Understanding the Drug Approval Process

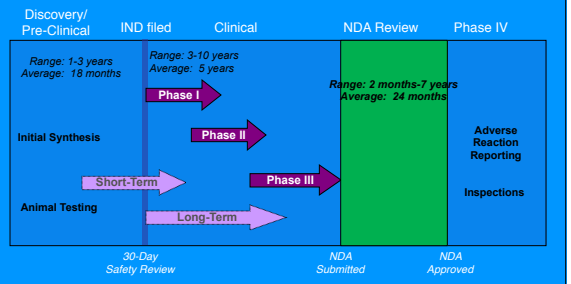
Understanding the Drug Approval Process

- For each of the following be able to give a brief description
  - Discovery
  - Phase I
  - Phase II
  - Phase III
  - NDA submission and Approval
  - Phase IV Post-Marketing
  - ANDA

The Drug Approval Process

- All new drugs require FDA approval prior to marketing.
- Proof that the drug is SAFE & EFFECTIVE and its benefits outweigh its risks.
- The burden of proof is on the manufacturer NOT the FDA.

New Drug Development and Approval Timeline



Testing Phases

- **Drug Discovery**
  - Synthesis – Screening
  - Begins in the laboratory for chemical analysis.
- **Pre-Clinical Animal testing**
  - Use animals and treat them as humanly as possible.
  - Test using different species.
  - Only a fraction of the drugs tested on animals reach clinical trials stage.

5

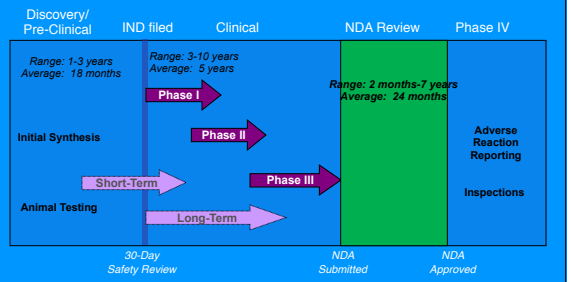
New Drug Approval Process

If Drug Discovery and Animal testing are successful:

- An Investigational New Drug Application **(IND)** is filed with the FDA by the manufacturer.
- The **IND** contains current findings and justification to move studies into humans.

6

New Drug Development and Approval Timeline



Phase I

- Objectives
  - Initiate human experience
  - Assess acute tolerability and laboratory safety
  - Define the drug's behavior in man
  - Assess early proof of concept

New Drug Approval Process

Clinical trials with humans

- **INFORMED CONSENT** is required for each patient/subject before enrolling into clinical trials.
- Requires for the patient to be **told all the risks and other treatment options** in a language they understand.
- Patients should also be **free to leave the trial** at any time.

9

Phase I

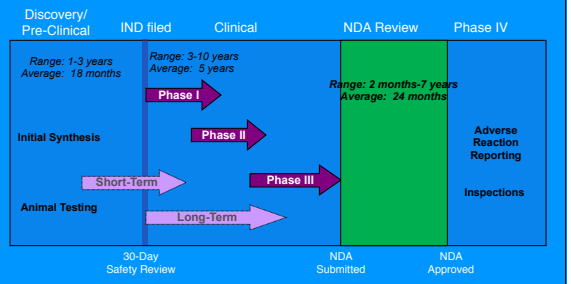
- Generally healthy male volunteers
- Subjects studied <100
- Usually blinded and placebo controlled
  - Inactive substance: not real medicine administered
  - Gives the impression that they're receiving the real medicine.
  - Used to compare against patients with the test drugs

10

Phase I

- Duration ~12 month
- About 2/3 go on to Phase II
- Less than ¼ will reach market
- Reasons for stopping
  - Safety
  - Intolerability
  - Poor bioavailability
  - Formulation issues

New Drug Development and Approval Timeline



Phase II

- Objectives
  - Establish early evidence of safety
  - Establish proof of concept
  - Narrow dose range
  - Up to several hundred patients.
  - Several months to two years.

13

Phase II

- Study Population
  - Target disease state
  - Tightly controlled patient selection
- Studies are comparative

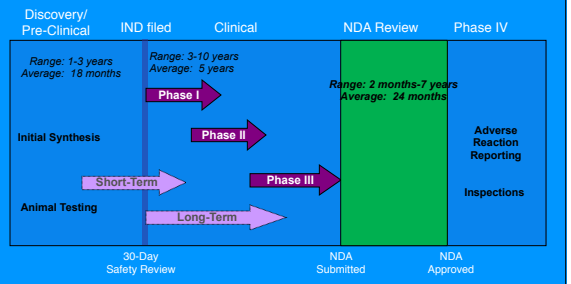
14

Phase II

- Duration 18 - 30 months
- Risk
  - Progression to Phase III 41%
  - Progression to launch 33%
- Reasons for Failure
  - Toxicity
  - Lack of efficacy

15

New Drug Development and Approval Timeline



16

Phase III

- Objectives
  - Unequivocal demonstration of efficacy and safety for the desired indication(s) at a specific dose.
    - **Safety**
    - **Dosage**
    - **Effectiveness.**

17

Phase III

- Controlled Trial
  - Group of patients (with similar condition or disease) who are given a placebo (or no drug) and used to compare the effect of the test drug.
  - Groups are placed on controlled or treatment arm randomly.
- Double-Blind Trial
  - The patient nor the doctor who is treating the patient knows in which arm of the study a particular patient is.

18

Phase III

- Study Population
  - Target disease state
  - Reduce exclusion criteria
  - 100s to 1,000s of patients studied
- Studies are conducted at multiple locations in multiple countries
- Data are pooled across treatment centers

Phase III

- Duration 2 - 3+ years
- Risk
  - Progression to NDA submission 79%
  - Progression to launch 65 - 71%
- Reasons for Failure
  - Economics
  - Efficacy
  - Safety

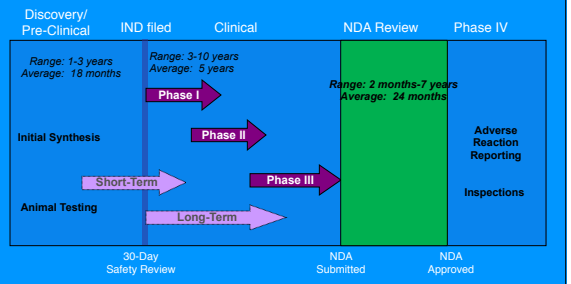
New Drug Application (NDA)

NDA

- Once proven safe and effective in the manufacturer's view, they may submit an **NDA** seeking approval to market the product.

21

New Drug Development and Approval Timeline



22

NDA Review

- Duration ~24 Months (2 months - 7 years)
- Respond to FDA Requests
- Phase IV Plan Being Put in Place

Phase IV

Phase IV

- Can be started after the NDA is approved.
- Life time of the drug.
- The main purpose is for safety.

Phase IV

- Studies to Broaden Use
  - Additional patient populations
    - Age
    - Sex
    - Childbearing potential
    - Pregnancy

25

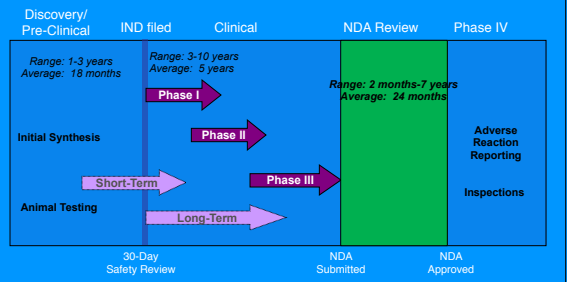
Marketed Drugs

- **Patent** is a right given to a manufacturer to exclusively market a new product for a specific period of time under a brand name.
- A patent is good for 20 **years.**

- **Hatch-Waxman Act of 1984**
- Extends patent up to **5 years** to compensate for lost time in NDA review before going to market.
- While the drug is under patent, a **generic drug** will NOT be marketed by other companies.

26

New Drug Development and Approval Timeline



Marketed Drugs

- Medical devices and biological products such as insulin and vaccines must also meet FDA testing and approval requirements.
- **The Center for Devices and Radiological Health (CDRH)** is responsible for devices.
- **The Center for Biologics Evaluation and Research (CBER)** is responsible for biological products made from living organisms.

Abbreviated New Drug Application

- Once the patent has expired other companies may market their version, a generic, of the brand drug if…….
- Approval to market a generic version requires submission of an ANDA.
- This is a much shortened process and application.

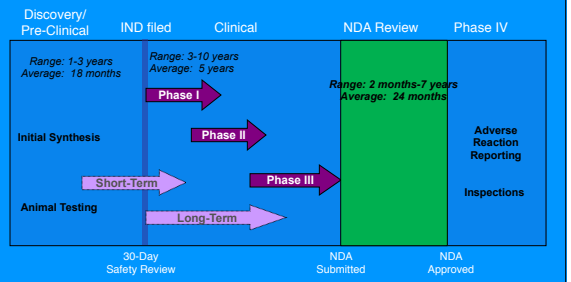
29

Abbreviated New Drug Application

- Basically, the generic manufacturer must show bioequivalency with the brand drug
- No safety or efficacy data required
- Preclinical, toxicology etc. is not needed.
- The FDA publishes this information in the "Orange Book".
- www.accessdata.fda.gov/scripts/cder/ob/default.cfm

30

New Drug Development and Approval Timeline



Terms to Know

- IND
- NDA
- Discovery
- Phase I, II, III, IV
- Efficacy
- Safety
- ANDA
- Informed Consent
- Placebo
- Comparative
- Bioequivalency
- Blinded
- Double-blinded
- Control group

This workforce solution is 100% funded by a grant awarded by the U.S. Department of Labor, Employment and Training Administration, TAACCCT grant agreement # TC-22505-11-60-A-25.The solution was created by the grantee and does not necessarily reflect the official position of the U.S. Department of Labor. The Department of Labor makes no guarantees, warranties, or assurances of any kind, express or implied, with respect to such information, including any information on linked sites and including, but not limited to, accuracy of the information or its completeness, timeliness, usefulness, adequacy, continued availability, or ownership. Massachusetts Community Colleges are equal opportunity employers. Adaptive equipment available upon request for persons with disabilities.