

Learn About Clinical Drug Development



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How are new drugs studied and approved?

- In this module, you will learn about:
 - Regulatory authorities
 - Phases of drug research
 - At what point in drug development children are typically involved in research



Why are research studies done for new medicines?

- Not all medicines have been studied in children
- Not all medicines work for all people
- Old medicines may be used for new medical conditions
- Medicines can be made into new dosage forms
 - Tablet or intravenous (parenteral)
 - Suspension/liquid
 - Topicals (creams or ointments)



What does it mean when a medication is approved?

- **Safe**- this means that it can be used without harm.
- **Effective**- this means that it has shown that the medication works for what it is intended.
- **Regulatory Approval**- this means that government review ensures that a medicine is BOTH SAFE and EFFECTIVE prior to being available to the public (outside of a clinical study).



What are Regulatory Agencies?

- Governmental offices that review data from clinical trials and have the authority to determine if a medicine is safe and effective for use in a patient population with a specific medical condition or disease
- Their role is very important to make sure patients have access to medicines that can make symptoms and diseases/medical conditions better



What are Regulatory Agencies?

- Each country or region has their own regulatory agency
- Here are some examples
 - **Food and Drug Administration (FDA)** <https://www.fda.gov/>
 - **European Medicines Agency (EMA)** <https://www.ema.europa.eu/en>
 - **Medicines and Healthcare Products Regulatory Agency (MHRA)**
<https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency>



How is a new medication studied?

- Laboratory research-does not involve humans
- Phases of Research-involve volunteers or patients
 - Phase 1
 - Phase 2
 - Phase 3
 - Phase 4



Laboratory Research

- Occurs before a medicine is studied in people
 - Also known as pre-clinical or non-clinical research
- Some reasons we do laboratory research:
 - To **find out** how a drug works (mechanism of action)
 - To **find out** how much of a drug is needed in the body to work
 - To **discover** what side effects a drug might have
 - To **test** how a drug is handled by the body (absorbed, distributed, metabolized, eliminated-pharmacokinetics)



Clinical Research Phases

- Clinical studies are divided into phases that involve different numbers and types of people participating in the study
- Phases of research follow different steps with phase 1 being the first step and phase 3 and 4 being the last steps before an investigational drug is reviewed and approved
- The goals of each phase, number, and type of people participating in the study differs

Clinical Research Phases -Drug Research

| | What is studied? | Who participants? | How many participants? | How long is the is a participant in this study? |
|---------|------------------------------------|--|------------------------|---|
| Phase 1 | Safety, pharmacokinetics | Healthy volunteers Patients with the condition (sometimes) | Small | Short |
| Phase 2 | Safety, pharmacokinetics | Adults with a medical condition | Small | Short |
| Phase 3 | Efficacy, safety, pharmacokinetics | Adults, adolescents, children, neonates with a medical condition | Large | Medium-Long |
| Phase 4 | Long-term safety and efficacy | Adults, adolescents, children, neonates with a medical condition | Large | Long |

When are pediatric patients enrolled in clinical trials?

- Children may be involved in any phase of research
- Traditionally, children have only been included in studies after a new medicine has been tested in adults (after adult phase 3 studies are done)
- More recently, adolescents and children have been included in phase 3 studies at the same time as the adult studies
- Studies in neonates can often be delayed until studies in children are complete



When are pediatric patients enrolled in clinical trials?

- In some cases studies may be done in pediatric patients earlier because the disease only happens in children, the disease is rare or in cases in which the disease is very severe or life-threatening
- Examples
 - Rare genetic diseases (Duchenne Muscular Dystrophy or Spinal Muscular Atrophy)
 - Cancers
 - Neonatal lung disease (bronchopulmonary dysplasia)

Clinical Research Phase Examples

- **Open-label Study to Evaluate the Pharmacokinetics of BREATHO in Adults ≥ 5 With Mild, Moderate, or Severe Asthma**
 - 14 adults
 - Open-label, no placebo group
 - Pharmacokinetic study
 - Goal of the study is safety and to determine the pharmacokinetics
 - Study lasts 2 months for each adult participant
 - What study phase would this be?

Clinical Research Phases -Drug Research

| | What is studied? | Who participants? | How many participants? | How long is the is a participant in this study? |
|---------|------------------------------------|--|------------------------|---|
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| Phase 2 | Safety, pharmacokinetics | Adults with a medical condition | Small | Short |
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| Phase 4 | Long-term safety and efficacy | Adults, adolescents, children, neonates with a medical condition | Large | Long |

Clinical Research Phase Examples

- **Efficacy and Safety of 2 Doses of BREATHO Compared to Placebo in Children With Severe Persistent Asthma**
 - 400 children
 - Two doses of medications compared to placebo
 - Goal of the study is to evaluate the efficacy (FEV₁) and safety of BRETHO for treating asthma symptoms
 - Study lasts 4 months for each child participant
 - What study phase would this be?

Clinical Research Phases

-Drug Research

| | What is studied? | Who participants? | How many participants? | How long is the is a participant in this study? |
|---------|--|--|------------------------|---|
| Phase 1 | Safety, pharmacokinetics | Healthy volunteers Patients with the condition (sometimes) | Small | Short |
| Phase 2 | Safety, pharmacokinetics | Adults with a medical condition | Small | Short |
| Phase 3 | Efficacy, safety, +/- pharmacokinetics | Adults, adolescents, children, neonates with a medical condition | Large | Medium-Long |
| Phase 4 | Long-term safety and efficacy | Adults, adolescents, children, neonates with a medical condition | Large | Long |

Clinical Research Phase Examples

- **A Study of GENEX for Duchenne Muscular Dystrophy**
 - 10 children
 - Single and Multiple Doses of GENE X in Patients With Duchenne Muscular Dystrophy
 - Goal of the study is to evaluate the safety and pharmacokinetics of GENEX in children with Duchenne Muscular Dystrophy
 - Study lasts 14 days for each child
 - What study phase would this be?

Clinical Research Phases -Drug Research

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| Phase 1 | Safety, pharmacokinetics | Healthy volunteers Patients with the condition (sometimes) | Small | Short |
| Phase 2 | Safety, pharmacokinetics | Adults with a medical condition | Small | Short |
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Now that trials are done, what data is needed to approve a new drug?

| | What is studied? | Who is involved in studies | What type of studies? | Comments? |
|----------|--|------------------------------|---|--|
| Option 1 | Disease only in adults | Adults | Phase 1, 2, 3 | Typically to be approved at least two phase 3 studies showing safe/efficacy |
| Option 2 | Disease in adults/ children | Adults/Children | Phase 1, 2, 3 Adults Phase 2, 3 Children | Sometimes no phase 2 in children is required |
| Option 3 | Rare disease or disease only in children | Children only or with adults | Phase 1, 2, 3 | To be approved at least two phase 3 studies showing safe/efficacy, sometimes one phase 2 that studies efficacy and one phase 3 is enough |

Thank you!



- Regulatory Agencies help determine whether or not a new drug is safe and effective for use in patients with a medical condition/disease
- Phases of research differ based on who is involved, what the disease is and what the goal of the study is.
- Goals of studies are safety, efficacy and pharmacokinetics
- Children can be involved in any phase of drug research