

GENERIC DRUGS PRODUCT DEVELOPMENT

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What is generic drug?

A generic drug product is **essentially identical to the brand name (reference) drug products** in terms of **active ingredients, dosage form, route of administration, quality, safety, efficacy, performance characteristics and therapeutic indication.**

ex: Phenytoin (generic) Dilantin (brand name)

- Brand drugs are protected by patent.
- The FDA Generic Drugs Program **conducts a rigorous pre-approval review to make sure generic medicines meet these requirements.**

Generic drugs must meet the same high standards as brand-name drugs to receive FDA approval

- FDA requires drug companies **to demonstrate that the generic medicine can be effectively substituted and provide the same clinical benefit as the brand-name** medicine. Generic drug applicants must show the generic medicine is the same as the brand-name in the following ways:
- The **active ingredient** in the generic medicine is the **same** as in the brand-name drug/innovator drug.
- The generic medicine has the **same strength, dosage form** (such as a tablet or an injectable), and **route of administration** (such as oral or topical).
- The generic medicine is **manufactured under the same strict standards** as the brand-name medicine.
- The **label is the same** as the brand-name medicine's label (with certain exceptions).
- The generic medicine is **bioequivalent** to the brand-name medicine.

- Generic medicines tend to **cost less than their brand-name counterparts because they do not have to repeat animal and clinical (human) studies** that were required of the brand-name medicines to demonstrate safety and effectiveness.
- In addition, multiple generic drugs are often approved for the same single product; this creates **competition in the marketplace**, typically resulting in lower prices.
- FDA established the **Drug Competition Action Plan** in 2017 **to further encourage robust and timely market competition for generic products** to increase competition so that consumers can get access to the medicines they need at more affordable prices.
- New **brand-name** drugs are usually **protected by patents** that prohibit others from selling generics of the same drug.
- Periods of marketing exclusivity for brand-name drugs can also impact the timing of generic drug approvals.

Selection of generic drug for manufacture

- The main objective for the selection of generic drug product manufacture is **the estimated sales volume for the branded product**.
- And the potential market share that the firm expects to have once the generic drug product is approved for marketing.
- The generic drug manufacturer needs to consider:
 - ✓ The **lead time** that is needed to make the product and **submission of an abbreviated new drug application** to the U.S. FDA for approval.
 - ✓ There is also a **financial incentive** to being the first generic drug product filed and approved by FDA.
 - ✓ A **time period of 180 days** exclusivity is given under certain conditions, for generic manufacturer who is to file first.

- Formulation consideration for generic drugs include:
 - ✓ The availability of raw materials, chemical purity, polymorphic form.
 - ✓ Particle size of the active pharmaceutical ingredients.
 - ✓ Any patents that the innovator company has filled, including patent for synthesis of the active pharmaceutical ingredients and composition of the dosage form.

Generic drug approval process

- The FDA office of generic drugs is responsible for reviewing the ANDA and approving the drug product marketing.
- www.fda.gov.org provides the **additional information for manufactures of generic drugs products that includes flow chart presentation of ANDA review process.**
- This process also describe about that **how FDA determines the quality, safety and efficacy of generic drugs prior to the approval** for marketing.
- Generic drug application reviewers focus on **bioequivalence data, chemistry and manufacture quality, microbiology data where relevant, request for plant inspection, and drug labeling information.**

- The ANDA for generic drug product approval is **based on the bioequivalence to the brand name product, appropriate chemistry, manufacturing information, and proper labeling.**
- Generic drug sponsors **do not have to perform the nonclinical animal toxicity studies or expensive clinical efficacy and safety studies** that are included in the new drug application.
- NDA which is submitted to the FDA for market approval of the brand name drug product.
- The ANDA contains data which is then **submitted to FDA's centre for drug evaluation and research for the generic drugs.**

- FDA approved generic drugs **must meet the same rigid standards as the innovator drugs.**
- To get FDA approval, a **generic drug product must contain same active ingredient as an approved drug product where the inactive constituents may vary.**
- The identical strength, dosage form, route of administration, same indication, bioequivalence, meet the batch requirement.
- The FDA's approved drug product with therapeutic equivalence, evaluation and list of the all approved products, both innovator and generic are included in the **orange book.**

Orange book

- On approval of NDA, FDA publishes patent information of drug are included in orange book.
- **Objective:**
 - ✓ It contains **therapeutic equivalence evaluations** for approved prescription drug products.
 - ✓ These evaluations are been **prepared to serve as public information.**
 - ✓ To advise **to state the health agencies, prescribers, pharmacists to promote public education** in area of **drug product selection.**
 - ✓ To review **the patterns of access and usage.**
 - ✓ To allow **discovery of repeated attempts** to bypass protections.
 - ✓ To **supply an additional form of users assurance.**

Contents of orange book:

- Introduction
- Content and exclusion
- Reference listed drugs
- General policies and legal status
- Drug product list
 - ✓ Prescription drug product list
 - ✓ OTC drug product list
 - **The orange book is comprises of 4 parts**
 - a. Approved prescription drug products with the therapeutic equivalence evaluations.**
 - b. Approved OTC drug products.**
 - c. Drug products with approval under section **505** of the FDC act.
 - d. A **cumulative list of approved drug** products that have never been marketed.

Steps for generic drug development process

- Concept development
 - System level design
 - Detail design
- Testing and refinement
 - Production ramp up

- **Concept and development:**
 - ✓ The needs of the target market are identified, alternative product concepts are generated and evaluated and a single concept is selected for further development.
- **System level design:**
 - ✓ It includes the definition of the product in to sub system and components.
 - ✓ The final assembly scheme for the production system is usually defined during this phase.
- **Detail design:**
 - ✓ it includes the complete specifications of the geometry, materials and tolerances of all the unique parts in the product and the identification of all the standards parts to be purchased from suppliers.
 - ✓ A process plan is established and tooling is designed for the each part to be fabricated with in the production system.

- **Testing and refinement:**

- ✓ It involves the **construction and evaluation of multiple pre-production version of the product.**
- ✓ **Early prototypes** are usually **built with production intent parts** (parts with **same geometry and material properties** as intended for the production version of the product).
- ✓ Early prototypes are tested to **determine whether the product will work as designed and whether it satisfies customers needs.**
- ✓ The goal of prototypes are usually **used to answer questions about performance and reliability** in order to **identify changes for the final product.**

- **Production ramp up:**

- ✓ The purpose is **to train the work force and to workout any remaining problems** in the **production process.**
- ✓ The artifacts produced during production ramp up are sometimes **supplied to the preferred customer** and are **carefully evaluated to identify any remaining flaws.**