# Drug Development Overview

## FDA: Basic Research to Clinical Use

**12 June 2012**

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**Division of Medical Imaging Products**
**Center for Drug Evaluation and Research**
**U.S. Food and Drug Administration**

# Outline

- **Therapeutic Drug vs Diagnostic Imaging Agent Development**
- **Preclinical Research to Clinical Studies**
  - **Appropriate FDA submission(s)**
  - **Introduction of upcoming talks in this session**

## Therapeutic Drugs

$800 million, 14 years

Basic Research, Target ID → Chemical Synthesis, Screening, Lead Selection → Preclinical Testing & Lead Optimization → Phase 1-3 Trials → NDA Review & Approval → Post-marketing Surveillance

$3.4 B annual revenue

$150 million, 10 years

ID of Diagnostic Opportunity → Chemical Synthesis → Assays & Preclinical Testing → Lead Selection → Lead Optimization → Phase 1-3 Trials → NDA Review & Approval → Post-marketing Surveillance

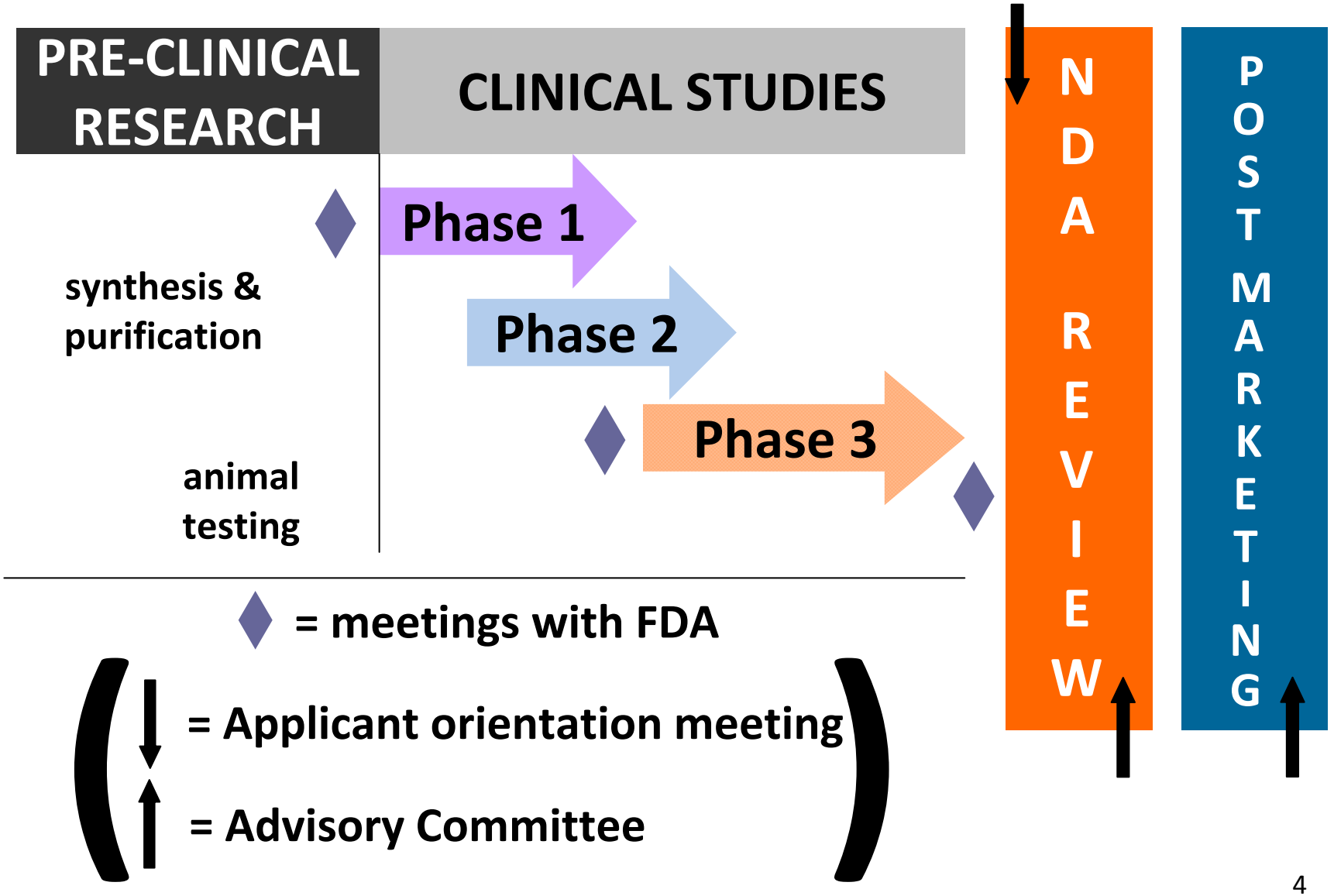
$400 M annual revenue

## Diagnostic Imaging Agents

adapted from Agdeppa (2009) AAPS Journal 11:286

# New Drug Development Process





# New Drug Development Process

**PRE-CLINICAL RESEARCH**

**CLINICAL STUDIES**

**Phase 1**

**Transitioning from eIND to Traditional IND**

**-- Dr. Siham Biade -- 10:00 AM**

**animal testing**

- **PK and**
- **proof of mechanism / concept**
- **toxicity**
- **translation to humans**

**What are the preclinical requirements for toxicology / pharmacology?**

# New Drug Development Process



**PRE-CLINICAL RESEARCH**

**CLINICAL STUDIES**

**Phase 1**

**CMC Issues in Radiopharmceutical INDs**

**-- Dr. Ravindra Kasliwal -- 10:45 AM**

**synthesis & purification**

**Considerations:**

- target affinity
- selectivity
- metabolism
- lipophilicity
- molecular weight / size
- signaling moiety selection / incorporation
- how the radiolabel is integrated into the imaging agent

- Radioactive drug substance
- Radioactive drug product

# New Drug Development Process

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**PRE-CLINICAL RESEARCH**

**CLINICAL STUDIES**

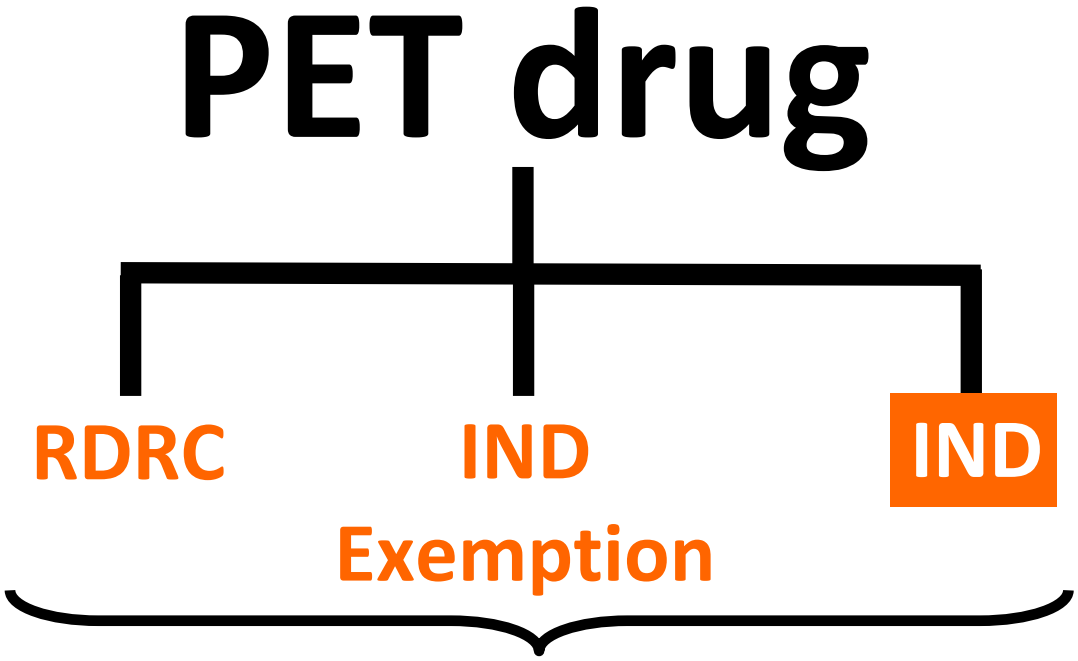
**Phase 1**

**synthesis & purification**

**animal testing**

**What do I submit to FDA before starting human studies?**

# *Which submission is most appropriate?*




**research or investigational use**

# Definitions

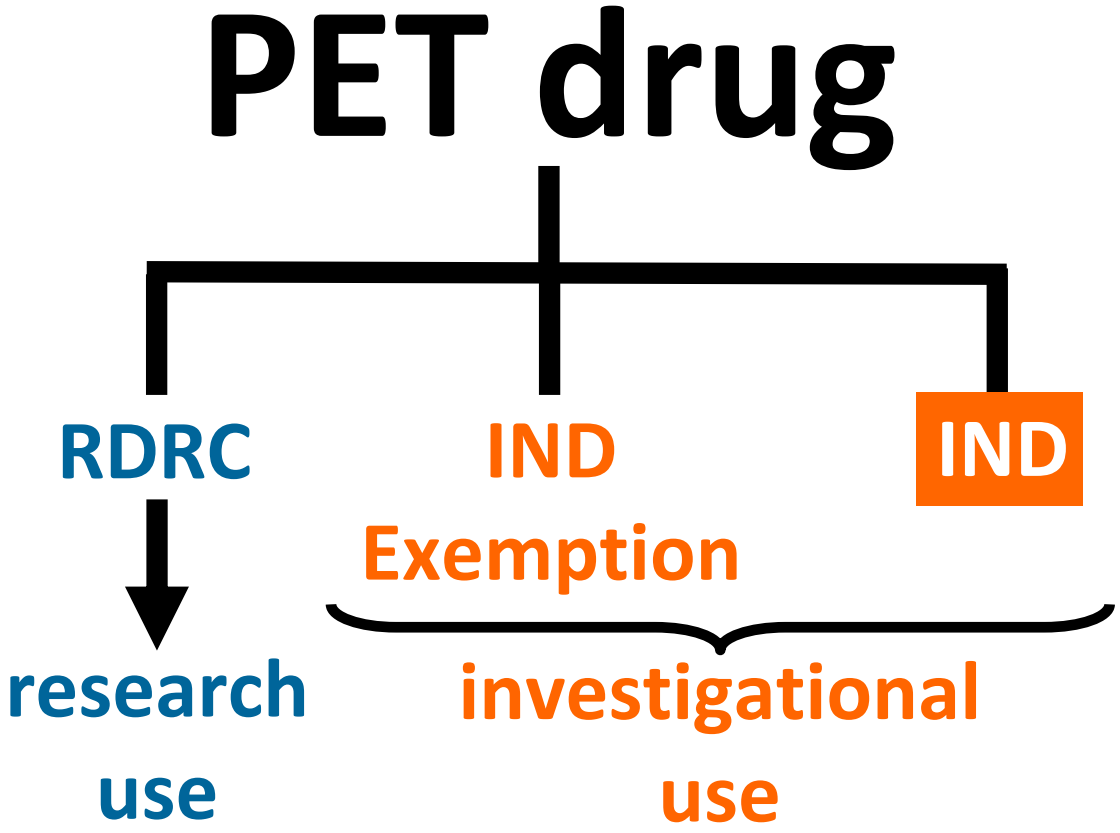
## Research use

- For basic science research
- Not using for immediate therapeutic, diagnostic, or similar purpose
- No intent to determine safety or effectiveness for clinical use

## Investigational use

- To establish the safety or effectiveness of a new use of the drug to support approval

# *Which submission is most appropriate?*



# RDRC

**NOT for 1st in human study!**

***IND not needed if study is approved by a Radioactive Drug Research Committee (RDRC)***

***RDRC research limited to:***

- **Basic science**
- **Not for diagnostic or therapeutic purpose**
- **Not an evaluation of drug's safety/efficacy**
- **Dose known not to cause any pharmacologic effect**
- **Radiation dose within specific limits**

# IND Exemption

## Before December 12, 2015

### C R I T E R I A

- PET drug used in the trial is made at a facility included in a submitted NDA/ANDA
- No intent to support new indication, labeling change, or advertising change
- No intent to promote/commercialize the drug
- No significant risk increase (e.g. dose, route of administration, patient population)
- Compliant with IRB/consent process

# IND Exemption

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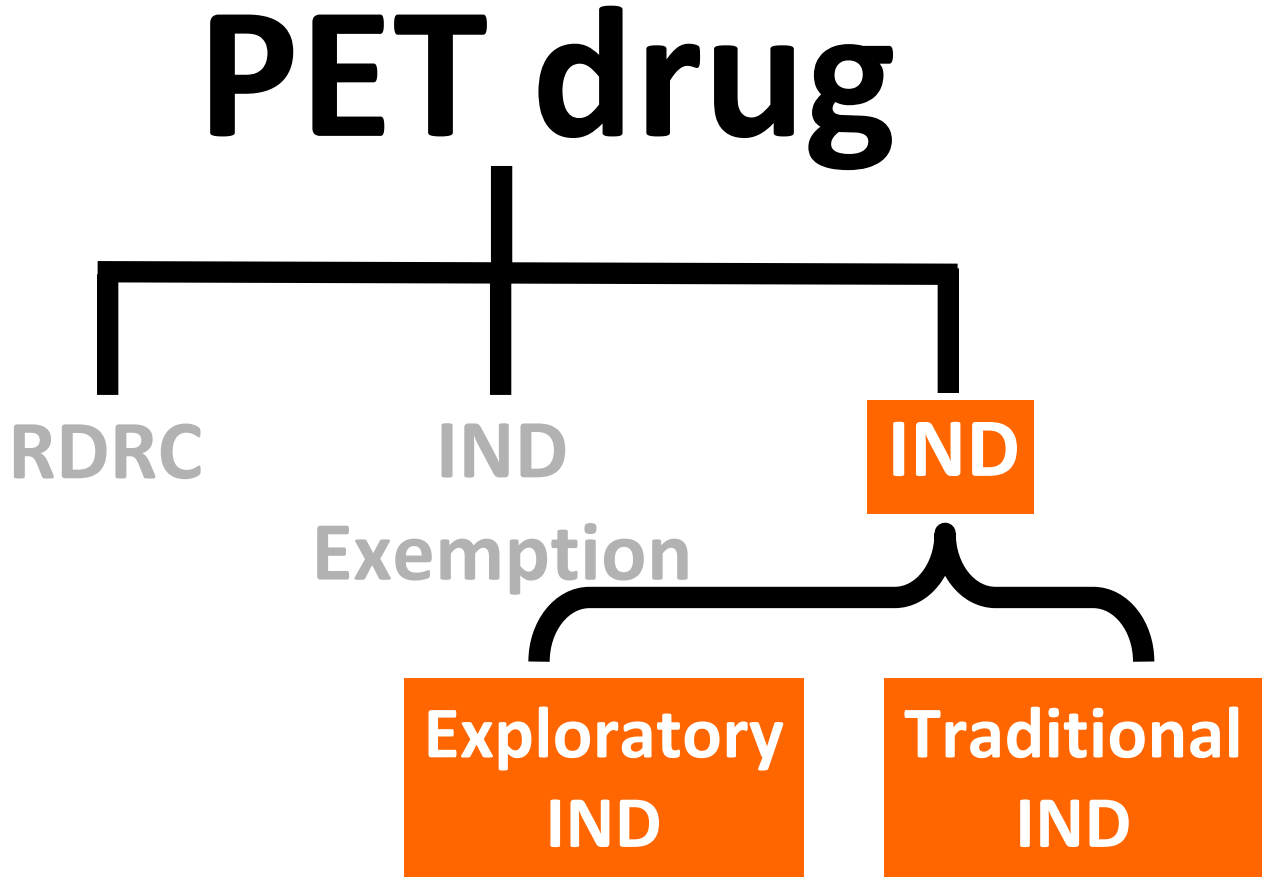
# *Which IND type is most appropriate?*



# Exploratory IND

## P U R P O S E

- An early Phase 1 approach to help distinguish earlier in the process those candidates that hold promise from those that do not.

## Potential A D V A N T A G E over Traditional IND

- Involve fewer resources than traditional IND;
- Sponsors can move ahead more efficiently with the development of promising candidates.

# *Exploratory IND*

## C R I T E R I A

- **Early Phase 1 study**
- **Assesses feasibility for further drug development**
- **Involves very limited human exposure**
- **Has no therapeutic or diagnostic intent (e.g. screening study, microdose study)**

# *How Can an Exploratory IND Study Help Sponsors?*

- **Determine mechanism of action:** same in humans and experimental system?
- **Provide pharmacokinetics information**
- **Select most promising lead product**
- **Explore biodistribution**

# New Drug Development Process

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**PRE-CLINICAL RESEARCH**

**CLINICAL STUDIES**

**Phase 1**

**synthesis & purification**

**animal testing**

**What do I submit to FDA before starting human studies?**

**ANSWER:**

**For investigational use, options are**

- **Exploratory IND (if qualify)**
- **Traditional IND**

**For research use, RDRC**

**RDRC: NOT 1st in human!**

# New Drug Development Process



## CLINICAL STUDIES

☐ for radio-pharmaceutical

Phase 1

---------- WHO? ----------

- small group of people (20-80)
- healthy participants and/or patients

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---------- WHAT? ----------

- initial human studies
- evaluate safety
- determine radiation absorbed dose
- determine safe mass dose
- determine metabolism
- determine pharmacokinetics
- gain early evidence of efficacy

# New Drug Development Process

**PRE-CLINICAL RESEARCH**

**CLINICAL STUDIES**

**Phase 1**

**Radiation Dose: What Do We Want?**

**-- Dr. Orhan Suleiman -- 10:15 AM**

**How is human radiation dose estimated?**

# New Drug Development Process



## CLINICAL STUDIES

### ------- WHO? -------

- larger groups of people
- patients with disease or condition under study

**Phase 2**

### --------- WHAT? ---------

- controlled clinical study
- evaluate efficacy of drug for a particular indication
- determine common short-term side effects and risks
- refine dose, population
- develop image reading method

clinicaltrials.gov

for imaging agent

# New Drug Development Process



## CLINICAL STUDIES

### ---------- WHO? ----------

- even larger groups of people
  - for imaging agent

Phase 3

though the sample size may depend on the study design

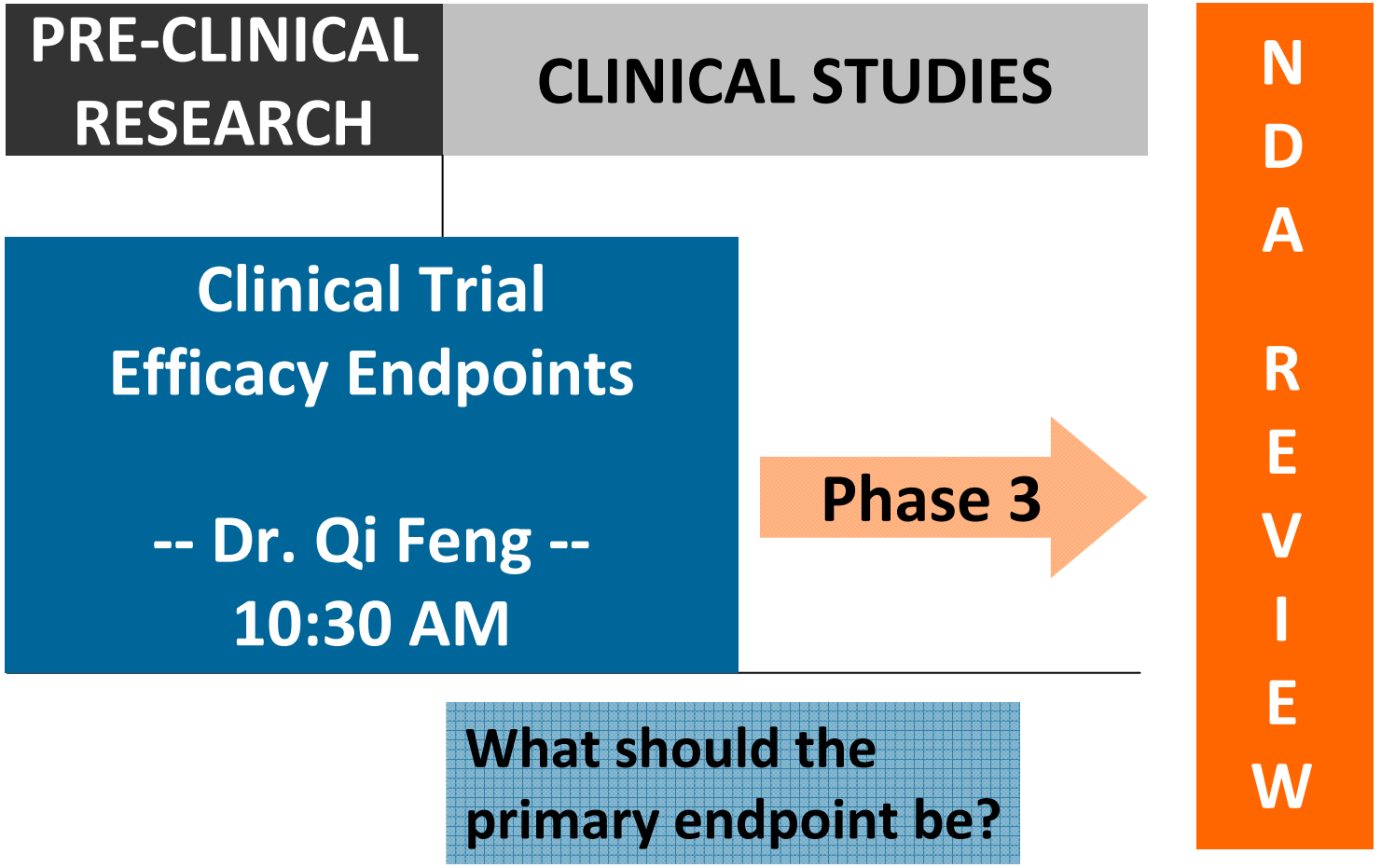
### ---------- WHAT? ----------

- expanded controlled and uncontrolled trials
- confirm efficacy, monitor side effects
- compare to commonly used treatments
- evaluate overall benefit-risk relationship of the drug
- gather data to inform adequate basis for labeling

clinicaltrials.gov

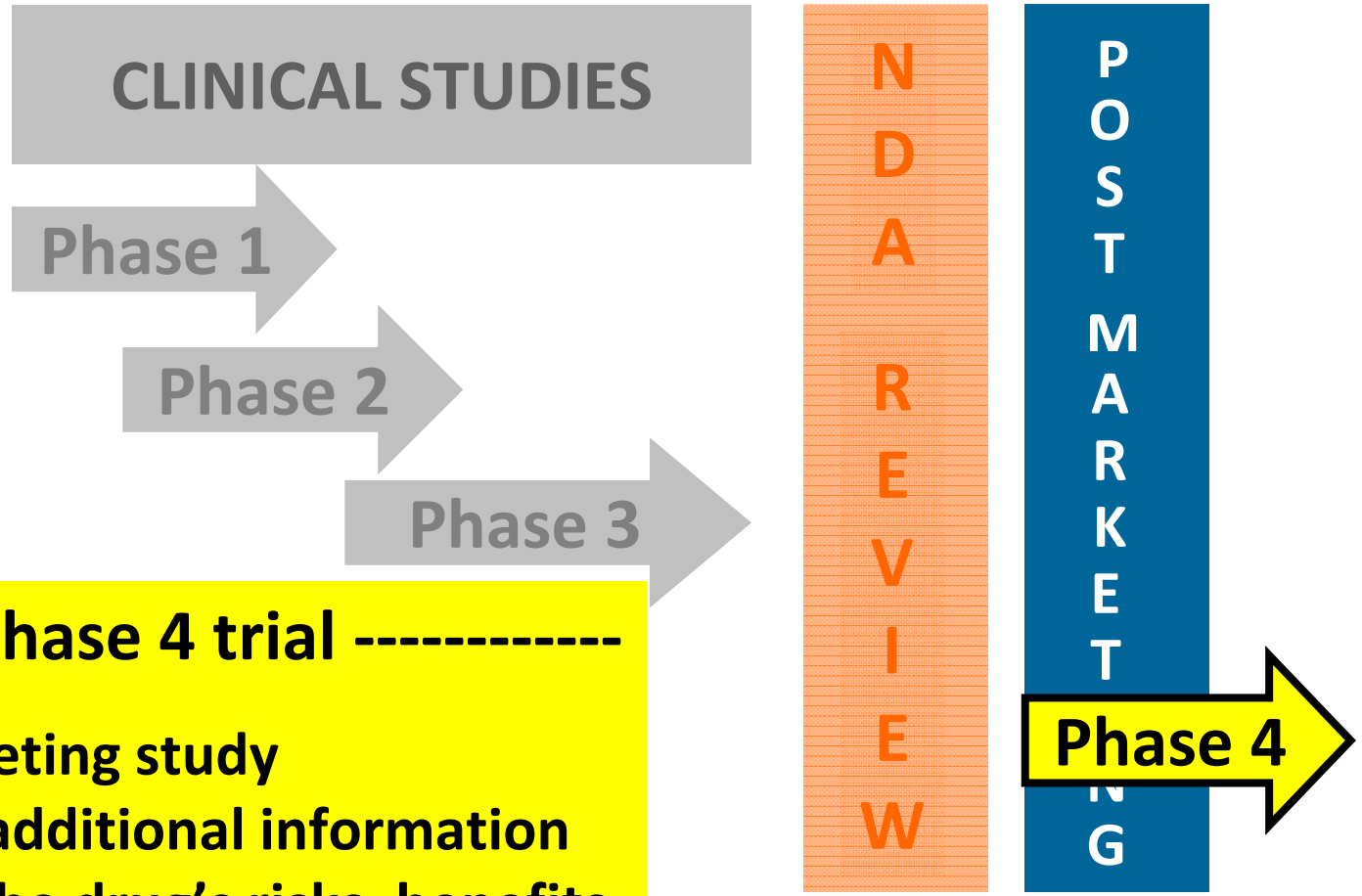
# New Drug Development Process





# New Drug Development Process






**---------- Phase 4 trial ----------**

- **post-marketing study**
- **delineate additional information including the drug's risks, benefits, and optimal use**

clinicaltrials.gov

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# New Drug Development

## www.fda.gov

## In search box, “New Drug Development and Review”

# *Thank you!*

# New Drug Development Process