Biological Product Approval, Vaccines, Emergency Use Authorization

KING & SPALDING

FDLI

Agenda

- Approval Standard
- BLA Submission
- FDA Review of BLAs
- Vaccines: Emergency Use Authorization
- Incentives for Biological Products

Approval Standard

PHS Act 351(a) Standard*

Approval if a BLA demonstrates that:

(i) the biological product … is safe, pure, and potent; and

(ii) the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent….”

*Certain FD&C Act requirements also apply

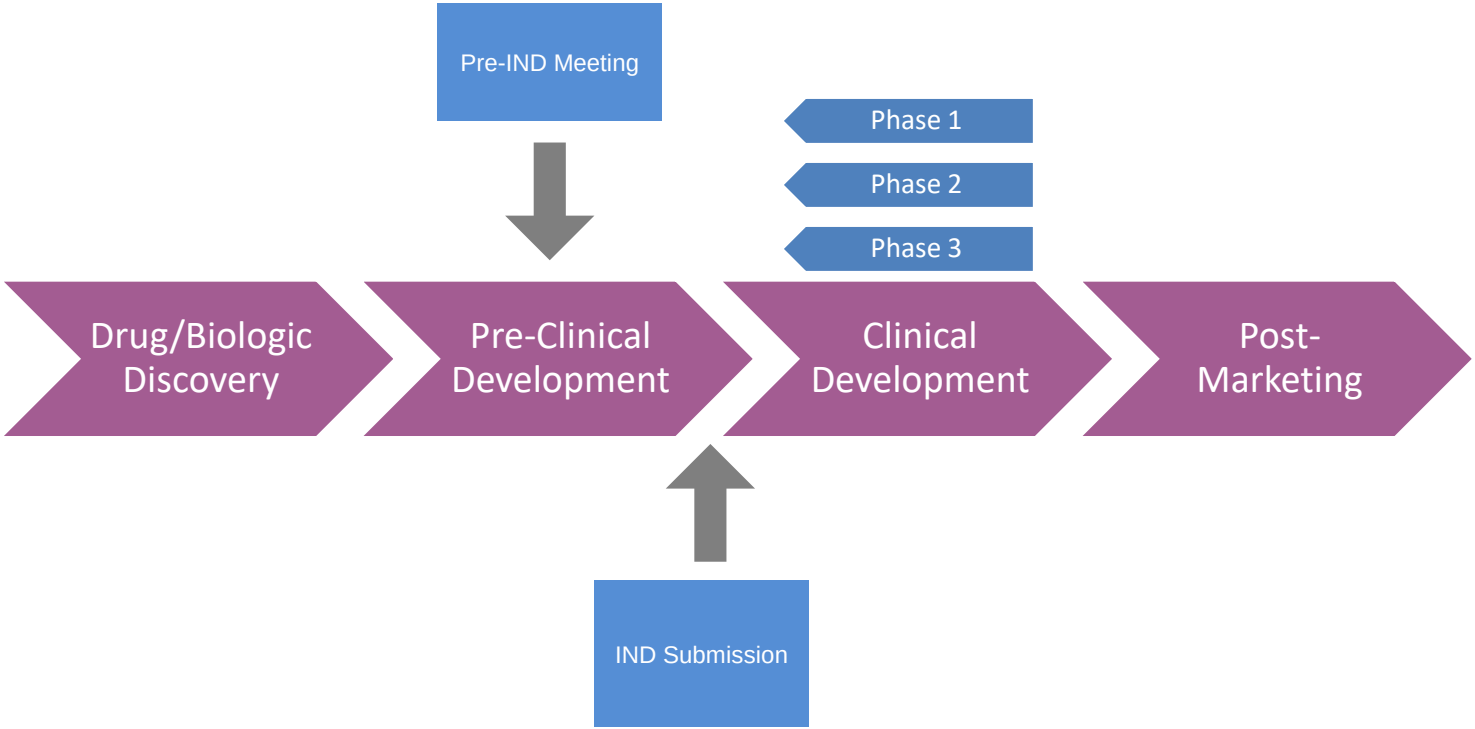
Safe, Pure & Potent

"the relative freedom from harmful effect to people affected directly or indirectly by a product when prudently administered"

"the relative freedom from extraneous matter"

the product will correspond with some measurable effect and will perform as intended and claimed

Stage of Development



Substantial Evidence

Potency interpreted to include efficacy

Requires substantial evidence of efficacy

Typically from adequate and well-controlled clinical studies

Diversity in Clinical Research

Federally-funded research must include

- women and minority groups unless demonstrably inappropriate

Diverse Women in Clinical Trials Initiative

- awareness about clinical trial participation by diverse women of different ages, races, ethnic backgrounds, and health conditions

Digital Health Tools in Clinical Investigations

- awareness of utility of digital health tools for improving clinical trial diversity

clinical trials should reflect the population most likely to use the drug if the drug is approved

PHS Act 351(k) Standard*

Approval if a BLA demonstrates that:

(i) the biological product is highly similar to a reference product notwithstanding minor differences in clinically inactive components; and

(ii) has no clinically meaningful differences from the reference product

(iii) additional requirements for interchangeability are met, if applicable

(iv) facility requirements at met

*Certain FD&C Act requirements also apply

Facility Requirements for Licensure

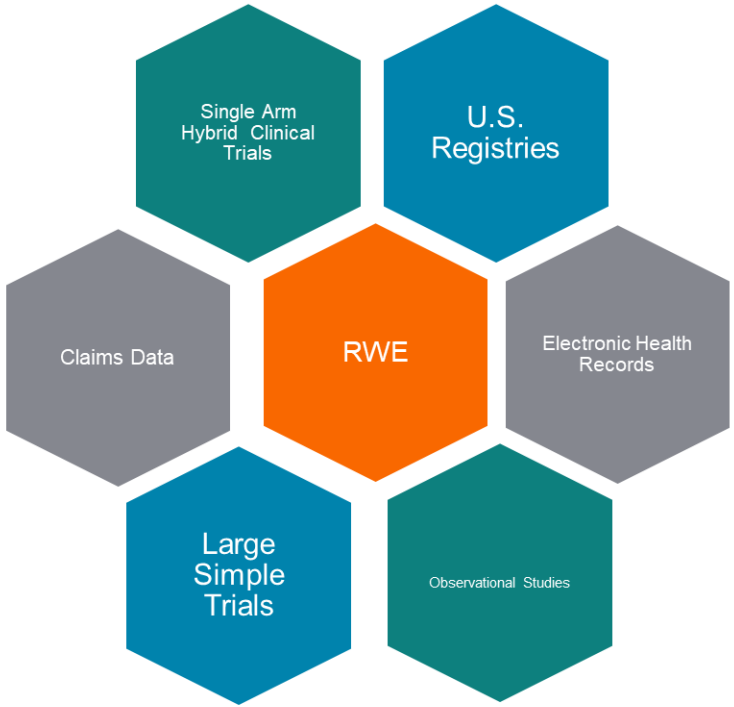
“The Process is the Product”

- Even minor changes in manufacturing can impact product performance
- Biologics regulations also require an inspection prior to approval.

Use of RWE

Use of RWD to generate RWE for regulatory decisions about potency/effectiveness. For example:

- New indications for an approved biologic
- Phase 4 studies
- Interchangeable biosimilars



Exception for section 361 HCT/Ps

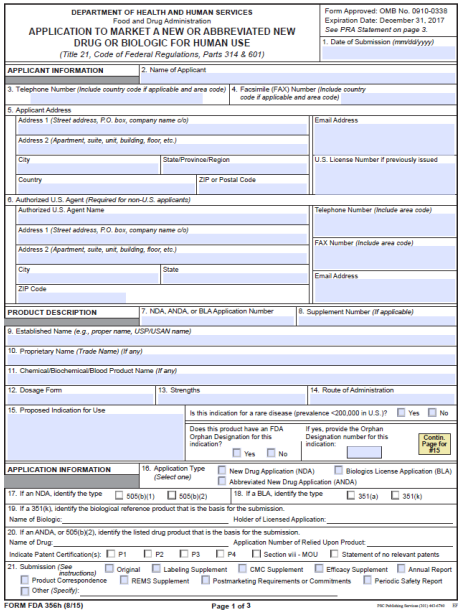
FDA will exempt HCT/Ps from the premarket review and approval processes and regulate them exclusively under section 361 of the Public Health Service Act if they meet certain criteria

(21 C.F.R. 1271.10(a))

BLA Submission

BLA Contents

- Nonclinical data
- Clinical data
- Statements of conformance
  - Good laboratory practices
  - Informed consent
  - Institutional review requirements
- Manufacturing locations
- Manufacturing methods
- Stability data
- Representative product samples and analytical results
- Financial certification/disclosure
- Labels, enclosures, containers
- Environmental assessment



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
APPLICATION TO MARKET A NEW OR ABBREVIATED NEW DRUG OR BIOLOGIC FOR HUMAN USE
(Title 21, Code of Federal Regulations, Parts 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: December 31, 2017
See PRA Statement on page 2.

1. Date of Submission (mm/dd/yyyy)

APPLICANT INFORMATION
2. Name of Applicant
3. Telephone Number (Include country code if applicable and area code)
4. Facsimile (FAX) Number (Include country code if applicable and area code)
5. Applicant Address
Address 1 (Street address, P.O. box, company name c/o)
Address 2 (Apartment, suite, unit, building, floor, etc.)
City
State/Province/Region
Country
ZIP or Postal Code
Email Address
U.S. License Number if previously issued
6. Authorized U.S. Agent (Required for non-U.S. applicants)
Authorized U.S. Agent Name
Address 1 (Street address, P.O. box, company name c/o)
Address 2 (Apartment, suite, unit, building, floor, etc.)
City
State
ZIP Code
Telephone Number (Include area code)
FAX Number (Include area code)
Email Address

PRODUCT DESCRIPTION
7. NDA, ANDA, or BLA Application Number
8. Supplement Number (If applicable)
9. Established Name (e.g., proper name, USP/USAN name)
10. Proprietary Name (Trade Name) (If any)
11. Chemical/Biochemical/Blood Product Name (If any)
12. Dosage Form
13. Strengths
14. Route of Administration
15. Proposed Indication for Use
Is this indication for a rare disease (prevalence <200,000 in U.S.)? Yes No
Does this product have an FDA Orphan Designation for this indication? Yes No
If yes, provide the Orphan Designation number for this indication:
Contin. Page for #15

APPLICATION INFORMATION
16. Application Type (Select one)
New Drug Application (NDA)
Abbreviated New Drug Application (ANDA)
Biologics License Application (BLA)
17. If an NDA, identify the type 505(b)(1) 505(b)(2)
18. If a BLA, identify the type 351(a) 351(k)
19. If a 351(k), identify the biological reference product that is the basis for the submission.
Name of Biologic:
Holder of Licensed Application:
20. If an ANDA, or 505(b)(2), identify the listed drug product that is the basis for the submission.
Name of Drug:
Application Number of Relied Upon Product:
Indicate Patent Certification(s): P1 P2 P3 P4 Section viii - MOU Statement of no relevant patents
21. Submission (See instructions) Original Labeling Supplement CMC Supplement Efficacy Supplement Annual Report
Product Correspondence REMS Supplement Postmarketing Requirements or Commitments Periodic Safety Report
Other (Specify):

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Master Files

- Submissions to FDA that provide detailed, confidential information about facilities, processes, or articles used in manufacturing, packaging, or storage
  - BLAs may cross-reference some Master Files (e.g., container closures)
  - Generally may not incorporate by reference information about:
    - Drug substance
    - Drug substance intermediate
    - Drug product
  - Proposed exception for NDAs “deemed” to be BLAs that previously cross-referenced Drug Master Files

Lot Release Protocol

- Potential requirement to submit data or product samples post-licensure for confirmatory review by FDA

FDA LOT RELEASE

Please submit final blister packaged drug product together with lot release protocols showing results of all applicable tests. You may not distribute any lots of product until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Unituxin to the Center for Drug Evaluation and Research (CDER) for release by the Director , CDER, under 21 CFR 610.2 We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Inclusion of Proposed Labeling

Label

- A display of written, printed, graphic matter upon the immediate container of an article
- 21 U.S.C. § 321(k)

Labeling

- All labels and other written, printed, or graphic matter (1) upon any articles, or any of its containers, or wrappers, or (2) accompanying such article
- 21 U.S.C. § 321(m)

Filing the BLA

"An application for a biologics license shall not be considered as filed until all pertinent information and data have been received by the Food and Drug Administration"

-21 C.F.R. 601.2(a)

FDA Review

PDUFA User Fees

- User fees are assessed for “human drug applications”:
  - Application
  - Annual (“Program Fee”)

FY 2021 and FY 2022 User Fee Rates:

User Fee Type	2021	2022
Application Fee – Clinical Data Required	**$2,875,842**	**$3,117,218**
Application Fee – No Clinical Data Required	$1,437,921	$1,558,609
Program Fee	$336,432	$369,413

PDUFA Review Goals

A. REVIEW PERFORMANCE GOALS

1. NDA/BLA Submissions and Resubmissions[2]

a. Review and act on 90 percent of standard NME NDA and original BLA submissions within 10 months of the 60 day filing date.

b. Review and act on 90 percent of priority NME NDA and original BLA submissions within 6 months of the 60 day filing date.

c. Review and act on 90 percent of standard non-NME original NDA submissions within 10 months of receipt.

d. Review and act on 90 percent of priority non-NME original NDA submissions within 6 months of receipt.

e. Review and act on 90 percent of Class 1 resubmitted original applications within 2 months of receipt.

f. Review and act on 90 percent of Class 2 resubmitted original applications within 6 months of receipt.

Expedited Programs

- Fast track designation
- Breakthrough therapy
- Priority Review
- Accelerated Approval
- Regenerative Medicine Advanced Therapy (“RMAT”) Designation

Interacting with FDA During Review

- Meetings and communications under PDUFA
- Information Requests
- Advisory committees
- Facility Inspections

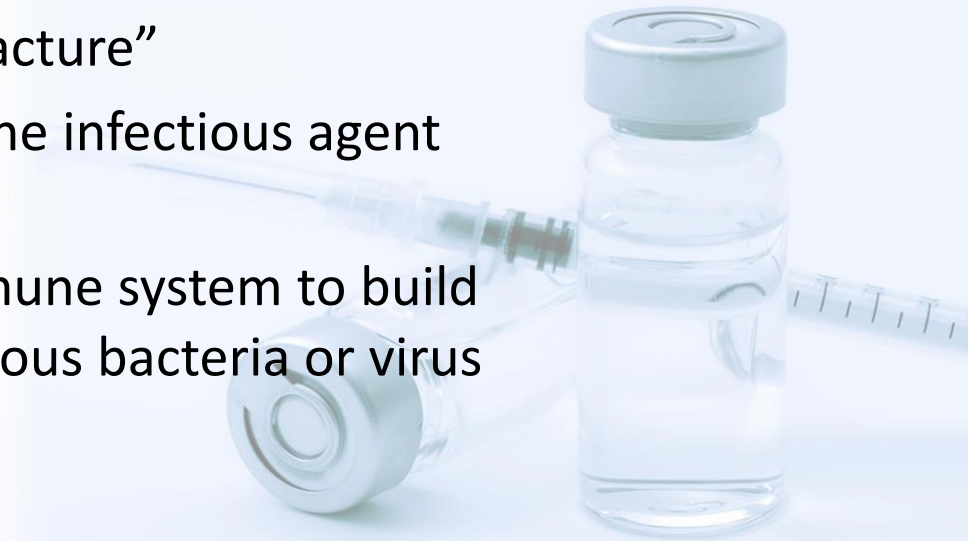
FDA's Decision

- Approval/Complete response letters
- Post-market Requirements and Commitments
- Risk Evaluation and Mitigation Strategies (REMS)
- Disclosure Implications
- Appeal/Dispute Resolution

Vaccines: Emergency Use Authorization

Vaccines

- Vaccines are “products intended to induce or increase an antigen specific immune response for prophylactic or therapeutic immunization, regardless of the composition or method of manufacture”
  - mechanism of action mimics the infectious agent that causes disease
  - This stimulates the body’s immune system to build up defenses against the infectious bacteria or virus without causing the disease

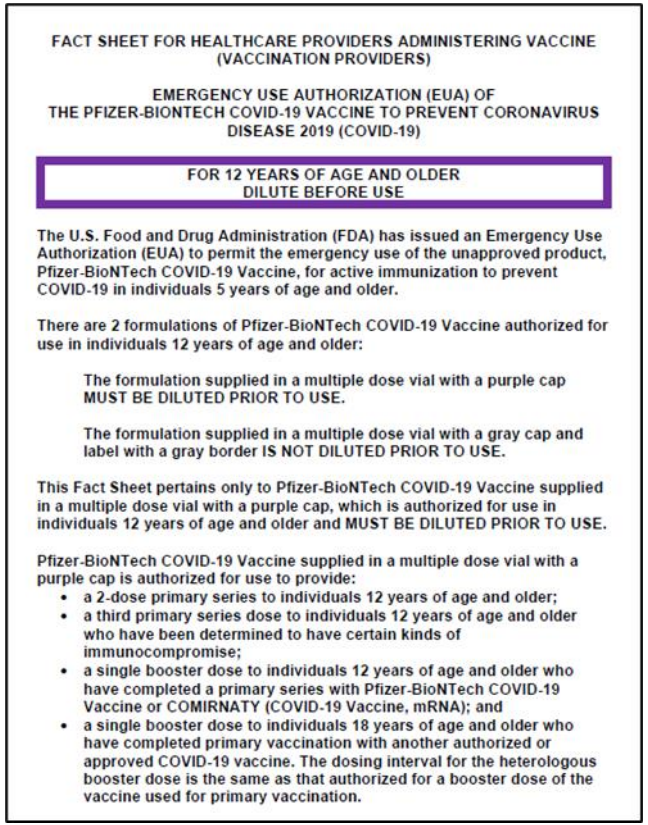


Emergency Use Authorization (EUA)

- FDA may authorize drug, device, or biological product for use in actual or potential emergency
- Only certain types of emergency declarations qualify
- If EUA is in effect for more than 1 year, FDA and sponsor must work to identify specific obstacles and actions toward approval

Criteria for Authorization

- Agent can cause serious or life-threatening disease or condition
- Totality of scientific evidence: it is reasonable to believe the product may be effective in diagnosis, treatment, or prevention
- Known and potential benefits outweigh the known and potential risks
- No adequate, approved and available alternative product exists



FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE (VACCINATION PROVIDERS)

EMERGENCY USE AUTHORIZATION (EUA) OF THE PFIZER-BIONTECH COVID-19 VACCINE TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19)

FOR 12 YEARS OF AGE AND OLDER
DILUTE BEFORE USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product, Pfizer-BioNTech COVID-19 Vaccine, for active immunization to prevent COVID-19 in individuals 5 years of age and older.

There are 2 formulations of Pfizer-BioNTech COVID-19 Vaccine authorized for use in individuals 12 years of age and older:

The formulation supplied in a multiple dose vial with a purple cap MUST BE DILUTED PRIOR TO USE.

The formulation supplied in a multiple dose vial with a gray cap and label with a gray border IS NOT DILUTED PRIOR TO USE.

This Fact Sheet pertains only to Pfizer-BioNTech COVID-19 Vaccine supplied in a multiple dose vial with a purple cap, which is authorized for use in individuals 12 years of age and older and MUST BE DILUTED PRIOR TO USE.

Pfizer-BioNTech COVID-19 Vaccine supplied in a multiple dose vial with a purple cap is authorized for use to provide:

- a 2-dose primary series to individuals 12 years of age and older;
- a third primary series dose to individuals 12 years of age and older who have been determined to have certain kinds of immunocompromise;
- a single booster dose to individuals 12 years of age and older who have completed a primary series with Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY (COVID-19 Vaccine, mRNA); and
- a single booster dose to individuals 18 years of age and older who have completed primary vaccination with another authorized or approved COVID-19 vaccine. The dosing interval for the heterologous booster dose is the same as that authorized for a booster dose of the vaccine used for primary vaccination.

Incentives for Biological Products

Reference Product Exclusivity

- Blocks biosimilar competition
- Beginning on the “date of first licensure,” FDA cannot:
  - file a biosimilar BLA for 4 years
  - make approval of a biosimilar BLA effective for 12 years
- Limitations on exclusivity for supplements and certain subsequent BLAs
  - “Umbrella exclusivity” unclear
- Pediatric exclusivity can add 6 months

Orphan Drug Exclusivity

- FDA cannot approve the “same drug” for the “same disease or condition” (indication) for 7 years
  - disease/condition affects fewer than 200,000 individuals in the US or no hope of covering the costs of manufacturing
  - exceptions for shortage and waiver
- Exclusivity possible for a clinically superior subsequent “same drug” in some circumstances
  - Consideration of clinical superiority is based on greater efficacy, greater safety, or a major contribution to patient care

Biological Product “Sameness”

- Whether something is a “same drug” can be critical
  - orphan drug exclusivity eligibility and scope
  - priority review vouchers
- Determining “sameness” can be difficult for biologics

Purple Book & Patent Listing

Purple Book
Database of Licensed Biological Products

- Upgraded Purple Book
- the Biological Product Patent Transparency Act
  - Added New mandates under section 351(k)(9) of the PHS Act
  - Patent Listing
  - Exclusivity

Thank You

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