How an Idea becomes a Treatment - *The Drug Development Process*

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The FDA's many roles

- Meeting with sponsors, investigators, patients/advocates
- Monitoring study safety & outcomes
- Drug review and approval
- Post-marketing surveillance
- Directing programs to expedite drug development for rare and serious conditions

IND Enabling Studies:
Test animals for toxicity; demonstrate potential efficacy; select dose(s) to be given in trials

FDA Review of IND Application:
FDA considers: potential risks of the drug and potential for benefit; FDA may request additional pre-clinical (animal) studies to address questions about risk and/or benefit. Sponsor *may not* proceed with clinical trials until FDA reviews & approves plan for studies in humans.

IND Application process:
Sponsor submits information about drug (how it's made), the drug's effects (e.g., toxicity, possible efficacy), results of animal studies, and proposed plan for clinical trials.

Keeping Patients Safe

- Data Safety & Monitoring Board (DSMB) oversees safety & monitors data quality
- IRBs oversee ethical conduct of research & protection of human subjects
- Study team monitors patient safety; documents & reports any adverse events
- Patients / families notify study team if there are side effects or any safety concerns

Develop and validate animal models

Manufacture drug for animal testing

Test initial safety in animals

Examine efficacy in animals

Select dose(s) to test in humans

IND Enabling Studies

Finalize protocol & safety plan

Establish Data Safety & Monitoring Board (DSMB)

Select sites & train study staff

Register on clinicaltrials.gov

Conduct trial & monitor participant safety

Review meeting prior to NDA

New Drug Application (NDA) submission

NDA review by FDA

Drug label development & review

Monitor for long-term safety & efficacy outcomes (sponsor)

Pre-Trial Development

Meet with FDA to plan studies (recurring)

Establish natural history

Develop & select outcome measures

Design the trial(s)

Investigational New Drug (IND) application submitted to FDA

Clinical Trials – Phase I, II, III*

Establish research infrastructure

Obtain ethics approval from institutional review board (IRB)

Recruit participants

Approval Process

Analyze data

Report results

FDA Advisory Councils

Facility Inspections

Post - Approval

Medwatch reporting system (clinicians)

The Phases of Clinical Research

- **Phase I:** Is it safe? What are (if any) the side effects? (*may not be able to move forward w/efficacy if safety is not demonstrated)*
- **Phase II:** Is the drug effective in a very specific population
- **Phase III:** Answers broader questions about effectiveness in more diverse populations; with other drugs, etc. *Does the treatment work? Does it provide a cure? Does it slow disease progression? Does it lessen symptoms?*

**Drug development programs do not always follow a linear Phase I-II-III process. There may be several studies done at any one phase, or an early-phase study may be skipped or combined with a later-phase study*

Natural History Studies

- *Gain understanding of disease & symptoms*
- *Learn how disease changes over time*
- *Have basis for comparison, to a treatment*

Early Stopping

A study might be stopped early because…

- It is not safe to continue
- The drug doesn't work
- The drug works and should be made available to all patients as soon as possible

Select Outcome Measures

To know if a drug is effective, researchers need to measure its effects on the individual and the disease. Does the drug slow disease progression? Does the drug treat certain specific symptoms? To answer these questions, researchers select outcome measures that can tell us if the drug has a meaningful impact on how the patient *feels, functions, and survives.*

New Drug Application (NDA):
Sponsors formally ask the FDA to approve drugs for marketing by submitting a NDA. The NDA includes a large amount of information about the drug: animal data, human data, how the drug acts (safety and efficacy), and how the drug is made (manufactured).

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