# The New Drug Approval Process: New Drug Research and Development

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# Overview

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# Preclinical Testing/Investigation

- In vitro “within glass” or In vivo “within the living”
- Typical nonclinical studies include:
  - Pharmacology studies
  - Toxicity studies
  - Toxicokinetic and nonclinical pharmacokinetic studies
  - Reproduction toxicity studies
  - Genotoxicity studies
  - Assessment of carcinogenic potential
- Other nonclinical studies conducted on a case-by-case basis
  - Phototoxicity
  - Immunotoxicity
  - Juvenile animal toxicity
  - Abuse liability
- Guidance for Industry M3(R2) Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals

# "Good Laboratory Practice" (GLP) Regulations

- 21 CFR Part 58
- Describes good laboratory practices for conducting nonclinical laboratory studies that support or are intended to support applications for research or marketing permits for products regulated by the FDA
- Includes:

| | |
|---|---|
| • Personnel<br>• Facilities<br>• Equipment<br>• SOPs | • Protocols<br>• Controls<br>• Records and Reports<br>• Disqualification |

# Preclinical Data Requirements

- Preclinical data is about basic safety
- Preclinical safety testing should consider:
  - Selection of the relevant animal species;
  - Age;
  - Physiological state;
  - The manner of delivery, including dose, route of administration, and treatment regimen; and
  - Stability of the test material under the conditions of use
- In some cases, lack of full GLP compliance does not necessarily mean that the data from these studies cannot be used to support clinical trials and marketing authorizations.

# Investigational New Drug (IND) Applications

- 21 CFR Part 312
- IND= a request for FDA for authorization to administer an investigational drug to humans.
- Must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved new drug application.
- Developers must include:
  - Animal study data and toxicity (side effects that cause great harm) data
  - Manufacturing information
  - Clinical protocols (study plans) for studies to be conducted
  - Data from any prior human research
  - Information about the investigator

# IND Content and Format

- Cover Sheet (Form FDA 1571)
- Table of Contents
- Introductory Statement
- General Investigational Plan
- Investigator's Brochure
- Protocol
- Chemistry, Manufacturing and Control Information
- Pharmacology and Toxicology Information
- Previous Human Experience with the Investigational Drug

# IND Protocols and Role

- Phase I – protocol outline
- Phase II and Phase III – detailed protocol describing all aspects of the trials
- The central focus of the initial IND submission should be on the general investigational plan and the protocols for specific human studies

# FDA IND Review Team

- Typically composed of:
  - ***Project Manager:*** Coordinates the team's activities throughout the review process, and is the primary contact for the sponsor.
  - ***Medical Officer:*** Reviews all clinical study information and data before, during, and after the trial is complete.
  - ***Statistician:*** Interprets clinical trial designs and data, and works closely with the medical officer to evaluate protocols and safety and efficacy data.
  - ***Pharmacologist:*** Reviews preclinical studies.
  - ***Pharmakineticist:*** Focuses on the drug's absorption, distribution, metabolism, and excretion processes. Interprets blood-level data at different time intervals from clinical trials, as a way to assess drug dosages and administration schedules.
  - ***Chemist:*** Evaluates a drug's chemical compounds. Analyzes how a drug was made and its stability, quality control, continuity, the presence of impurities, etc.
  - ***Microbiologist:*** Reviews the data submitted, if the product is an antimicrobial product, to assess response across different classes of microbes.

# IND Review Process

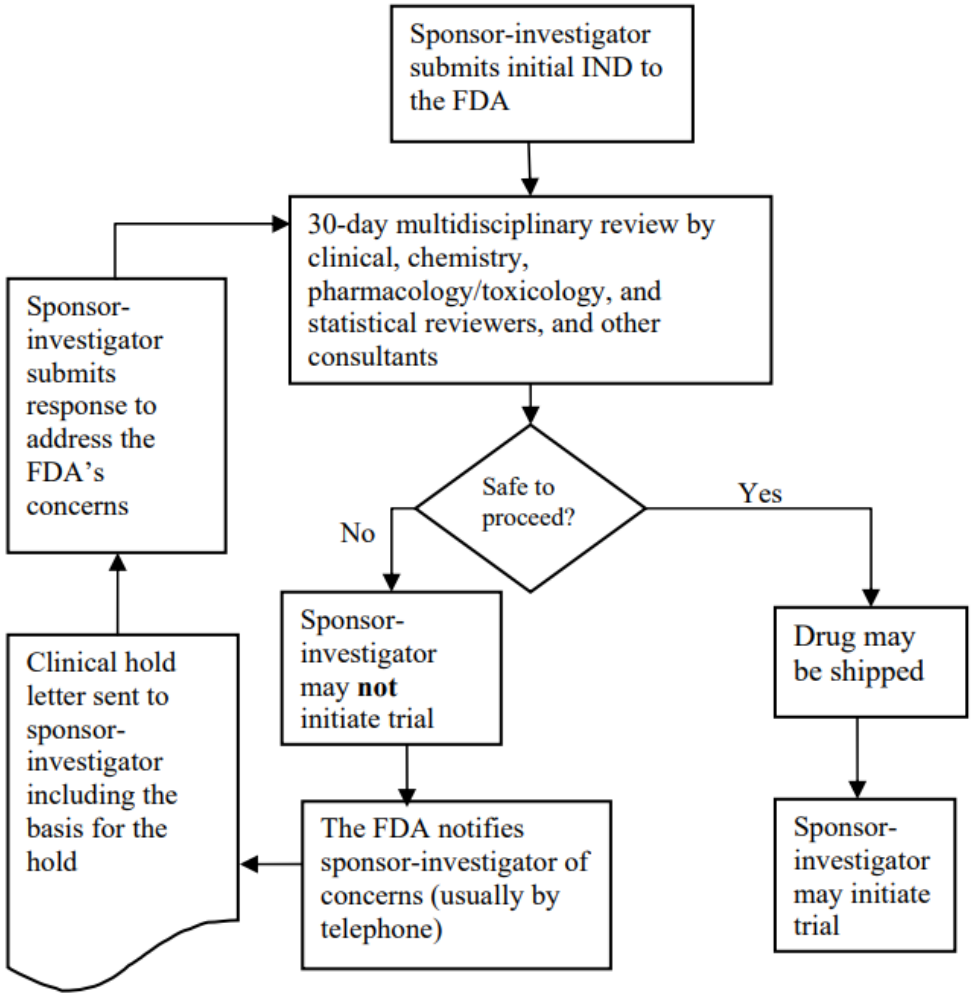
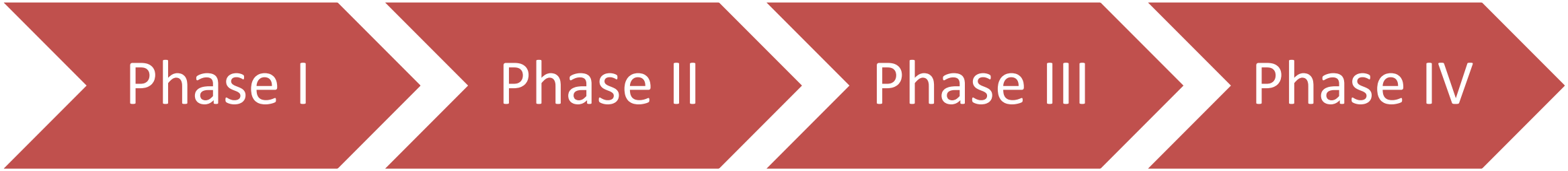



Figure from: Investigational New Drug Applications Prepared and Submitted by Sponsor-Investigators Guidance for Industry (May 2015)

# IND Approval

- The FDA review team has 30 days to review the original IND submission.
- The process protects volunteers who participate in clinical trials from unreasonable and significant risk in clinical trials. FDA responds to IND applications in one of two ways:
  - Approval to begin clinical trials
  - Clinical hold to delay or stop the investigation. FDA can place a clinical hold for specific reasons, including:
    - Participants are exposed to unreasonable or significant risk
    - Investigators are not qualified
    - Materials for the volunteer participants are misleading
    - The IND application does not include enough information about the trial's risks
- A clinical hold is rare
  - FDA may provide comments intended to improve the quality of a clinical trial.

# Clinical Trials



# Designing Clinical Trials

- Who qualifies to participate (selection criteria)?
- How many people will be part of the study?
- How long the study will last?
- Whether there will be a control group and other ways to limit research bias?
- How the drug will be given to patients and at what dosage?
- What assessments will be conducted, when, and what data will be collected?
- How the data will be reviewed and analyzed?

# Phase I

- Study Participants: 20 to 100 healthy volunteers or people with the disease/condition
- Length of Study: Several months
- Purpose: Safety and dosage
- According to FDA: Approximately 70% of drugs move to the next phase

# Phase II

- Study Participants: Up to several hundred people with the disease/condition
- Length of Study: Several months to 2 years
- Purpose: Efficacy and side effects
- According to FDA: Approximately 33% of drugs move to the next phase

# Phase III

- Study Participants: 300 to 3,000 volunteers who have the disease or condition
- Length of Study: 1 to 4 years
- Purpose: Efficacy and monitoring of adverse reactions
- According to FDA: Approximately 25-30% of drugs move to the next phase

# Phase IV

- Post-approval
- Study Participants: Several thousand volunteers who have the disease/condition
- Purpose: Safety and efficacy

# Question

- Why is diversity in clinical trials important?

# Inclusion of Demographic Subgroups in Clinical Trials

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- Sec. 907 of the Food and Drug Administration Safety and Innovation Act (FDASIA) directed FDA to investigate how well demographic subgroups (sex, age, race and ethnicity) in applications for medical products – drugs, biologics and devices, submitted to the agency for marketing approval:
  - 1) Are included in clinical trials; and
  - 2) If subgroup-specific safety and effectiveness data are available.
- Sec. 907 also required the FDA to provide Congress with an action plan detailing "recommendations for improving the completeness and quality of analyses of data on demographic subgroups in summaries of product safety and effectiveness data and in labeling; on the inclusion of such data, or the lack of availability of such data, in labeling; and on improving the public availability of such data to patients, health care professionals, and researchers" and to indicate the center(s) tasked with each recommendation. Congress directed the Agency to issue the action plan one year following the publication of the Sec. 907 report.

# FDA Guidance on Diversity in Clinical Development



- Draft guidance, “Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Subgroups in Clinical Trials”
  - Recommends that sponsors of medical products develop and submit a Race and Ethnicity Diversity Plan to the agency early in clinical development
- Contents of Plan
  - Define enrollment goals
  - Describe the planned assessment of race and ethnicity in addition to other covariates with known potential to affect the safety and effectiveness of the medical product

# FDA Action Plan Priority Areas

- Plan outlines the agency's current policies and practices, and presents 27 action items focused on three priorities:
  - 1. **Quality**: to improve the completeness and quality of demographic subgroup data;
  - 2. **Participation**: to identify barriers to subgroup enrollment in clinical trials and employ strategies to encourage greater participation;
  - 3. **Transparency**: to improve the public availability of demographic subgroup data.

# Question

- How can I meet with the FDA?

# Meetings with FDA

- Drug developers are free to ask for help from FDA at any point in the drug development process, including:
  - Pre-IND application, to review FDA guidance documents and get answers to questions that may help enhance their research
  - After Phase 2, to obtain guidance on the design of large Phase 3 studies
  - Any time during the process, to obtain an assessment of the IND application
- FDA's suggestions are not binding
  - Drug developers are not required to take FDA's suggestions.
  - If clinical trials are thoughtfully designed, reflect what developers know about a product, safeguard participants, and otherwise meet Federal standards, FDA allows flexibility in clinical trial design

# Informed Consent – 21 CFR § 50.25

- (1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
- (2) A description of any reasonably foreseeable risks or discomforts to the subject.
- (3) A description of any benefits to the subject or to others which may reasonably be expected from the research.
- (4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
- (5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the FDA may inspect the records.
- (6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
- (7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.
- (8) A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

# Informed Consent is More than a Signature

- Informed Consent Information Sheet, Draft Guidance for IRBs, Clinical Investigators, and Sponsors (July 2014)
- Informed consent involves providing a potential subject with
  - Adequate information to allow for an informed decision about participation in the clinical investigation
  - Facilitating the potential subject's comprehension of the information
  - Providing adequate opportunity for the potential subject to ask questions and to consider whether to participate
  - Obtaining the potential subject's voluntary agreement to participate
  - Continuing to provide information as the clinical investigation progresses or as the subject or situation requires

# Institutional Review Boards (IRBs)

- *Institutional Review Board (IRB)* means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. 21 CFR § 56.102
- The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects.

# 21 CFR PART 56—IRBs

- Organization and Personnel
  - Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution
- Functions and Operations
- Records and Reports
- Administrative Actions for Noncompliance

# Obligations of Sponsors

- Select qualified investigators
- Ensure proper monitoring of the investigation(s)
- Ensuring that the investigation(s) is conducted in accordance with the general investigational plan and protocols contained in the IND
- Maintain an effective IND with respect to the investigations
- Ensure that FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug

# Obligations of Investigators

- Ensure that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations
- Protect the rights, safety, and welfare of subjects under the investigator's care
- Obtain the informed consent of each human subject to whom the drug is administered
- Reports:
  - Progress
  - Safety
  - Final
  - Financial disclosure

# Role of Contract Research Organizations (CROs)

- *Contract research organization* means a person that assumes, as an independent contractor with the sponsor, one or more of the obligations of a sponsor:
  - Design of a protocol
  - Selection or monitoring of investigations
  - Evaluation of reports
  - Preparation of materials to be submitted to the FDA. 21 CFR § 312.3
- A sponsor may transfer responsibility for any or all of its obligations to a CRO

# Adverse Event Reporting (AER)

- Sponsor must notify FDA and all participating investigators (i.e., all investigators to whom the sponsor is providing drug under its INDs or under any investigator's IND) in an IND safety report of potential serious risks, from clinical trials or any other source, as soon as possible, but in no case later than 15 calendar days after the sponsor determines that the information qualifies for reporting
- In each IND safety report, the sponsor must identify all IND safety reports previously submitted to FDA concerning a similar suspected adverse reaction, and must analyze the significance of the suspected adverse reaction in light of previous, similar reports or any other relevant information
- Sponsor must notify FDA of any *unexpected fatal or life-threatening suspected adverse reaction* as soon as possible but in no case later than 7 calendar days after the sponsor's initial receipt of the information

# What Qualifies for an IND Safety Report?

- ***Serious and unexpected suspected adverse reaction*** - any suspected adverse reaction that is both serious and unexpected. The sponsor must report an adverse event as a suspected adverse reaction only if there is evidence to suggest a causal relationship between the drug and the adverse event
- ***Findings from other studies*** - epidemiological studies, pooled analysis of multiple studies, or clinical studies, that suggest a significant risk in humans exposed to the drug. Ordinarily, such a finding would result in a safety-related change in the protocol, informed consent, investigator brochure (excluding routine updates of these documents), or other aspects of the overall conduct of the clinical investigation
- ***Findings from animal or in vitro testing*** - that suggest a significant risk in humans exposed to the drug, such as reports of mutagenicity, teratogenicity, or carcinogenicity, or reports of significant organ toxicity at or near the expected human exposure. Ordinarily, any such findings would result in a safety-related change in the protocol, informed consent, investigator brochure (excluding routine updates of these documents), or other aspects of the overall conduct of the clinical investigation
- ***Increased rate of occurrence of serious suspected adverse reactions*** - clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure

# Clinical Holds

- A clinical hold is an order issued by FDA to the sponsor of an IND application to delay a proposed clinical investigation or to suspend an ongoing investigation
  - When a proposed study is placed on clinical hold, subjects may not be given the investigational drug
  - When an ongoing study is placed on clinical hold, no new subjects may be recruited to the study and given the investigational drug; patients already in the study are expected to be taken off therapy involving the investigational drug unless treatment continuation is specifically permitted by FDA in the interest of patient safety

# Grounds for imposition of clinical hold:

- The grounds for imposition of clinical hold for a proposed or ongoing Phase 1 investigation include the following:
  - Human subjects are or would be exposed to an unreasonable and significant risk of illness or injury; or
  - The clinical investigators named in the IND are not qualified by reason of their scientific training and experience to conduct the investigation described in the IND; or
  - The investigator brochure is misleading, erroneous, or materially incomplete; or
  - The IND application does not contain sufficient information needed to assess the risks to subjects of the proposed studies; or
  - The IND application is for the study of an investigational drug intended to treat a life-threatening disease or condition that affects both genders, and men or women with reproductive potential who have the disease or condition being studied are excluded from eligibility because of a risk of reproductive toxicity (i.e., affecting reproductive organs) or developmental toxicity (i.e., affecting potential offspring).
- The grounds for imposition of clinical hold for a proposed or ongoing Phase 2 or Phase 3 investigation include the following:
  - Any of the conditions described above as for Phase 1 investigations; or
  - The plan or protocol for the investigation is clearly deficient in design to meet its stated objectives.

# Use of Foreign Studies

- FDA will accept as support for an IND or application for marketing approval, a well-designed and well-conducted foreign clinical study not conducted under an IND, subject to certain conditions at 21 CFR § 312.120
- Sponsors wishing to use foreign clinical studies must submit additional data from the foreign study to the FDA

# Exemptions from the IND Requirement

- Three most commonly occurring scenarios when clinical investigations may be exempted from the IND application requirements refer to certain limited situations of clinical investigations with:
  - Approved marketed drugs
  - Bioavailability or bioequivalence studies
  - Clinical investigations involving radioactive drugs considered safe for certain research uses
- IND almost always required but see Investigational New Drug Applications (INDs) — Determining Whether Human Research Studies Can Be Conducted Without an IND, Guidance (September 2013)

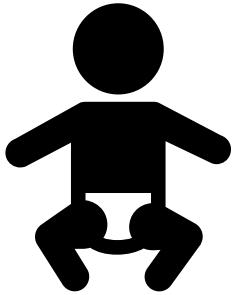
# Notice of Initiation of Disqualification Proceedings and Opportunity to Explain (NIDPOE)

- If FDA has information indicating that an investigator (including a sponsor-investigator) has *repeatedly or deliberately* failed to comply with the requirements of an IND, IRB, or Protection of Human Subjects, or has repeatedly or deliberately submitted to FDA or to the sponsor false information in any required report, the FDA will give the investigator an opportunity to explain
- If an explanation is offered and accepted by the FDA, the disqualification proceeding ends
- If an explanation is offered but not accepted, the investigator will be given an opportunity for a regulatory hearing

# Disqualification of Investigators/Debarment

- A disqualified clinical investigator is not eligible to receive investigational drugs, biologics, or devices, and is not eligible to conduct any clinical investigation that supports an application for a research or marketing permit for products regulated by FDA
- FDA publishes a Debarment list (“Investigator blacklist”)

# Pediatrics



- Pediatric Research Equity Act of 2003 (PREA)
  - Requires pediatric studies for certain drug and biological products
- Prior to this, drug developers typically did not conduct pediatric studies
- Waivers available

# Pediatric Exclusivity

- Encourage sponsors or holders of approved applications to voluntarily perform the pediatric studies described in a Written Request issued by FDA, in order to qualify for an additional 6 months of marketing exclusivity
- Section 505(A) of The Food and Drug Administration Modernization Act of 1997 enabled FDA to:
  - Issue Written Requests for pediatric studies prior to approval of a new drug application if FDA has determined that information related to the use of the drugs in the pediatric population may produce health benefits
  - Issue Written Requests to holders of approved applications for pediatric studies if it has determined that information related to the use of the drug in the pediatric population may produce health benefits

# Expanded Access

- Expanded Access= Using Investigational Drugs for Treatment Use
- Draft Guidance published November 2022 - Expanded Access to Investigational Drugs for Treatment Use, Questions and Answers
- Criteria:
  - The patient or patients to be treated have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;
  - The potential patient benefit justifies the potential risks of the treatment use and those potential risks are not unreasonable in the context of the disease or condition to be treated; and
  - Providing the investigational drug for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use

# Types of Expanded Access

- Individual patients, including for emergency use
  - The physician must determine that the probable risk to the person from the investigational drug is not greater than the probable risk from the disease or condition; and the FDA must determine that the patient cannot obtain the drug under another IND or protocol
- Intermediate-size patient populations
  - There is enough evidence that the drug is safe at the dose and duration proposed for expanded access use to justify a clinical trial of the drug in the approximate number of patients expected to receive the drug under expanded access; and
  - There is at least preliminary clinical evidence of effectiveness of the drug, or of a plausible pharmacologic effect of the drug to make expanded access use a reasonable therapeutic option in the anticipated patient population
- Treatment IND or treatment protocol
  - The sponsor is actively pursuing marketing approval of the drug for the expanded access use with due diligence

# Right to Try

- An eligible patient is a patient who has:
  - Been diagnosed with a life-threatening disease or condition
  - Exhausted approved treatment options and is unable to participate in a clinical trial involving the eligible investigational drug (this must be certified by a physician who is in good standing with their licensing organization or board and who will not be compensated directly by the manufacturer for certifying)
  - And has provided, or their legally authorized representative has provided, written informed consent regarding the eligible investigational drug to the treating physician
- An eligible investigational drug is an investigational drug:
  - For which a Phase 1 clinical trial has been completed
  - That has not been approved or licensed by the FDA for any use
  - For which an application has been filed with the FDA or is under investigation in a clinical trial that is intended to form the primary basis of a claim of effectiveness in support of FDA approval and is the subject of an active investigational new drug application submitted to the FDA
  - Whose active development or production is ongoing, and that has not been discontinued by the manufacturer or placed on clinical hold by the FDA

# Orphan Drugs

- The Orphan Drug Act (ODA) provides for granting special status to a drug or biological product ("drug") to treat a rare disease or condition upon request of a sponsor. This status is referred to as orphan designation (or sometimes "orphan status")
- Orphan Drug Designation
  - Disease/condition affects <200,000 persons in the U.S.
- Granting an orphan designation request does not alter the standard regulatory requirements and process for obtaining marketing approval - Safety and effectiveness of a drug must be established through adequate and well-controlled studies.

# Orphan Drug Exclusivity

- 7 years of marketing exclusivity
- Also, a marketing application for a prescription drug product that has received orphan designation is not subject to a prescription drug user fee unless the application includes an indication for other than the rare disease or condition for which the drug was designated
- Current topic note:
  - FDA granted orphan drug designation to remdesivir (drug for COVID-19) in March 2020, before the number of cases in the US surpassed 200,000.
  - Sponsor then requested FDA to rescind this status

# Clinical Trial Registration and Reporting

- Registration on **ClinicalTrials.gov** is required for studies that meet the definition of an "applicable clinical trial" (ACT) and either were initiated after September 27, 2007, or initiated on or before that date and were still ongoing as of December 26, 2007.
- ACTs, as defined in section 402(j) of the PHS Act, include the following:
  - Controlled clinical investigations (other than phase 1 investigations) of any U.S. Food and Drug Administration (FDA)-regulated drug or biological product for any disease or condition
  - Certain studies of FDA-regulated medical devices, excluding small clinical trials to determine feasibility and certain clinical trials to test prototype devices, but including FDA-required pediatric postmarket surveillances of a device product
- ACTs generally include interventional studies (with one or more arms) of FDA-regulated drug, biological, or device products that meet one of the following conditions:
  - The trial has one or more sites in the United States
  - The trial is conducted under an FDA investigational new drug application or investigational device exemption
  - The trial involves a drug, biological, or device product that is manufactured in the United States or its territories and is exported for research

# What is available/reported to ClinicalTrials.gov?



- Participant Flow. A tabular summary of the progress of participants through each stage of a study, by study arm or comparison group. It includes the numbers of participants who started, completed, and dropped out of each period of the study based on the sequence in which interventions were assigned.
- Baseline Characteristics. including age, sex/gender, race, ethnicity (if collected under the protocol), and any other measure(s) that were assessed at baseline and are used in the analysis of the primary outcome measure(s)
- Outcome Measures and Statistical Analyses.
  - A brief description of each arm or comparison group used for submitting an outcome measure for the clinical trial
  - Result(s) of scientifically appropriate tests of the statistical significance of the primary and secondary outcome measures, if any.
- Adverse Events. A tabular summary of all anticipated and unanticipated Serious adverse event and a tabular summary of anticipated and unanticipated other adverse events exceeding a specific frequency threshold. For each serious or other adverse event, the summary includes the adverse event term, affected organ system, number of participants at risk, and number of participants affected, by study arm or comparison group.

# Who is responsible for Clinical Trial Registration and Reporting?

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- Responsible party means, with respect to a clinical trial, the **sponsor of the clinical trial**, as defined in 21 CFR 50.3; or the **principal investigator** of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee, so long as the principal investigator is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements under this part for the submission of clinical trial information. For a pediatric postmarket surveillance of a device product that is not a clinical trial, the responsible party is the entity who FDA orders to conduct the pediatric postmarket surveillance of the device product.

42 CFR § 11.10(a)

# When and Why must registration and reports be made to ClinicalTrials.gov?



- 21 calendar days after the first human subject is enrolled
- Failure to Register and Submit information is a prohibited act under one or more provisions of section 301(jj) of the Federal Food, Drug, and Cosmetic Act
  - Civil or Criminal Penalties
  - Grants
- 42 CFR PART 11 - CLINICAL TRIALS REGISTRATION AND RESULTS INFORMATION SUBMISSION

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# ClinicalTrials.gov

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ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

**Explore 356,869 research studies in all 50 states and in 218 countries.**

**See listed clinical studies related to the coronavirus disease (COVID-19)**

ClinicalTrials.gov is a resource provided by the U.S. National Library of Medicine.

**IMPORTANT**: Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

Before participating in a study, talk to your health care provider and learn about the risks and potential benefits.

## Find a study (all fields optional)

**Status**

- ○ Recruiting and not yet recruiting studies
- ● All studies

**Condition or disease** (For example: breast cancer)

**Other terms** (For example: NCT number, drug name, investigator name)

**Country**

Search | Advanced Search

Help | Studies by Topic | Studies on Map | Glossary

# Medical Publisher Policies

- FDA generally prohibits manufacturers of new drugs from distributing products in interstate commerce for any intended use that FDA has not approved as safe and effective
- Scientific and medical information that concerns the safety or effectiveness of an approved drug or approved or cleared medical device for an unapproved new use that is not included in the product's approved labeling or statement of intended uses (including unapproved new uses of approved drugs and approved or cleared devices) is often published in journal articles or reference publications.
- A scientific or medical journal article that is distributed should:
  - Be published by an organization that has an editorial board that uses experts who have demonstrated expertise in the subject of the article under review by the organization and who are independent of the organization to review and objectively select, reject, or provide comments about proposed articles; and that has a publicly stated policy, to which the organization adheres, of full disclosure of any conflict of interest or biases for all authors, contributors, or editors associated with the journal or organization;
  - Be peer-reviewed and published in accordance with the peer-review procedures of the organization; and
  - Not be in the form of a special supplement or publication that has been funded in whole or in part by one or more of the manufacturers of the product that is the subject of the article

# 21st Century Cures Act

- Patient-focused drug development
- Real-World Evidence is the clinical evidence regarding the usage and potential benefits, or risks of a medical product derived from analysis of Real-World Data:
  - Electronic health records (EHRs)
  - Claims and billing activities
  - Product and disease registries
  - Patient-generated data including in home-use settings
  - Data gathered from other sources that can inform on health status, such as mobile devices

# Novel clinical trial designs

- FDA encourages sponsors to seek early interaction with FDA regarding details of their complex innovative clinical trial designs
- Examples:
  - Simulations
  - Sequential Multiple Assignment Randomized Trials (SMARTs) are designed to inform the development of adaptive interventions.
    - Patients move along multiple stages and are randomly assigned to one of several treatment options at each stage

# Qualification of drug development tools

- Drug Development Tools (DDTs) are methods, materials, or measures that have the potential to facilitate drug development
  - Examples of DDTs may include, but are not limited to:
    - A biomarker used for clinical trial enrichment
    - A clinical outcome assessment (COA) used to evaluate clinical benefit
    - An animal model used for efficacy testing of medical countermeasures
- Qualification is a conclusion that within the stated context of use, the DDT can be relied upon to have a specific interpretation and application in drug development and regulatory review
- Once qualified, DDTs will be publicly available to be used in any drug development program for the qualified context of use

# Questions

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