Navigating FDA: Drug Development Requirements

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NIA Healthy Aging Start-Up Bootcamp to Foster Diversity & Accelerate Innovation

OFFICE OF EXTRAMURAL RESEARCH | OFFICE OF THE DIRECTOR | NATIONAL INSTITUTES OF HEALTH

Welcome

Michael W. Washabaugh, Ph.D.
Complex Systems Biologist

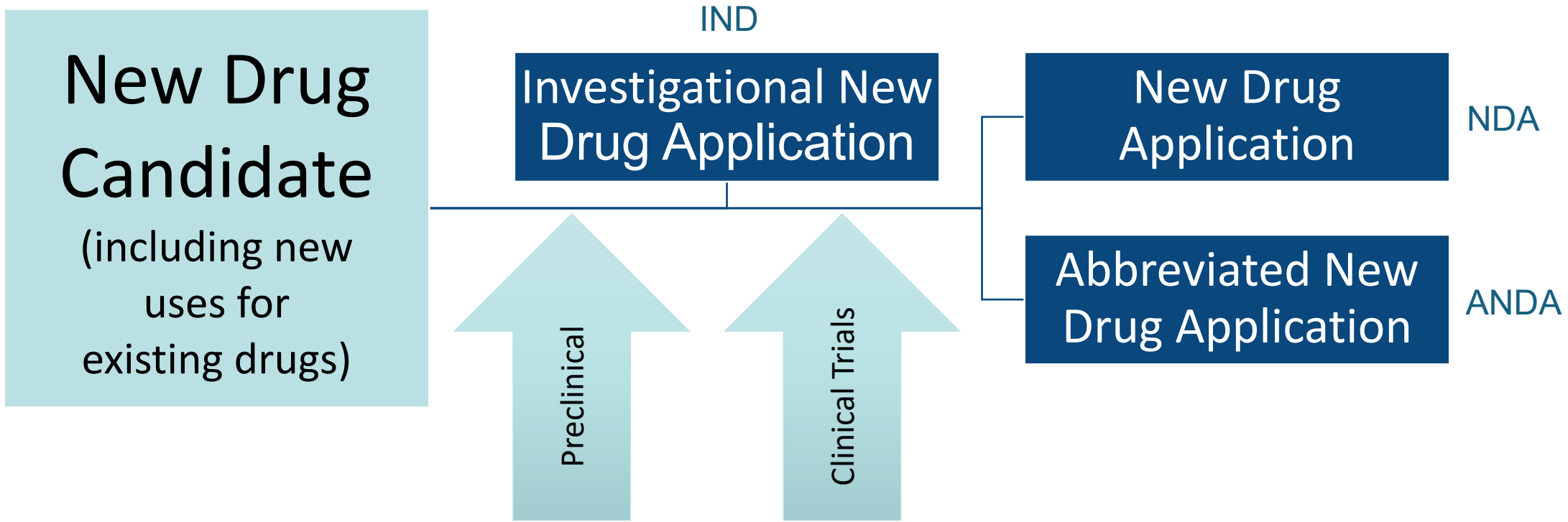
SEED Presenter from MITRE Health FFRDC

- Now
  - MITRE (https://www.mitre.org/about/corporate-overview)
  - Health FFRDC
  - Supports NIH OER, program officers and funded innovators as a Subject Matter Expert and provides an industrial perspective
- Before
  - 30+ years of experience developing drugs, vaccines, therapeutic antibodies, cellular and viral products in academia, large pharma and small biotech
  - Translation of product candidates from discovery into early-stage development to regulatory approval, launch and life-cycle management
  - Numerous approved products in several therapeutic areas

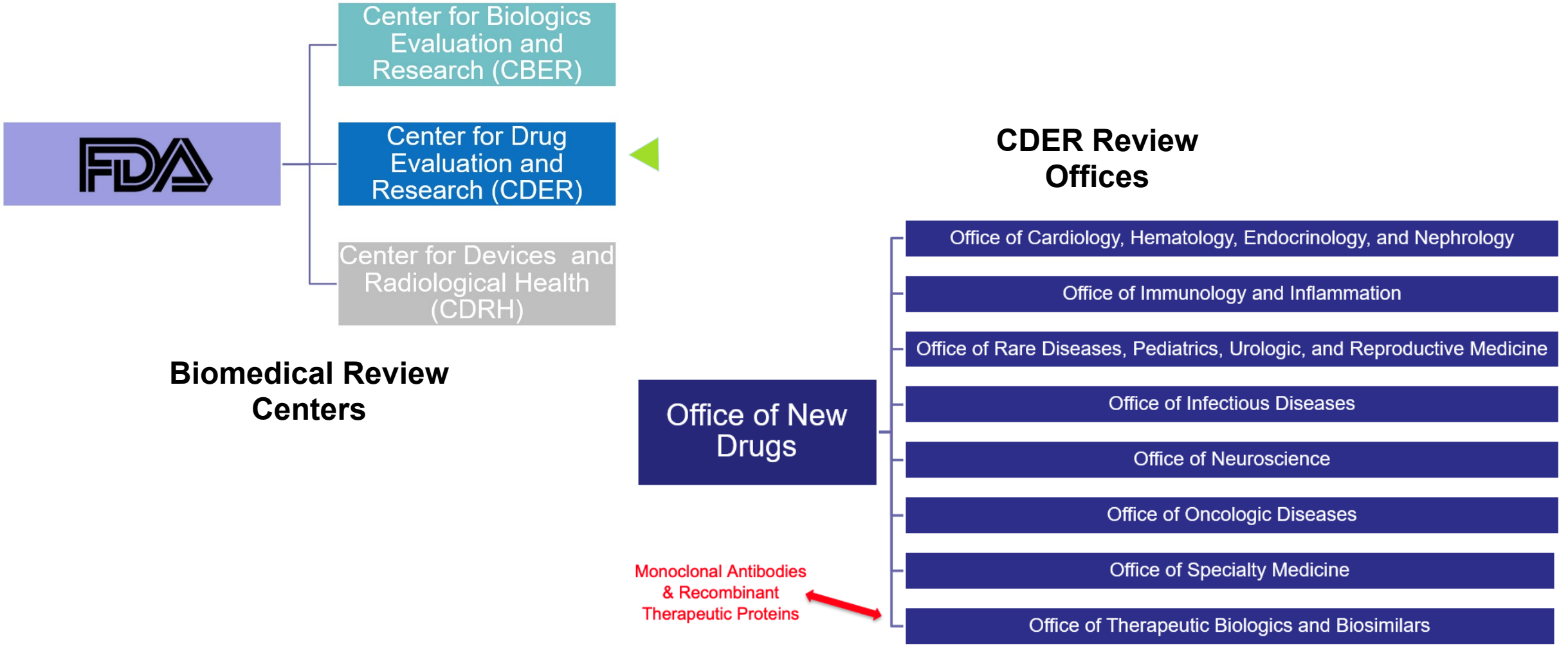
Overview

- Drug Development
  - A *small-molecule drug* is an organic compound that affects a biological process with a relatively low molecular weight, below 900 Da
  - Chemically defined, so less testing burden and characterization than biologics
- FDA
  - U.S. health agency that regulates the country's foods and drugs, among other products
  - Focus on CDER, which regulates most prescription, generic and over-the-counter drugs
  - Reviews applications, manages cGMP regulations, determines which medications require a medical prescription, monitors advertising of approved medications, and collects & analyzes safety data about marketed pharmaceuticals
- High-level understanding of how to research and develop a regulatory plan for your product candidate
  - What information can I find on my own and how do I use that information to guide my research?
  - When and how do I meet with FDA?

Developing a New Drug



FDA



https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cder-offices-and-divisions

Learning about Regulations

- See Appendix
- Legal/formal information FDA.gov
  - Approval databases
  - Learn websites
- Practical information about your drug
  - Regulatory consultant [ideally with experience in your therapeutic area(s)]
  - Other online resources
    - Manufacturer websites
    - CRO/CMO websites (white papers & templates)
    - University/Clinical websites (webinars, templates & “how to” guides)
    - NIH websites (NCATS, NCI, NHLBI, NIAID, NIDCR …)
    - Videos, blogs, podcasts & patient advocacy organizations

Not quite ready for a meeting?

CBER Office of Communication, Outreach & Development

- Industry.Biologics@fda.hhs.gov
  (800) 835-4709 or (301) 827-1800

CDER Small Business & Industry Assistance

- CDERSmallBusiness@fda.hhs.gov
  (866) 405-5367 or (301) 796-6707

CDRH Division of Industry & Consumer Education

- DICE@fda.hhs.gov
  (800) 638-2041 or (301) 796-7100

When to meet with FDA

- See Appendix (Pre-IND and IND meetings)
- Before Human Studies – CDER Consultation Meeting
  - Informal, non-binding regulatory consultation
  - Typically, early in development for very novel products
  - Not all CDER Office/Divisions/Branches participate
- You have a minimum of three critical questions
- You (or a knowledgeable regulatory professional) can't find the information you need to move your development work forward in the public domain
- Your work will stop without official guidance from FDA
- Three types of meetings:

  A – Urgent (clinical program is on hold)

  B – Important (planning of a clinical program is impacted)

  C – Anything not A or B

https://www.fda.gov/media/109951/download

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https://twitter.com/nihseed

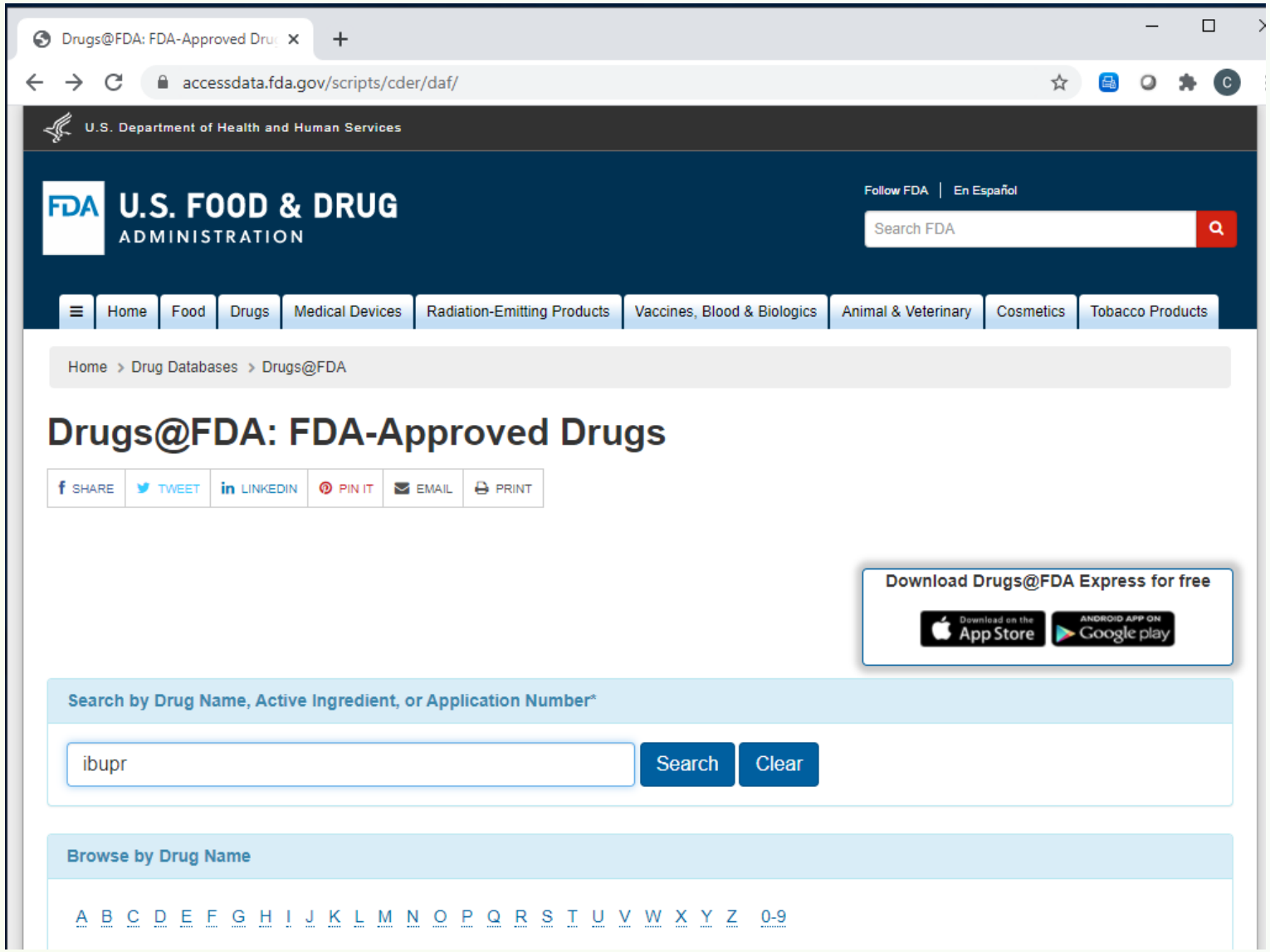
NIH SEED
https://www.linkedin.com/company/nihseed

Sign up for NIH and SEED updates:
https://seed.nih.gov/subscribe

The NIH Guide for Grants and Contracts:
http://grants.nih.gov/grants/guide/listserv.htm

Appendix

FDA.gov Resources (3.1)



CDER

FDA.gov Resources (3.2)

Drugs@FDA: FDA-Approved Drugs

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ADVIL ALLERGY SINUS
ADVIL COLD AND SINUS

CDER

FDA.gov Resources (3.3)

Drugs@FDA: FDA-Approved Drugs

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New Drug Application (NDA): 018989
Company: GLAXOSMITHKLINE

EMAIL

Products on NDA 018989

CSV | Excel | Print

Drug Name	Active Ingredients	Strength	Dosage Form/Route	Marketing Status	TE Code	RLD	RS
ADVIL	IBUPROFEN	200MG	TABLET;ORAL	Over-the-counter	None	Yes	Yes

Showing 1 to 1 of 1 entries

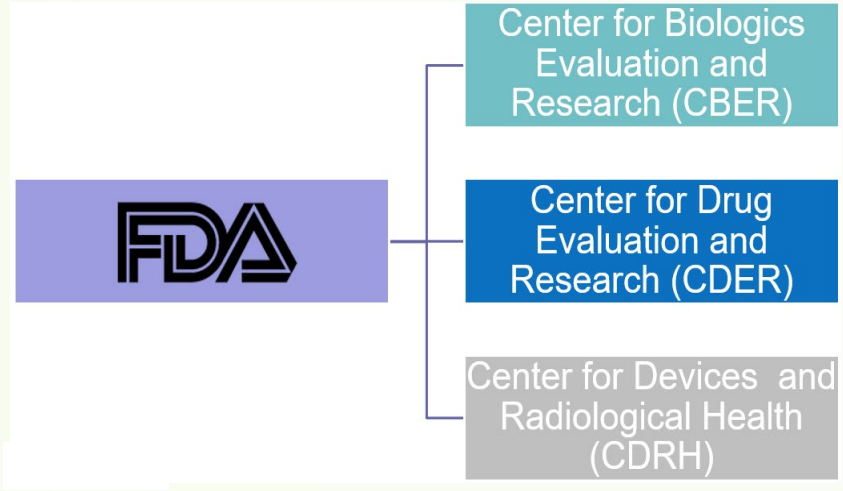
Approval Date(s) and History, Letters, Labels, Reviews for NDA 018989

Labels for NDA 018989

Other OTC Drugs with the Same Active Ingredient, Strength and Dosage Form/Route

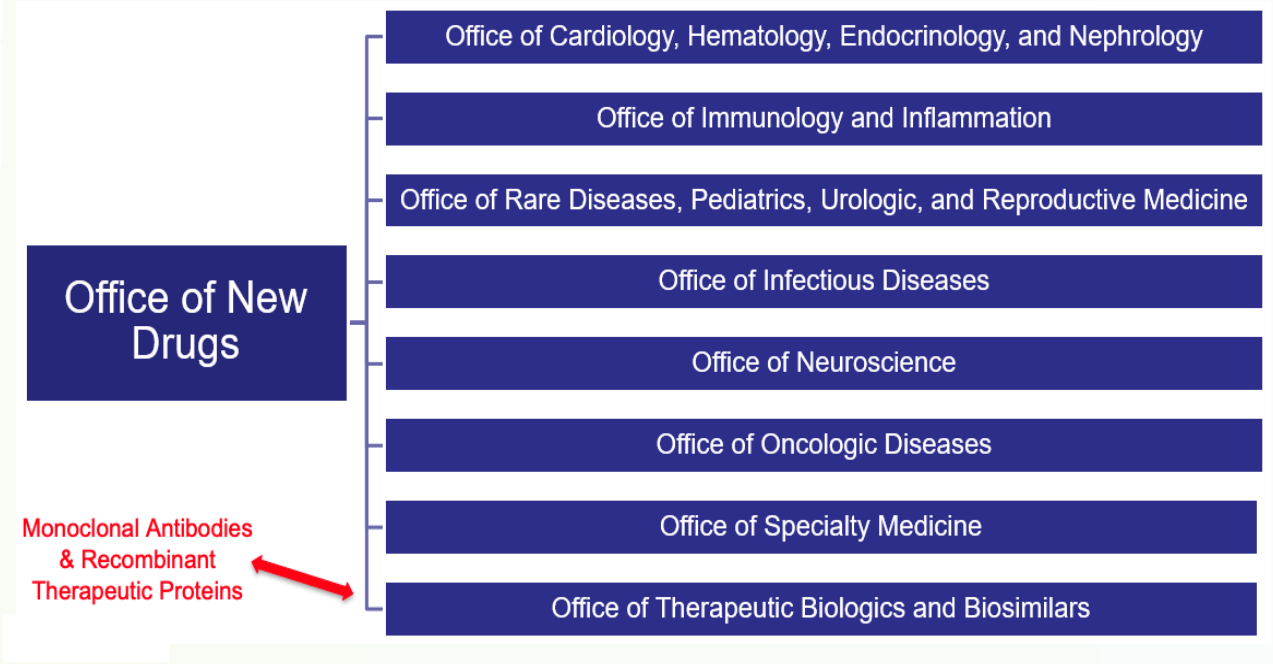
CDER

FDA.gov Resources (4)



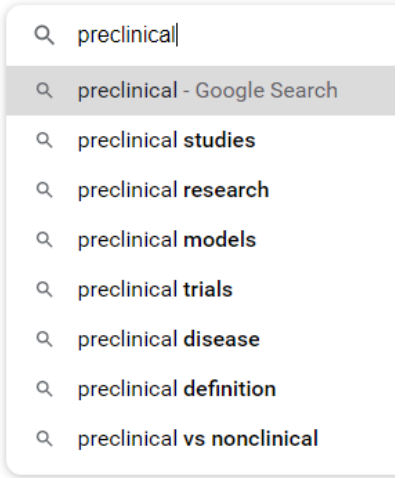
Biomedical Review Centers

CDER Review Offices



https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cder-offices-and-divisions

Internet Searches



www.fda.gov › patients › drug-development-process

Step 2: Preclinical Research | FDA

Jan 4, 2018 — Usually, **preclinical** studies are not very large. However, these studies must provide detailed information on dosing and toxicity levels. After ...

en.wikipedia.org › wiki › Preclinical_development

Preclinical development - Wikipedia

In drug development, **preclinical** development, also named **preclinical** studies and nonclinical studies, is a stage of research that begins before clinical trials (testing in humans) can begin, and during which important feasibility, iterative testing and drug safety data are collected, typically in laboratory animals.

Types of preclinical ... · Animal testing · Choice of species

www.profil.com › knowledge-center › trial-stages

The phases of preclinical and clinical trials

Preclinical studies. Deciding whether a drug is ready for clinical trials (the so-called move from bench to bedside) involves extensive **preclinical** studies that yield ...

www.covance.com › services › preclinical

Preclinical CRO, Studies and Testing | Covance Nonclinical

Preclinical. Plan your next **preclinical** study or partner with us for an IND/CTA-enabling package to get you from research to clinical trials faster. Save ...

www.medicinenet.com › script › main › art

Definition of Preclinical study - MedicineNet

Preclinical study: A study to test a drug, a procedure, or another medical treatment in animals. The aim of a **preclinical** study is to collect data in support of the safety of the new treatment. **Preclinical** studies are required before clinical trials in humans can be started.

www.merriam-webster.com › dictionary › preclinical

Preclinical | Definition of Preclinical by Merriam-Webster

Preclinical definition is - of, relating to, or concerned with the period preceding clinical manifestations. How to use **preclinical** in a sentence.

Multicenter preclinical studies as an innovative method to ...

Mar 27, 2019 — One potential explanation for this finding is that **guidelines** and standards for multicenter **studies** are just emerging, and there has yet to be any ...

by VT Hunniford · 2019 · Cited by 1 · Related articles

www.x-mol.com › paperRedirect

Improving Translation from Preclinical Studies to Clinical ...

Background: Several cellular and molecular targets and mechanisms have been investigated in **preclinical studies** of acute kidney injury (AKI), but translation in ...

by M Fiorentino · 2018 · Cited by 9 · Related articles

www.cellandgene.com › doc › best-practices-in-preclini...

Best Practices In Preclinical Development Of Cell Therapy ...

Dec 19, 2019 — **Preclinical studies** must be customized to support the feasibility of the ... Drawing from current regulatory **guidance** documents and industry ...

by N Manley · Related articles

www.who.int › biologicals › publications › clinical_gui... PDF

annex 1 who guidelines on clinical evaluation of vaccines

Preclinical and laboratory **research** data include details of the development and production of a vaccine together with reports of control testing, which should be ...

www.researchgate.net › publication › 319492003_The_E...

(PDF) The Early Preclinical Development Program for Locally ...

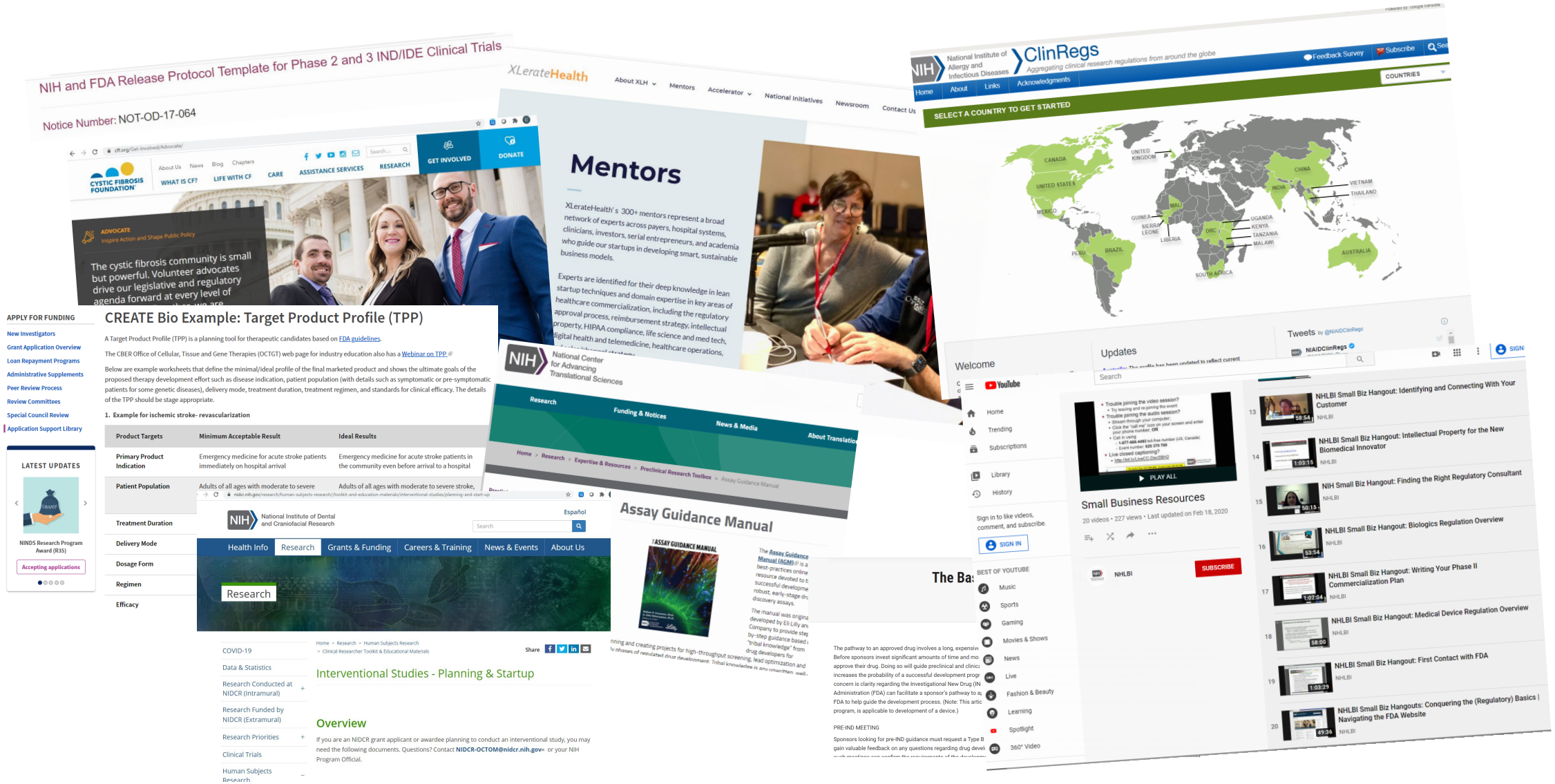
PDF | Background: Although regulatory **guidance** defines which **preclinical** data are required in ... Find, read and cite all the **research** you need on ResearchGate.

www.amazon.com › Guidelines-Preclinical-Evaluation-...

Guidelines for Preclinical Evaluation and Clinical Trials in ...

This book provides comprehensive **guidelines** for the design, implementation, and interpretation of **preclinical studies** and clinical trials of agents undergoing ...

Internet Searches



Chemistry, Manufacturing and Controls (CMC)

FDA Guidance “CGMP for Phase 1 Investigational Drugs”

TABLE OF CONTENTS

Describes FDA expectations for:

- People (training),
- Records (for everything and everyone involved in the manufacture of the drug),
- Manufacturing processes and controls (in process, post-manufacture, stability, and retention),
- Facilities and equipment (specifications and maintenance),
- Clinical material (packaging, labeling, and distribution).

Scale up of manufacturing involves considering all these components – as well as optimizing your processes by minimizing steps, duplicating supply chain options, evaluating yields, cleaning of manufacturing facilities during and between batches and products,

https://www.fda.gov/media/70975/download

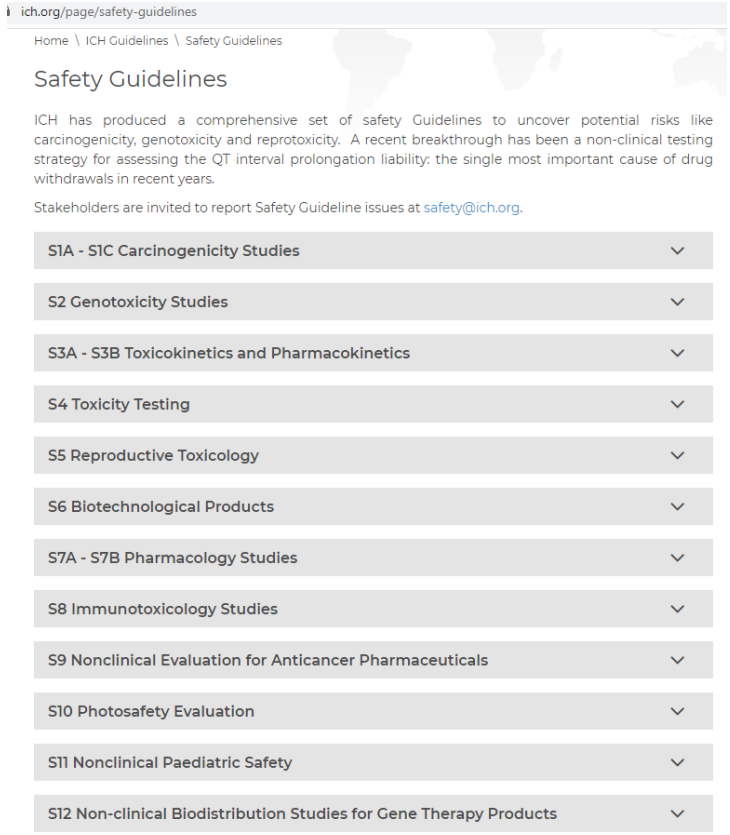
CMC

Research plan options:

- Development of specific, sensitive, and accurate assays to assess purity, potency, identity, and strength of interim and final materials
- Optimization of manufacturing processes to maximize yield, maintain sterility, define acceptance/rejection criterion (raw materials through final finished product), storage and shipping conditions for batch processes
- Evaluation of storage conditions – sensitivity to light, humidity, temperature, mechanical agitation
- Development/characterization of Working and Master cell banks

Preclinical

"Proof of concept" that your drug (i) might work and (ii) is not likely to cause harm



ICH Guidelines are based upon best practices for drug development world-wide within the pharmaceutical industry
4 categories – Quality, **Safety**, Efficacy, Multidisciplinary

Need to assess:

- Toxicity (e.g., genotoxicity, reproductive toxicity, carcinogenicity)
- Selection of animal models and their applicability to the disease/indication and population or interest
  - Including sex (as a biological variable)
- Maximum tolerated and minimum effective doses
- Route of administration and dosing regimen
- Immunogenicity/ tolerance

Preclinical

Research plan options

- Development or validation of small and larger animal models appropriate for your therapy
- Absorption, distribution, metabolism, elimination studies
- Evaluation of formulation and route of administration
- Dosing range studies (Minimum Effective Dose, No Adverse Event Limit, Maximum Tolerated Dose)
- Single and repeat dose studies (14-day, 28-day, 3-month (more?))

Pre-IND Meetings

"Type B" meetings

- meetings requested to discuss a planned developmental step with FDA (before an IND, EUA, or marketing submission, discuss REMS elements, "breakthrough" program meetings, "End of Phase" meetings
- Formats – ~~face to face~~, virtual, written response only
- Timelines
  - 14 days for FDA to accept the request
  - 60 days to conduct the meeting
  - Sponsor MUST submit briefing packet NLT 30 (50) days before the scheduled meeting date

https://www.fda.gov/media/109951/download

IND Meetings

- Generally “Type A” meetings
  - meetings requested to discuss stalled clinical plan
    - Confirm meeting type with review division before submitting request
  - Formats – ~~face to face~~, virtual, written response only
  - Timelines
    - 14 days for FDA to accept the request
    - 30 days to conduct the meeting
    - Sponsor must submit briefing packet WITH the meeting request