Generic Drugs

Today's Discussion

- What is a Generic Drug?
- Why Should You be Interested?
- Marketing Issues
- Information Sources

What is a Generic Drug?

Brand vs. Generic

What is the Main Consumer Concern Regarding Generics?

- **Do the quality and performance of generic drugs compare to brand drugs?**

Often triggered by brand companies and physicians

Legislative History

- **1906 Pure Food and Drug Act - establishes regulation of Food and Drugs.**
- **1938 Food, Drug and Cosmetic Act - introduced safety standards.**
- **1962 Kefauver-Harris Amendments to the FDA&C Act - tightened safety standards and introduced requirement that drugs must be effective.**
- ***1984 Hatch-Waxman Act* - created an *abbreviated* mechanism for approval of generic copies of all drugs originally approved after 1962, by stating that pre-clinical and clinical testing does not have to be repeated for generics.**

Definition of a Generic Drug

A drug product that is comparable to a brand/reference listed drug product in dosage form, strength, route of administration, quality and performance characteristics, and intended use.

Prior to this, companies had to independently establish the safety and efficacy of their generics.

When can a Generic Drug be Marketed?

- After patent & exclusivity protection ends, or
- patent owner waives its rights, and
- FDA requirements are met

Patent Protection

- **17 years from the date the patent was issued or 20 years from the date *submitted to the Patent Office*, not FDA**

Approximately 12 years of marketing protection

Exclusivity

- **Award/reward of marketing protection of 3 to 5 years for innovative development to an existing product (i.e. new uses, strengths)**
- **6 months for pediatrics**

What are the Basic Generic Drug Requirements?

- Same active ingredient(s)
- Same route of administration
- Same dosage form
- Same strength
- Same conditions of use
- Inactive ingredients already approved in a ***similar*** NDA

NDA vs. ANDA Review Process

Brand Name Drug (NDA) Requirements	Generic Drug (ANDA) Requirements
1. Chemistry	1. Chemistry
2. Manufacturing	2. Manufacturing
3. Controls	3. Controls
4. Labeling	4. Labeling
5. Testing	5. Testing
6. Animal Studies	
7. Clinical Studies	6. Bioequivalence
8. Bioavailability	

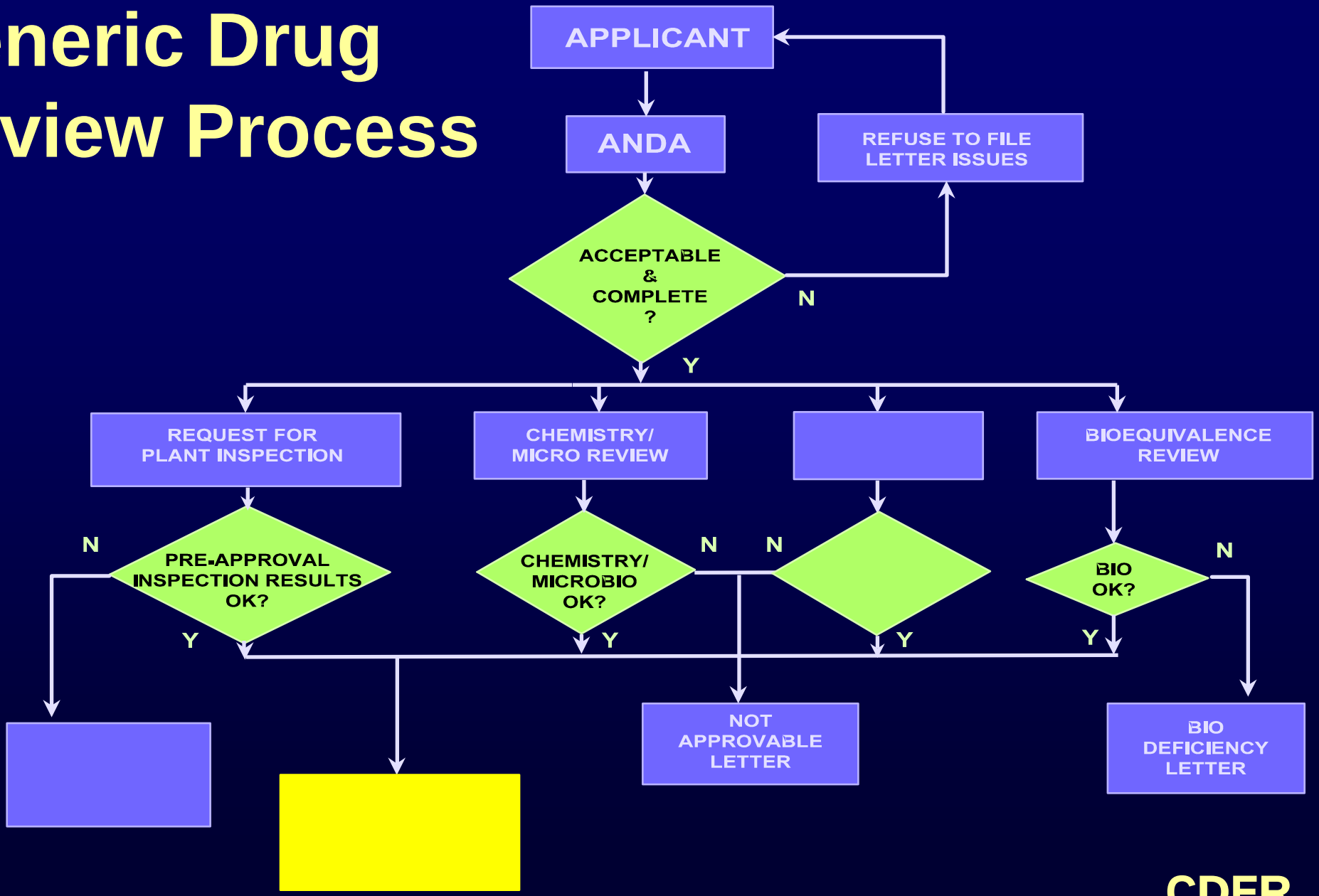
What is Bioequivalence?

A generic drug is considered to be bioequivalent to the brand name drug if:

- **The rate and extent of absorption do *not* show a significant difference from the listed drug, *or***

- **The extent of absorption does *not* show a significant difference and any difference in rate is intentional or *not* medically significant**

Generic Drug Review Process



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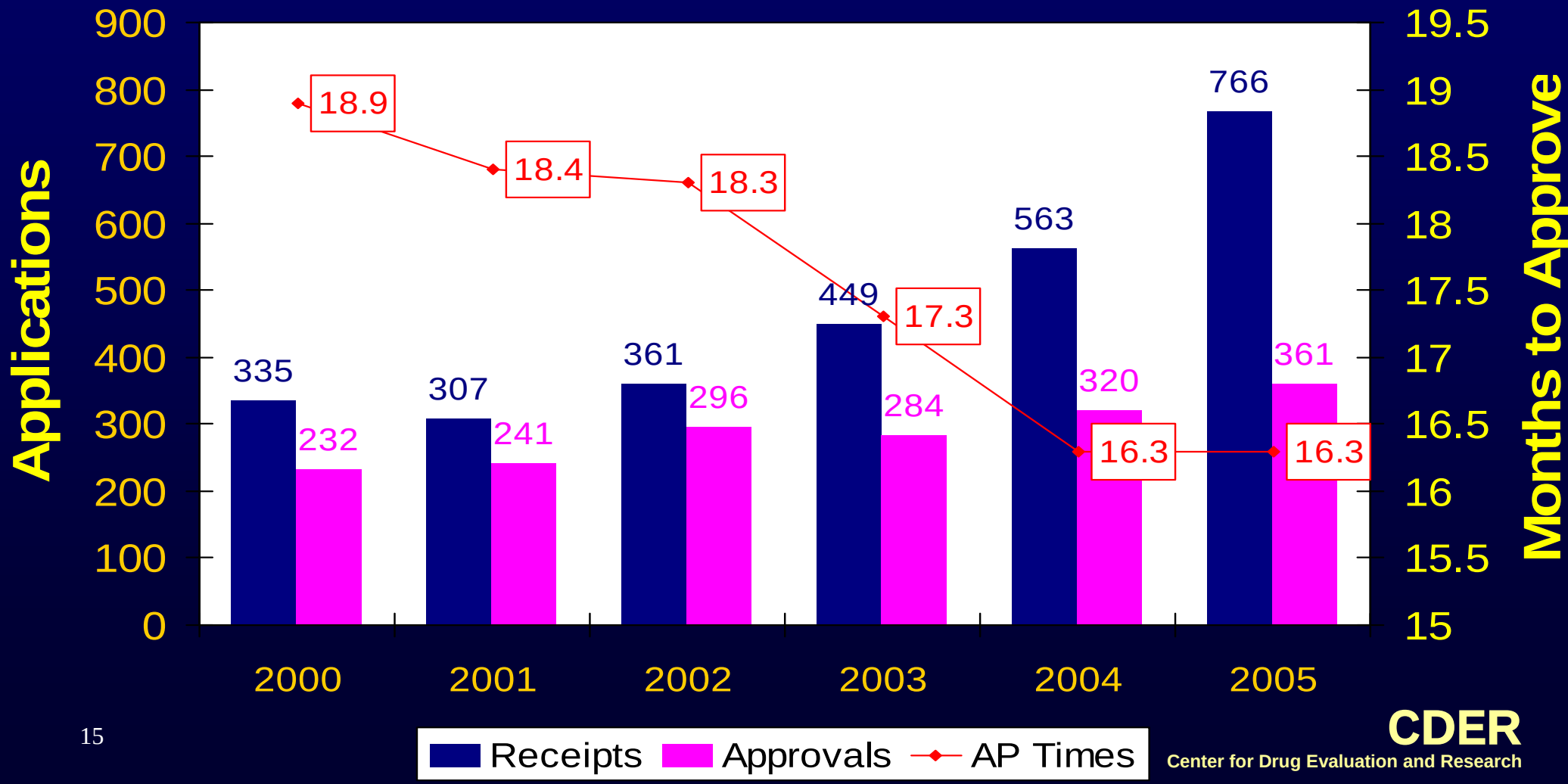
Center for Drug Evaluation and Research

Statistics



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Post-Marketing

- **Same policies & systems as new/brand drugs**
- **Product quality surveys – a recent review of 1,159 studies submitted to OGD revealed that the average difference between generics and their respective brand drugs was 3%**

How is Quality Assured?

- First 5 steps of review identical to NDA
- Bioequivalence same as NDAs
- FDA has experience with the product
- Product is known to be safe
- Scientific literature published
- Over half produced by brand manufactures
- Post-approval product surveys

To make sure your generic drug meets your approval, it first has to get ours.

When FDA approves your generic drugs, it ensures they are safe and effective. All generic drugs are put through a rigorous, multi-step approval process. From quality and performance to manufacturing and labeling, everything must meet FDA's high standards. We make it tough to become a generic drug in America so it's easy for you to feel confident. Visit www.fda.gov/cder/ or call 1-888-INFO-FDA to learn more.

Generic Drugs: Safe. Effective. FDA Approved.

U.S. Department of Health and Human Services
Food and Drug Administration

The Ultimate Endorsement for Generics

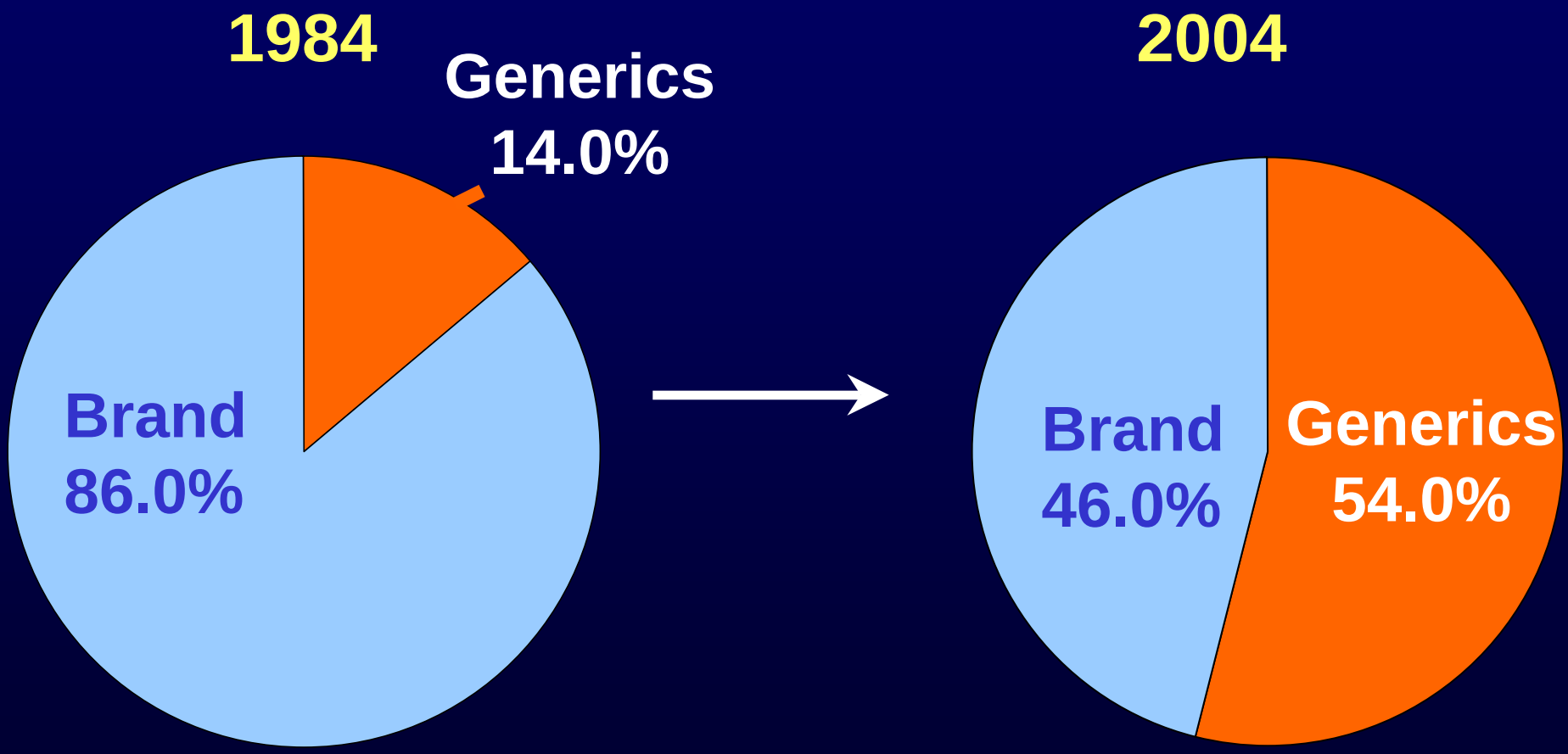
- Drug Shortages
  - Product rationalization
  - Supply disruption

Why Should You be Interested?

Economics

Frequency of Generic Drugs Use?

Prescription Drugs

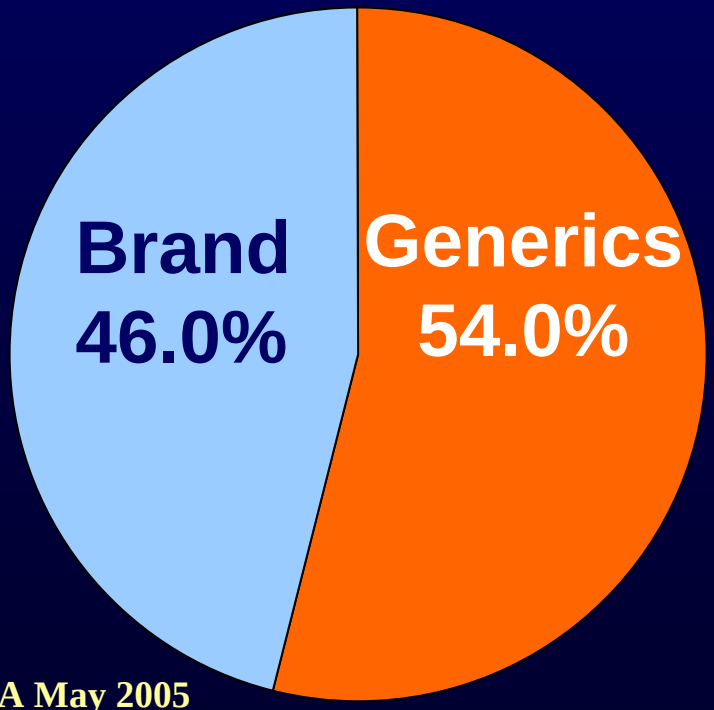


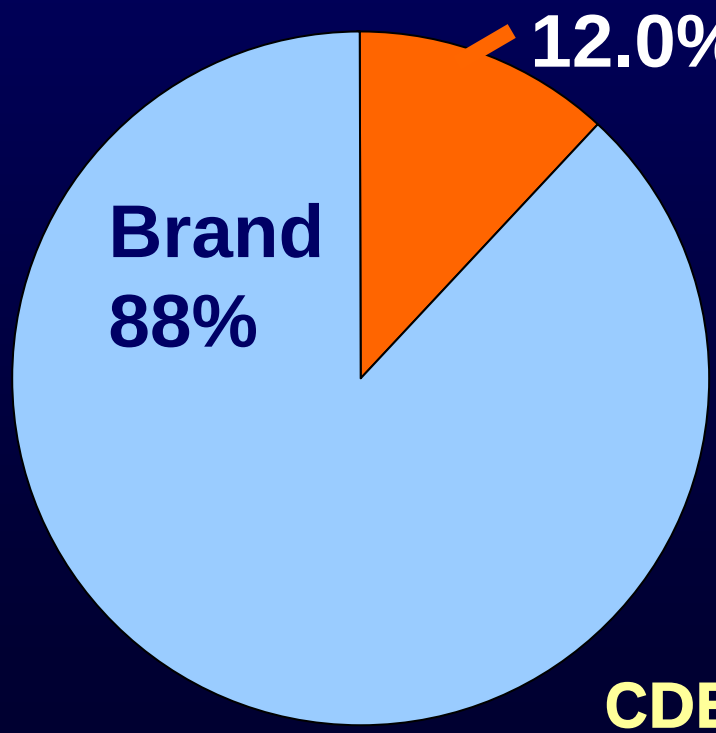
Market Share vs. Dollar Volume?
$250 billion

Prescription Volume

2005

Sales





Estimated Savings Through Generic Drug Use

$67 per retail prescription

or

$10.0 Billion a Year

DHHS Dec. 2004 "if consumers were to buy generic products whenever possible ... we estimate savings to be approximately $17 billion."

Future

Over $100 billions worth of drug products losing protection in the next five years

Top Selling Drugs U.S.

Drug name (maker)	Treatment area	Sales
1. Lipitor (Pfizer)	Cholesterol	$8.4 billion
2. Zocor (Merck)	Cholesterol	$4.4 billion
3. Nexium (AstraZeneca)	Ulcer	$4.4 billion
4. Prevacid (TAP/Abbott)	Acid reflux	$3.8 billion
5. Advair Diskus (GlaxoSmithKline)	Asthma	$3.6 billion
6. Plavix (Bristol-Myers Squibb)	Heart attack	$3.5 billion
7. Zoloft (Pfizer)	Depression	$3.1 billion
8. Epogen (Amgen)	Anemia	$3.0 billion
9. Procrit (Johnson & Johnson)	Anemia	$3.0 billion
10. Aranesp (Amgen)	Anemia	$2.8 billion

SOURCE: Bloomberg News, Feb. 2006

Marketing Issues

Applicant Issues

- Submission of a complete application – avoid being “refused to receive”
- Efforts underway to accept electronic submissions
- Proper patent and exclusivity certification – watch for additions
- Assure that any and all Drug Master Files (DMFs) are properly referenced and submitted to the Agency
- Assure all facilities ready for inspection

Critical Path Initiative

- Medical product development path is becoming increasingly challenging, inefficient and costly
- Need to update tools used to assess safety and efficacy
- "Toolkit" should contain powerful new scientific and technical methods to improve predictability and efficiency along the critical path from laboratory concept to commercial product

Question Based Review

- Specifications based on benefit to the consumer - eliminate non-scientific controls with no value to product quality
- Product specific risk assessment
  - Reduce supplements
  - Use FDA resources effectively
- Keep review up to date with advances in manufacturing and formulation science
  - Quality by Design
  - Process Analytical Technology

Quality by Design

- Understanding the product as it is developed and designed
- Understanding critical attributes
- Designing product and process to be robust with regard to these attributes
- Knowing what happens to those attributes if changes are made in production
- Provide the tools to utilize risk based approaches

Process Analytical Technology

- **A system for designing, analyzing, and controlling manufacturing through timely measurements (i.e., during processing) of critical quality and performance attributes of raw and in-process materials and processes with the goal of ensuring final product quality.**

International Conference on Harmonization (ICH)

- To harmonize the interpretation and application of technical guidelines and requirements
- To reduce or eliminate duplicate testing during research and development in participating countries

Approaches to Streamline the Review Process

- Reduce the number of review cycles
- Improved/increased communications
  - telephone calls for clarifications
  - email communications
- Revision of first-in, first-reviewed policy to utilize review expertise

- **Applicant (internet) access to dissolution and bioequivalence information (frees up reviewer time)**
- **Process enhancements**
  - **Early DMF review**
  - **Early dissolution review**
  - **Clustered application reviews**

Information Sources

APPROVED DRUG PRODUCTS

WITH THERAPEUTIC EQUIVALENCE EVALUATIONS

26 TH EDITION

THE PRODUCTS IN THIS LIST HAVE BEEN APPROVED UNDER SECTIONS 505 AND 507 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF MANAGEMENT
DIVISION OF DATABASE MANAGEMENT

2006

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Center for Drug Evaluation and Research

"Orange Book"

- **All FDA approved drug products listed (NDA's, ANDA's and non-monograph OTC's)**
- **Therapeutic equivalence codes for NDAs & ANDAs**
  - **"A" = Substitutable**
  - **"B" = Inequivalent, NOT substitutable**
- **Expiration dates: patent and exclusivity**
- **Reference Listed Drugs - brand drugs identified by FDA for generic companies to compare their proposed products against**

Orange Book Internet Address

http://www.accessdata.fda.gov/ob/

Office of Generic Drugs Home Page

http://www.fda.gov/cder/ogd/index.htm

Application Process Page

http://www.fda.gov/cder/regulatory/applications/anda.htm

Inactive Ingredient Database

http://www.accessdata.fda.gov/scripts/cder/iig/index.cfm

Dissolution Methods Database

http://www.accessdata.fda.gov/scripts/cder/dissolution/index.cfm

Questions?

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Center for Drug Evaluation and Research
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