

Navigating FDA: Drug Development Requirements

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

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Welcome



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

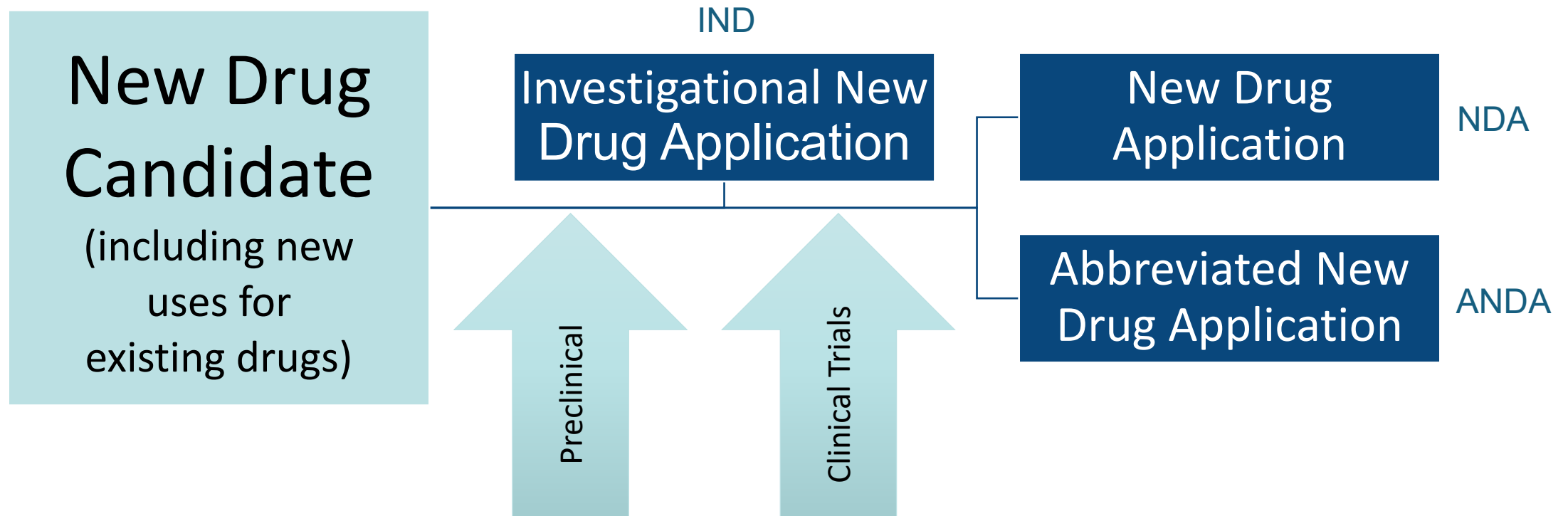
SEED Presenter from MITRE Health FFRDC

- 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

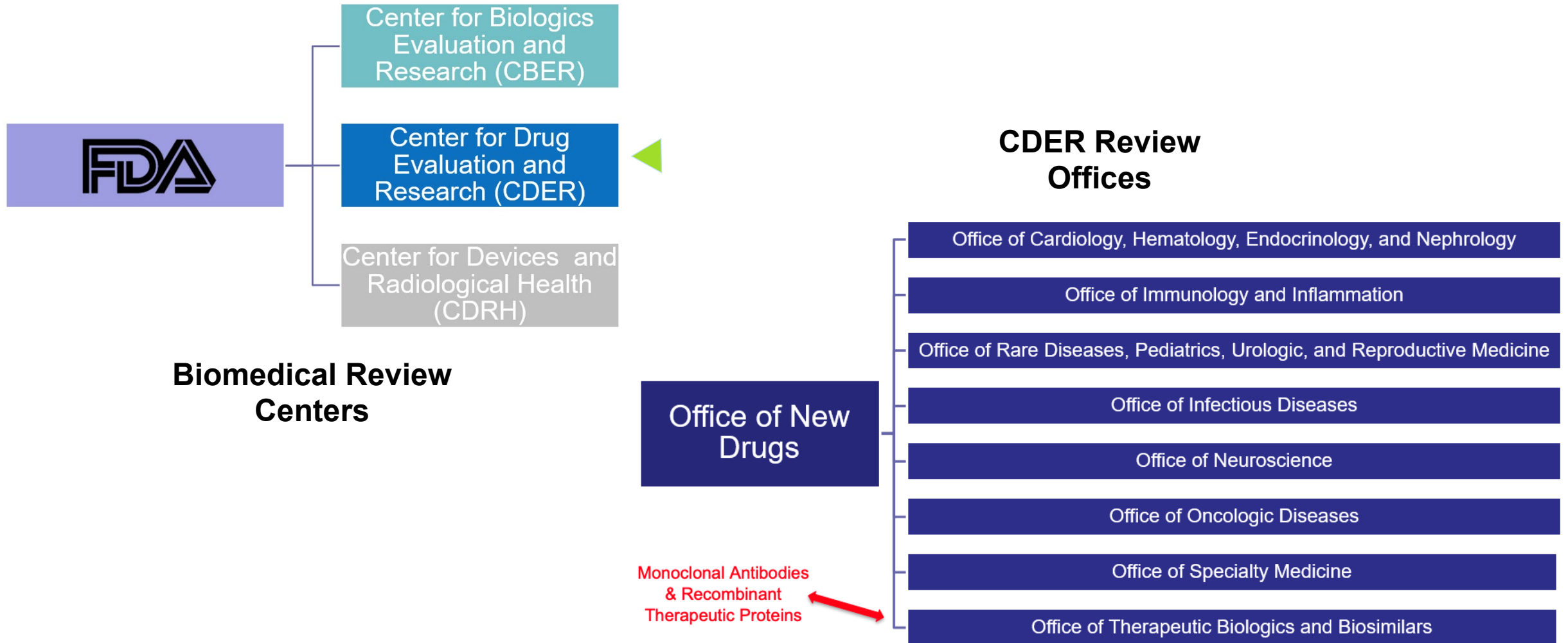
Overview

- 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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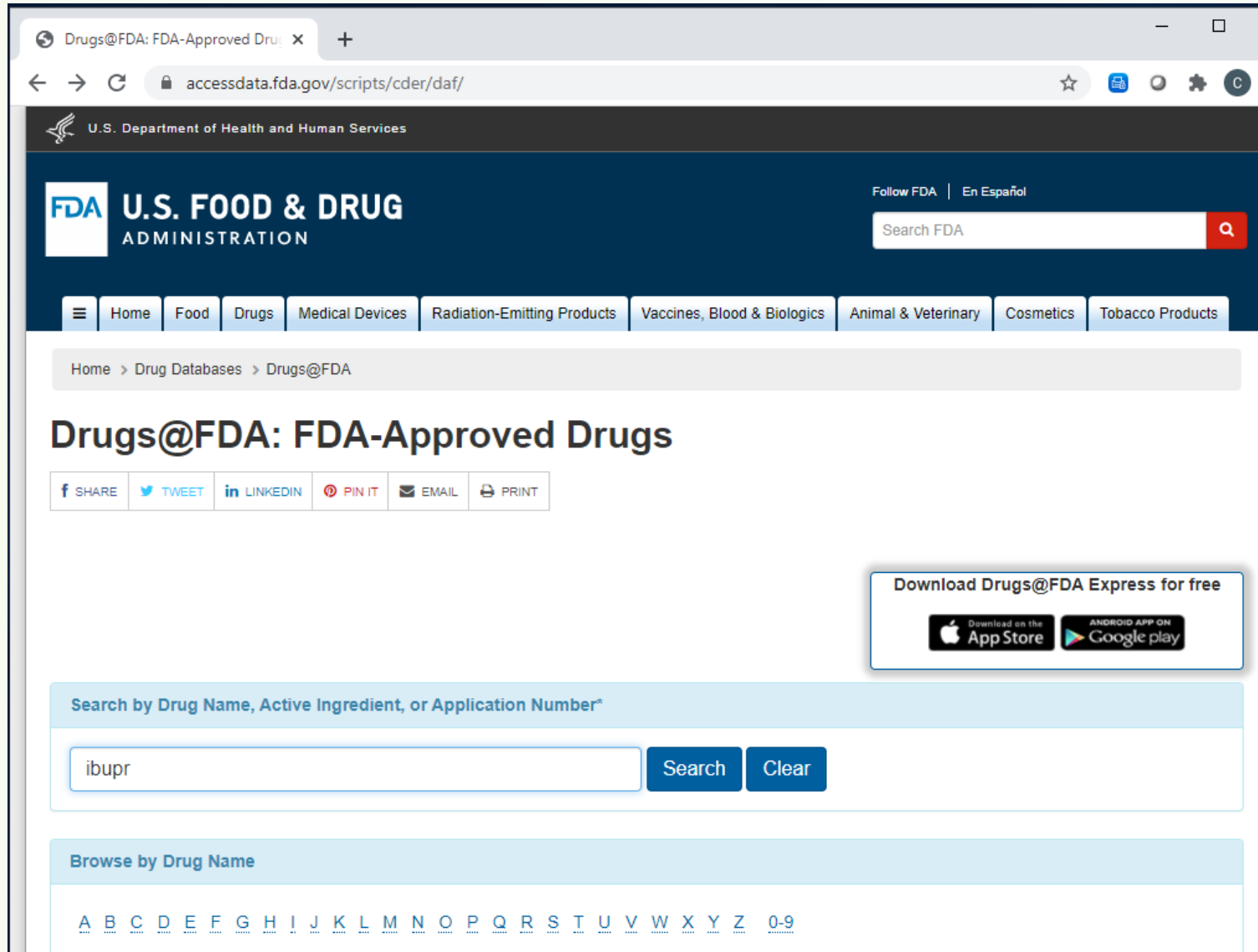
<https://seed.nih.gov/subscribe>

The NIH Guide for Grants and Contracts:

<http://grants.nih.gov/grants/guide/listserv.htm>

Appendix

FDA.gov Resources (3.1)



The screenshot shows the Drugs@FDA website interface. The browser address bar displays `accessdata.fda.gov/scripts/cder/daf/`. The page header includes the U.S. Department of Health and Human Services logo and the U.S. Food & Drug Administration logo. A search bar is located in the top right corner. Below the header, a navigation menu lists various product categories: Home, Food, Drugs, Medical Devices, Radiation-Emitting Products, Vaccines, Blood & Biologics, Animal & Veterinary, Cosmetics, and Tobacco Products. The main content area is titled "Drugs@FDA: FDA-Approved Drugs" and includes social media sharing options (Facebook, Twitter, LinkedIn, Pinterest, Email, Print). A prominent banner encourages downloading the "Drugs@FDA Express" app for free, with links to the App Store and Google Play. Below this, a search section titled "Search by Drug Name, Active Ingredient, or Application Number*" features a text input field containing "ibupr", a "Search" button, and a "Clear" button. At the bottom, a "Browse by Drug Name" section displays a horizontal list of letters from A to Z, followed by a "0-9" link.

CDER

FDA.gov Resources (3.2)

Drugs@FDA: FDA-Approved Drugs

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Search Results for "ibupr"

[Products listed on this page may not be equivalent to one another.](#)

« ‹ 1 2 › »

ACHES-N-PAIN

ADVIL

ADVIL ALLERGY AND CONGESTION RELIEF

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

CSVExcelPrint

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

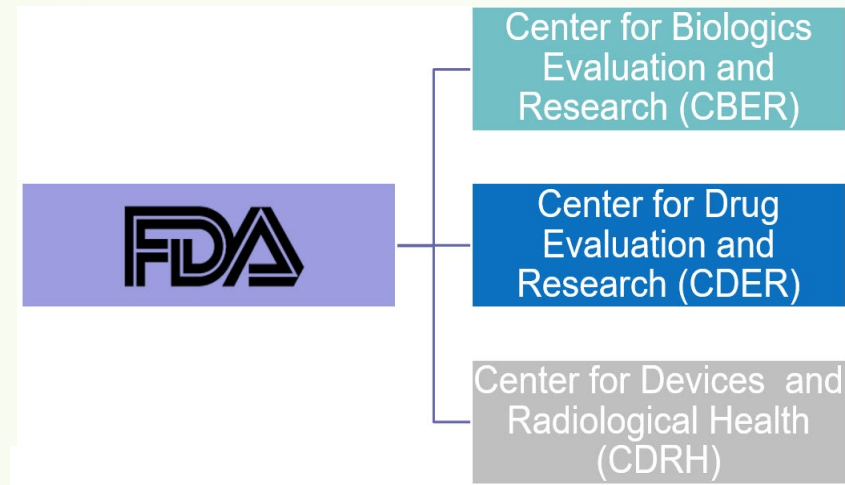
Other OTC Drugs with the Same Active Ingredient, Strength and Dosage Form/Route

CDER

NIH SEED

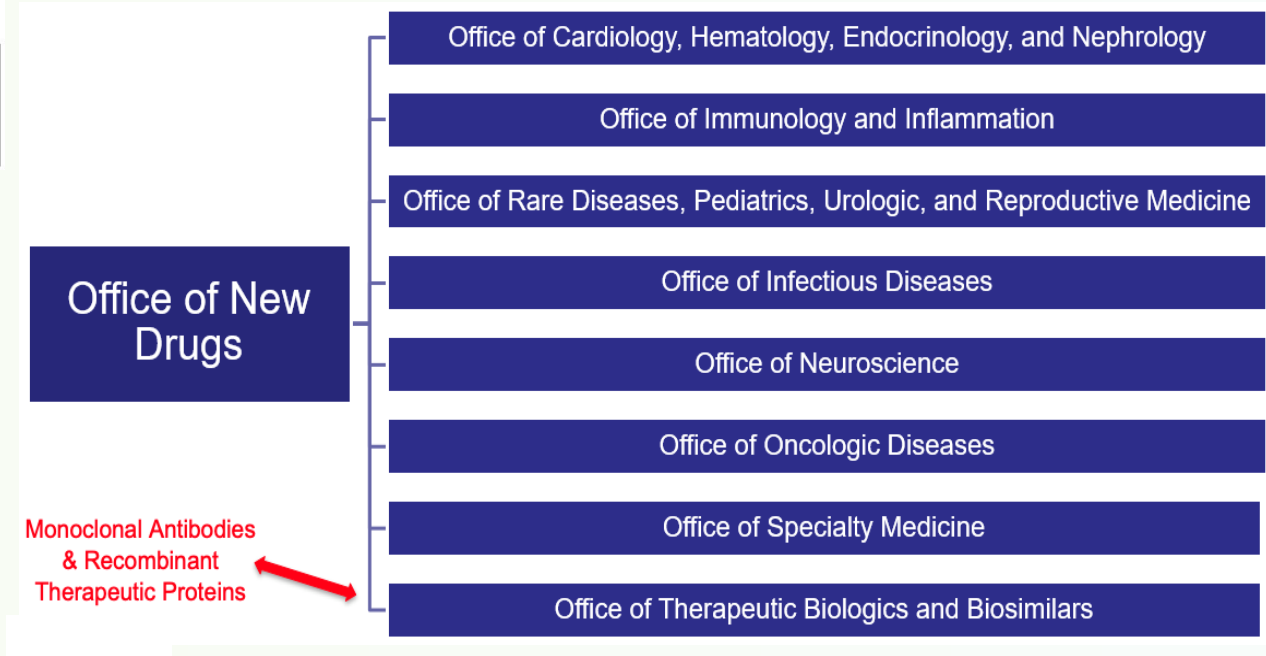
13

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

- preclinical|
- preclinical - Google Search
- preclinical studies
- preclinical research
- preclinical models
- preclinical trials
- preclinical disease
- preclinical definition
- preclinical vs nonclinical

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.

www.sciencedirect.com › content

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

NIH and FDA Release Protocol Template for Phase 2 and 3 IND/IDE Clinical Trials

Notice Number: NOT-OD-17-064

MENTORS

XLerateHealth's 300+ mentors represent a broad network of experts across payers, hospital systems, clinicians, investors, serial entrepreneurs, and academia who guide our startups in developing smart, sustainable business models.

Experts are identified for their deep knowledge in lean startup techniques and domain expertise in key areas of healthcare commercialization, including the regulatory approval process, reimbursement strategy, intellectual property, HIPAA compliance, life science and med tech, digital health and telemedicine, healthcare operations,

CREATE Bio Example: Target Product Profile (TPP)

A Target Product Profile (TPP) is a planning tool for therapeutic candidates based on [FDA guidelines](#).

The CBER Office of Cellular, Tissue and Gene Therapies (OCTGT) web page for industry education also has a [Webinar on TPP](#).

Below are example worksheets that define the minimal/ideal profile of the final marketed product and shows the ultimate goals of the proposed therapy development effort such as disease indication, patient population (with details such as symptomatic or pre-symptomatic patients for some genetic diseases), delivery mode, treatment duration, treatment regimen, and standards for clinical efficacy. The details of the TPP should be stage appropriate.

1. Example for Ischemic stroke- revascularization

Product Targets	Minimum Acceptable Result	Ideal Results
Primary Product Indication	Emergency medicine for acute stroke patients immediately on hospital arrival	Emergency medicine for acute stroke patients in the community even before arrival to a hospital
Patient Population	Adults of all ages with moderate to severe	Adults of all ages with moderate to severe stroke,
Treatment Duration		
Delivery Mode		
Dosage Form		
Regimen		
Efficacy		

Assay Guidance Manual

The Assay Guidance Manual (AGM) is a best practices online resource devoted to a successful development of a drug. The manual was originally developed by Eli Lilly and Company to provide step-by-step guidance based on "tribal knowledge" from drug developers for running and creating projects for high-throughput screening, lead optimization and preclinical research. Tribal knowledge is also considered useful to choose of regulated drug development. Tribal knowledge is also considered useful.

ClinRegs

National Institute of Allergy and Infectious Diseases
Aggregating clinical research regulations from around the globe

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SELECT A COUNTRY TO GET STARTED

COUNTRIES

World map showing countries: CANADA, UNITED STATES, MEXICO, GUATEMALA, BRAZIL, PERU, UNITED KINGDOM, GUINEA, SIERRA LEONE, LIBERIA, DR Congo, UGANDA, KENYA, TANZANIA, MALAWI, SOUTH AFRICA, INDIA, CHINA, VIETNAM, THAILAND, AUSTRALIA.

Small Business Resources

20 videos • 227 views • Last updated on Feb 18, 2020

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Updates: This profile has been updated to reflect current

Tweets by @NIADClinRegs

NHLBI Small Biz Hangout: Identifying and Connecting With Your Customer

NHLBI Small Biz Hangout: Intellectual Property for the New Biomedical Innovator

NIH Small Biz Hangout: Finding the Right Regulatory Consultant

NHLBI Small Biz Hangout: Biologics Regulation Overview

NHLBI Small Biz Hangout: Writing Your Phase II Commercialization Plan

NHLBI Small Biz Hangout: Medical Device Regulation Overview

NHLBI Small Biz Hangout: First Contact with FDA

NHLBI Small Biz Hangouts: Conquering the (Regulatory) Basics | Navigating the FDA Website

Chemistry, Manufacturing and Controls (CMC)

FDA Guidance “CGMP for Phase 1 Investigational Drugs”

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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>

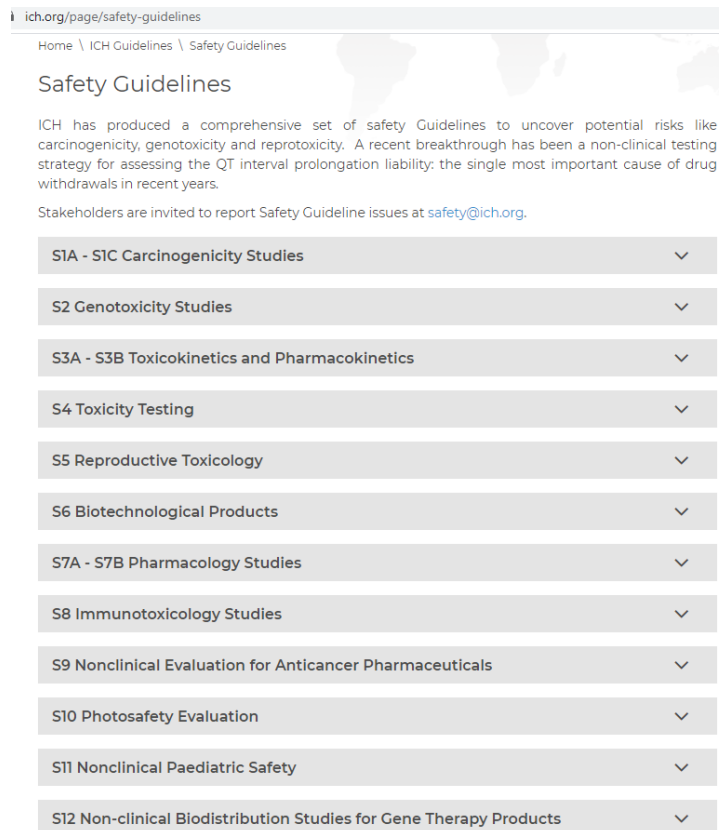
CMC

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