about 1 year
- About 70% of drugs will pass this phase

Phase 2



- Typically involves 100-300 individuals who have the target disease
- Emphasis is on effectiveness
- Patients receiving the drug are compared to similar patients receiving a placebo or another drug
- Lasts about 2 years
- About 33% of drugs will pass this phase

Phase 3



- Typically involves 1000-3000 patients
- Emphasis is on safety and effectiveness
- Investigates through well-controlled studies different populations and different dosages as well as uses of new drug in combination with other drugs
- Lasts about 3 years; 25-30% of drugs will pass this phase
- ~7 products out 100,000 that started in the laboratory will make to this stage

New Drug Application

Pre-NDA period: FDA and drug sponsors meet

Submission of NDA: Formal step asking the FDA to consider approving a drug for marketing

FDA has 60 days to decide whether it will file it for approval consideration

If filed, a review team is assigned to evaluate the new drug

FDA Role



The review team evaluates the research on the safety of the drug and its effectiveness



The FDA reviews the information to go on the drug label



It inspects the facilities where the drug will be manufactured



The application will be classified as “approvable” or “not approvable”

FDA Role

If approvable, the FDA requests additional information from the sponsor

The NDA is again reviewed

Following drug approval, sponsors of the drug will be required to continually assess the safety of the drug

Phase 4



Post-market surveillance of the drug to continually assess the safety of the drug



May include incidence and severity of rare adverse reactions, cost-effectiveness analyses, comparative trials, and quality of life studies

Expedited Programs



Fast track designation



Breakthrough therapy designation



Accelerated approval



Priority review designation



These programs allow faster and more frequent communication and guidance from FDA as the studies are being conducted, so the process brings efficiency in time and resources



Concepts for Expedited Review

Serious Condition

- AIDS, Alzheimer's, heart failure and cancer

Available Therapy

- preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s)

Unmet Medical Need

- providing a therapy where none exists
- providing a therapy which may be potentially better than available therapy



Emergency Use Authorizations

- FDA Commissioner may allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions when there are no adequate, approved, and available alternatives.
- [Coronavirus Disease 2019 \(COVID-19\) Emergency Use Authorizations for Medical Devices](#)
 - [Personal Protective Equipment EUAs](#)
 - [In Vitro Diagnostic EUAs](#)
 - [Ventilators and Other Medical Device EUAs](#)



Emergency Use Authorizations

2020 Remdesivir Emergency Use Authorization

Zika Virus Emergency Use Authorization

2015 Enterovirus D68 (EV-D68) Emergency Use Authorization

2014 Ebola Virus Emergency Use Authorization

2013 Coronavirus Emergency Use Authorization (Potential Emergency)

2013 H7N9 Influenza Emergency Use Authorization (Potential Emergency)



FDA Office of Orphan Products Development (OOPD)

- **Developing Products for Rare Diseases & Conditions**
- The [Orphan Drug Designation program](#) provides orphan status to drugs and biologics which are defined as those intended for the safe and effective treatment, diagnosis or prevention of rare diseases/disorders that affect fewer than 200,000 people in the U.S., or that affect more than 200,000 persons but are not expected to recover the costs of developing and marketing a treatment drug.



FDA Office of Orphan Products Development (OOPD)

- The [Rare Pediatric Disease Priority Review Voucher Program](#) says that a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product.
- The [Humanitarian Use Device \(HUD\) program](#) designates medical devices that are intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year as eligible for Humanitarian Device Exemption.



Resources

- <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/default.htm>
- <https://www.fda.gov/ForPatients/Approvals/Fast/default.htm>
- <https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/default.htm>
- <https://www.fda.gov/downloads/Drugs/Guidances/UCM358301.pdf>
- www.ja-online.com/industry/Drug_Development_and_Approval.ppt
- <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations>