



USFDA

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INTRODUCTION

- The **U.S. Food and Drug Administration (FDA or USFDA)** is a science-based regulatory agency within the U.S. Department of Health and Human Services (HHS) – Food and Drug Administration Act of 1988

Mission of FDA

- The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.
- The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.
- To participate with representatives of other countries to reduce the burden of regulation, coordinate regulatory requirements, and achieve appropriate equivalent arrangements.

- As determined to be appropriate by the Secretary of Health and Human Services, to carry out the tasks above by consulting with experts in science, medicine, and public health, and by cooperating with consumers, users, manufacturers, importers, packers, distributors, and retailers of regulated products.
- FDA accomplishes its task by establishing and enforcing high product standards and other regulatory requirements authorized or mandated by the Federal Food, Drug and Cosmetic Act (FD&C Act), its amendments, and other public health laws.

WHAT FDA REGULATES

- FDA is the federal agency responsible for ensuring that foods are safe, wholesome and sanitary; human and veterinary drugs, biological products, and medical devices are safe and effective; cosmetics are safe; and electronic products that emit radiation are safe.
- FDA also ensures that these products are honestly, accurately and informatively represented to the public.

- Some of the agency's specific responsibilities include:

1. Biologics

- product and manufacturing establishment licensing
- safety of the nation's blood supply
- research to establish product standards and develop improved testing methods

2. Cosmetics

- safety
- labeling

3. Drugs

- product approvals
- OTC and prescription drug labeling
- drug manufacturing standards

4. Foods

- labeling
- safety of all food products (except meat and poultry)
- bottled water

5. Medical Devices

- premarket approval of new devices
- manufacturing and performance standards
- tracking reports of device malfunctioning and serious adverse reactions

6. Radiation-Emitting Electronic Products

- radiation safety performance standards for microwave ovens, television receivers, diagnostic x-ray equipment, cabinet x-ray systems (such as baggage x-rays at airports), laser products, ultrasonic therapy equipment, mercury vapor lamps, and sunlamps

7. Veterinary Products

- livestock feeds
- pet foods
- veterinary drugs and devices

8. Tobacco Products, including:

- cigarettes
- cigarette tobacco
- roll-your-own tobacco
- smokeless tobacco

WHAT FDA DOES NOT REGULATE

I) ADVERTISING

II) ALCOHOL

III) CONSUMER PRODUCTS

IV) DRUGS OF ABUSE

V) HEALTH INSURANCE

VI) MEAT AND POULTRY

VII) PESTICIDES

VIII) RESTAURANTS AND GROCERY STORES

IX) WATER

- **The agency is organized into the following major subdivisions, each focused on a major area of regulatory responsibility:**

Sr. No	Component	Full Form	Regulates
A	CBER	Center For Biologics Evaluation And Research	Biological Products
B	CDRH	Center For Devices And Radiological Health	Safety and Effectiveness of New Medical Devices Before they are Marketed
C	CDER	Center For Drug Evaluation And Research	Health of by Assuring Prescription and OTC Drugs are Safe and Effective
D	CSFAN	Center For Food Safety And Applied Nutrition	Food Supply is Safe, Sanitary, Wholesome, and Honestly Labeled, and Cosmetic Products are Safe and Properly Labeled.
E	CVM	Center For Veterinary Medicine	Assure that Animal Food Products are Safe.
F	NCTR	National Center For Toxicological Research	Human Toxicity
G	OC	Office Of The Commissioner	
H	ORA	Office Of Regulatory Affairs	Products Comply with Appropriate Public Health Laws and Regulations.

CFR Title 21

- C.F.R – Code of federal Regulation is a codification of general rules and regulations also known as administrative law published in the federal register by the executive department and agencies of federal government of united states
- Title 21 of the CFR is reserved for rules of the Food and Drug Administration.
- CFR 21 was received from the Government Printing Office (GPO) and contains the most recently received revision.
- Food and Drugs: Parts 1 to 1499 different types of parts to food, drug , cosmetic and medical devices and etc

- 21 CFR part 11- Electronic submission and Electronic signature
- 21 CFR part 50- Protection of human subjects
- 21 CFR part 54- Financial Disclosure by Clinical Investigators
- 21 CFR part 56- Institutional Review Board
- 21 CFR part 101-Food Labeling.
- 21 CFR part 104-Nutritional quality guidelines for foods
- 21 CFR part 106- Infant Formula Quality Control Procedures
- 21 CFR part 110- CGMP Practices in manufacturing packing or holding human food.

- 21 CFR part 210- CGMP Practices in manufacturing, packing or holding of Drugs: General
- 21 CFR part 211- CGMP Practices for finished pharmaceuticals
- 21 CFR part 225- CGMP Practices for medicated feeds.
- 21 CFR part 312- Investigational new drug application
- 21 CFR part 314- Application for FDA Approval to Market a New Drug
- 21 CFR part 600 to 680- For biological products

About FDA Product Approval

- The Food and Drug Administration's regulatory approaches to marketing approval of the products it regulates are as varied as the products themselves. These differences are dictated by the laws FDA enforces and the relative risks that the products pose to consumers.
- Some products — such as new drugs and complex medical devices — must be proven safe and effective before companies can put them on the market. The agency also must approve new food additives before they can be used in foods. Other products — such as x-ray machines and microwave ovens -- must measure up to performance standards. And some products — such as cosmetics and dietary supplements — can generally be marketed with no prior approval.

What is the approval process for a new prescription drug?

- Drug companies seeking FDA approval to sell a new prescription drug in the United States must test it in various ways. First are laboratory and animal tests. Next are tests in humans to see if the drug is safe and effective when used to treat or diagnose a disease.
- After testing the drug, the company then sends FDA an application called a New Drug Application (NDA). Some drugs are made out of biologic materials. Instead of an NDA, new biologic drugs are approved using a Biologics License Application (BLA).

- Whether an NDA or a BLA, the application includes:
 1. The drug's test results
 2. Manufacturing information to demonstrate the company can properly manufacture the drug
 3. The company's proposed label for the drug. The label provides necessary information about the drug, including uses for which it has been shown to be effective, possible risks, and how to use it.
- If a review by FDA physicians and scientists shows the drug's benefits outweigh its known risks and the drug can be manufactured in a way that ensures a quality product, the drug is approved and can be marketed in the United States.

NDA and BLA - Similarities

There are many similarities:-

- Regulations
- Guidance documents
- PDUFA (The Prescription Drug User Fee Act 1992)

NDA and BLA - Similarities

Specific Similarities Include

- IND regulations, Fast Track designation, Special Protocol Assessment (SPA)
- Financial Disclosure, CTD format
- Labeling and Advertising (21CFR 201-202)
- Pediatric study requirements and waivers
- Accelerated Approval
- Orphan Exclusivity

Most differences are due to

- Type of Product
- Not due to which
- FDA Center Regulates The Product

Unique to NDAs

- Patent Exclusivity (Generics, 505b2, & Orange Book)
- Pediatric Exclusivity (written requests)
- NOA Field Copies
- Regulations more detailed (NOA content; Filing criteria etc.)

Unique to BLAS

- U.S. License
- Product and facility must meet "Product standards" prior to License issuance
- Review includes
 - Application review
 - Facility inspection (Pre-approval, review members participate)
 - Method validation (complete)
 - Compliance check
- Cooperative manufacturing arrangements permitted
 - Divided, Shared, Contract
- FDA "official" release (21 CFR 610.2) of each product lot (at discretion of FDA)
- Container & Packaging, Label Requirements
- Specific information will be required depending on the type of BLA (e.g., Blood, Vaccines).

ORANGE BOOK

- Its official title is Approved Drug Product with Therapeutic Equivalence Evaluations.
- Commonly known as Orange Book due to the orange cover of the original print version, it is the FDA's list of all drugs approved in United States as safe and effective.
- In addition to listing all approved drugs, the Orange Book is also the authoritative source of information on the therapeutic equivalence of drug product.

Contents of the Orange Book

PREFACE TO THIRTIETH EDITION

1.	INTRODUCTION
1.1	Content and Exclusion
1.2	Therapeutic Equivalence-Related Terms
1.3	Statistical Criteria for Bioequivalence
1.4	Reference Listed Drug

1.5	General Policies and Legal Status
1.6	Practitioner/User Responsibilities
1.7	Therapeutic Equivalence Evaluations Codes
1.8	Description of Special Situations
1.9	Therapeutic Equivalence Code Change for a Drug Entity
1.10	Change of the Therapeutic Equivalence Evaluation for a Single Product
1.11	Discontinued Section
1.12	Changes to the Orange Book
1.13	Availability of the Edition

2.	HOW TO USE THE DRUG PRODUCTS LISTS
2.1	Key Sections for Using the Drug Product Lists
2.2	Drug Product Illustration
2.3	Therapeutic Equivalence Evaluations Illustration

DRUG PRODUCT LISTS

	Prescription Drug Product List
	OTC Drug Product List
	Drug Products with Approval under Section 505 of the Act Administered by the Center for Biologics Evaluation and Research List
	Discontinued Drug Product List
	Orphan Products Designations and Approvals List
	Drug Products Which Must Demonstrate in vivo Bioavailability Only if Product Fails to Achieve Adequate Dissolution

APPENDICES

A.	Product Name Index A-1
B.	Product Name Index Listed by
C.	Uniform Terms

PATENT AND EXCLUSIVITY INFORMATION ADDENDUM

Differences between EMA and US-FDA requirements for solid oral dosage form

- The EMA in general recommends one single fasting BE study; In the currently approved guidelines one single-dose fasting study is considered to be sufficient for oral solid IR formulations of BCS Class I if the labeling does not highlight food effects.
- But the US-FDA recommends the conduct of two BE studies, one fasting- and one fed-state study for both IR and MR formulations in general.
- If an RLD is listed in the USA and only a similar (not the same) product is approved in the EU, the bioequivalence needs to be confirmed against both the RLD and the EU reference product.

Comparison of Key Factors or Requirement Criteria for BCS Based Biowaiver

Regulatory Authority	Solubility of Drug Substance	Permeability of Drug Substance	BCS Class of Drug Substance	In-vitro Dissolution Similarity of Test and Reference Product
USA (3) *	<p>Highest dose strength is soluble in ≤ 250 ml of buffers</p> <p>pH range: 1-7.5</p> <p>Temp.: $37 \pm 1^\circ\text{C}$</p> <p>Methodology:</p> <ul style="list-style-type: none"> • Shake Flask Method • Acid or Base Titration 	<p>Highly Permeable: Extent of absorption in humans is $\geq 90\%$</p> <p>Methodology:</p> <ul style="list-style-type: none"> • Absolute Bioavailability study • Mass Balance study • In-vivo perfusion study • In-vitro excised human or animal Intestinal study • In-vitro epithelial cell culture study 	Class I	<p>Rapidly Dissolving: $\geq 85\%$ of the labeled amount of the drug substance dissolves within 30 minutes.</p> <p>Apparatus: USP Type I at 100 rpm or Type II at 50 rpm</p> <p>Dissolution Media: 900 ml of following media</p> <ol style="list-style-type: none"> (1) 0.1 N HCl or Simulated Gastric Fluid USP without enzymes; (2) pH 4.5 buffer; (3) pH 6.8 buffer or Simulated Intestinal Fluid USP without enzymes. <p>N = 12</p>
EU (4)	<p>Highest dose strength is soluble in ≤ 250 ml of buffers</p> <p>pH range: 1-6.8</p> <p>Temp.: $37 \pm 1^\circ\text{C}$</p> <p>Methodology:</p> <ul style="list-style-type: none"> • Shake Flask Method 	<p>Highly Permeable: Extent of absorption in humans is $\geq 85\%$</p> <p>Methodology:</p> <ul style="list-style-type: none"> • Absolute Bioavailability study • Mass Balance study 	Class I, Class III	<p>Class I</p> <p>Rapidly Dissolving: $\geq 85\%$ of the labeled amount of the drug substance dissolves within 30 minutes.</p> <p>Class III</p> <p>Very Rapidly Dissolving: $\geq 85\%$ of the labeled amount of the drug substance dissolves within 15 minutes.</p> <p>Apparatus: USP Type I at 100 rpm or Type II at 50 rpm</p> <p>Dissolution Media: 900 ml of following media</p> <ol style="list-style-type: none"> (1) 0.1 N HCl or Simulated Gastric Fluid USP without enzymes; (2) pH 4.5 buffer; (3) pH 6.8 buffer or Simulated Intestinal Fluid USP without enzymes. <p>N = 12</p>

References

- www.fda.gov
- **Comparison of global regulatory guidelines for availability of different biowaiver provisions and application requirements of biopharmaceutics classification system (BCS) based biowaiver; international journal of drug regulatory affairs; 2015, 3(3), 8-20**
- **EMA versus US-FDA regulatory requirements regarding bioequivalence of orally administered generics**

A white, hand-drawn style thought bubble sticker is centered on a brown corkboard. The bubble has a small tail pointing downwards. The text 'Thank you!!' is written inside the bubble in a black, casual, handwritten font. The corkboard is set against a dark, textured background.

Thank
you!!