

Regulation of Biopharmaceuticals in the United States of America

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Overview

- FDA Organization
- Laws Relevant to Biotechnology Drugs for Humans
- Follow-on Biologics (Biosimilars)
- Regulation of Biological Products

U.S. Food and Drug Administration

Center for Drug Evaluation and Research

- Synthetic Drugs
- Biotechnology Products

Center of Biologics Evaluation and Research

- Blood & Blood Products
- Vaccines
- Cellular, Tissue, and Gene Therapies

U.S. Food and Drug Administration

Center for Veterinary Medicine

- Synthetic Veterinary Drugs
- Transgenic Animals

Center for Devices and Radiological Health

- Healthcare Devices
- Radiation-emitting devices

U.S. Food and Drug Administration

Center for Food Safety and Applied Nutrition

- Human Food
- Animal Feed
- Cosmetics

Office of Regulatory Affairs

- Facility Inspections

National Center for Toxicological Research

U.S. Department of Agriculture

Animal & Plant Health Inspection Service

- Bioengineered Plants

Center for Veterinary Biologics

- Vaccines for Animals

Center for Drug Evaluation and Research

Office of New Drugs

- Clinical Trial Review
 - Six Review Offices

Office of Pharmaceutical Science

- Product Quality Review
 - Office of Biotechnology Products
 - Office of New Drug Quality Assessment
 - Office of Generic Drugs

Laws for Human Drugs

LAW

U.S. FOOD DRUG &
COSMETIC ACT



“TRADITIONAL” DRUGS
AND PROTEIN HORMONES

PRODUCTS

U.S. PUBLIC HEALTH
SERVICE ACT

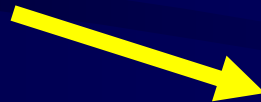


BIOLOGICAL DRUG
PRODUCTS

APPLICATIONS

LAW

U.S. FOOD DRUG &
COSMETIC ACT



U.S. PUBLIC HEALTH
SERVICE ACT



APPLICATION

NEW DRUG APPLICATION
(NDA)

ABBREVIATED NDA
(ANDA)

BIOLOGIC LICENSE
APPLICATION (BLA)

ABBREVIATED
BLA

Categorical Examples

NDA

h-GROWTH HORMONE

INSULIN

CALCITONIN

BLA

MONOCLONAL
ANTIBODIES

INTERFERONS

INTERLEUKINS

GROWTH FACTORS

What is a Follow-on Product?

A product for which a sponsor relies to some extent on the finding of safety and efficacy of an approved reference product.

What is a Follow-on Product?

Not a single answer...

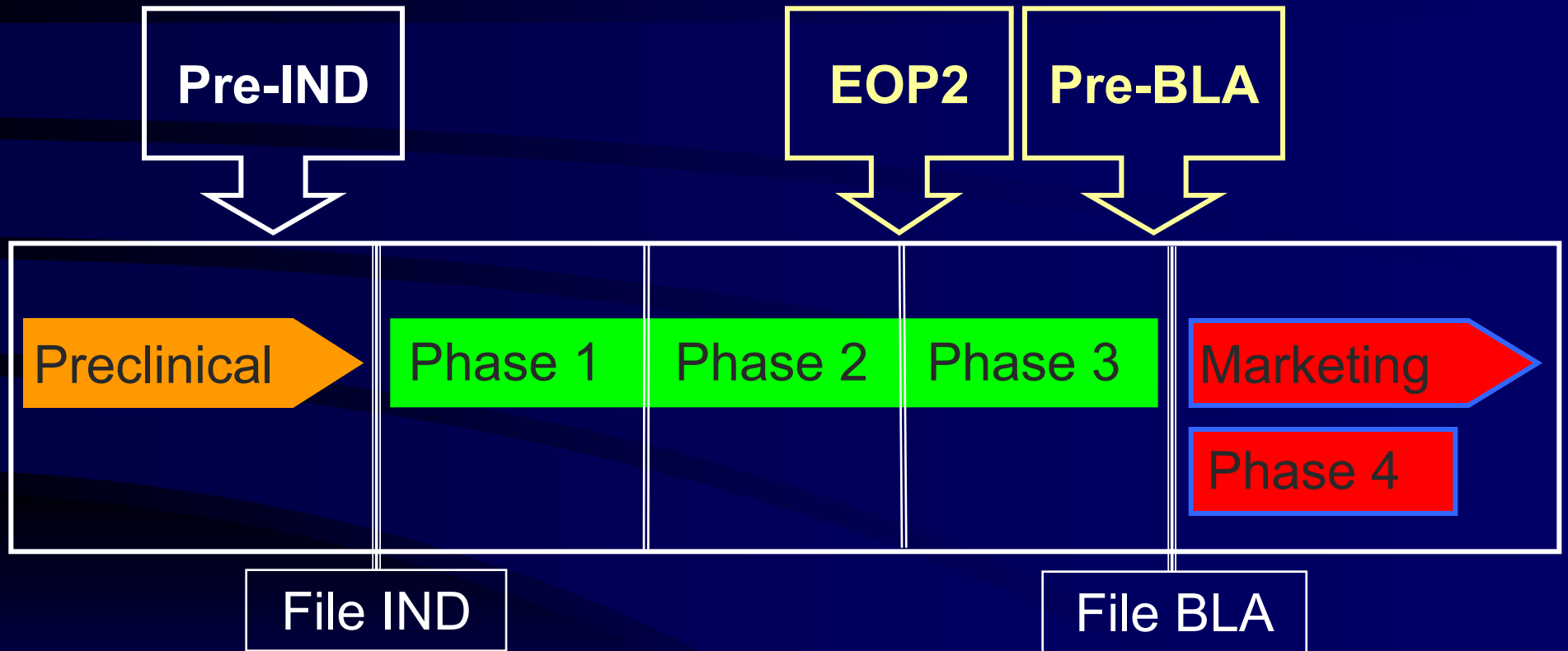
- Product intended to be interchangeable with comparator product
 - High degree of similarity
- Product intended to be similar to comparator product
 - Similar, but not interchangeable
 - Improved (e.g., 2nd Generation Product)

Waiting for new laws...



Four laws have been written, but, until one is passed, we cannot approve a biosimilar biological product in the USA.

Product Development



Safety

- Safety means the **relative freedom from harmful** effect to persons affected, directly or indirectly, by a product when prudently administered, **taking into consideration** the **character of the product** in relation to the **condition of the recipient at the time**.
- **Proof of safety** shall consist of **adequate tests** by methods reasonably applicable to show the biological product is safe **under the prescribed conditions of use**, including results of significant human experience during use.

Effectiveness

- Effectiveness means a **reasonable expectation** that, in a significant proportion of the target population, the pharmacological or other **effect of the biological product**, when used under adequate directions, for use and warnings against unsafe use, will serve a **clinically significant function** in the diagnosis, cure, mitigation, treatment, or prevention of disease in man.

Proof of Effectiveness

- Proof of effectiveness shall consist of **controlled clinical investigations** ..., **unless** this requirement is waived on the basis of a showing that **it is not reasonably applicable** to the biological product **or essential to the validity of the investigation**, and that an **alternative method of investigation is adequate** to substantiate effectiveness.

Surrogate Endpoints

- Alternate methods, such as **serological response evaluation** in clinical studies and appropriate animal and other laboratory assay evaluations **may** be adequate to **substantiate effectiveness** where a **previously accepted correlation** between data generated in this way and clinical effectiveness **already exists**.

Product & Manufacturing Facility

- Approval of a biologics license application or issuance of a biologics license shall constitute a determination that the establishment(s) and the product meet applicable requirements to ensure the continued safety, purity, and potency of such products” including but not limited to GMPs.

Thank You

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For Additional Information

CDER –

<http://www.fda.gov/cder/regulatory/applications/default.htm>

CBER –

<http://www.fda.gov/cber/guidelines.htm>

USDA/CVB –

http://www.aphis.usda.gov/animal_health/vet_biologics/