What's new in CDER, 2006

ORA San Francisco District Office

Alameda, California

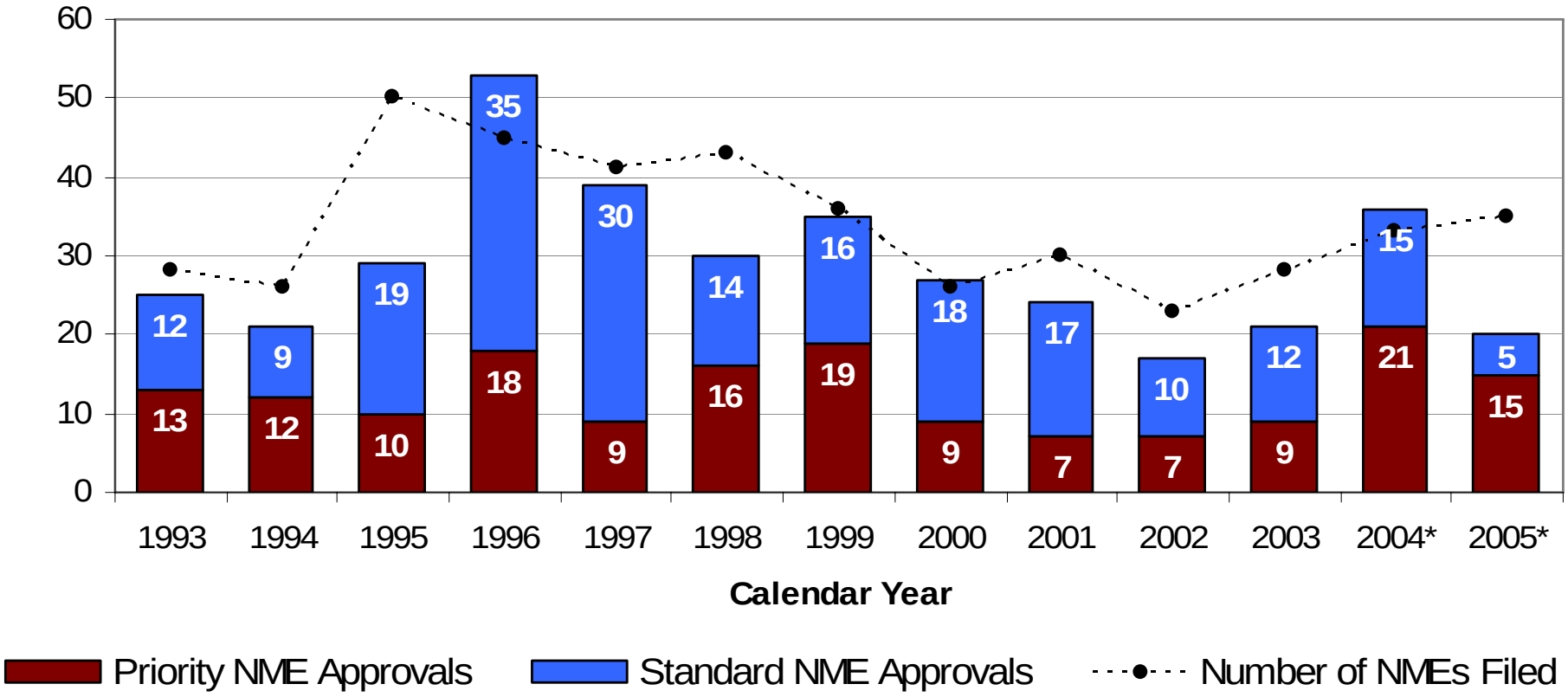
January 23, 2006

Steven K. Galson, M.D., MPH
Director
Center for Drug Evaluation and Research
Food and Drug Administration

Outline

- 2005 new drug approval statistics and trends and what they mean for the pharmaceutical industry
- CDER's Drug Safety Initiative
- Recent improvements in drug regulation, review and communication
- Q&A

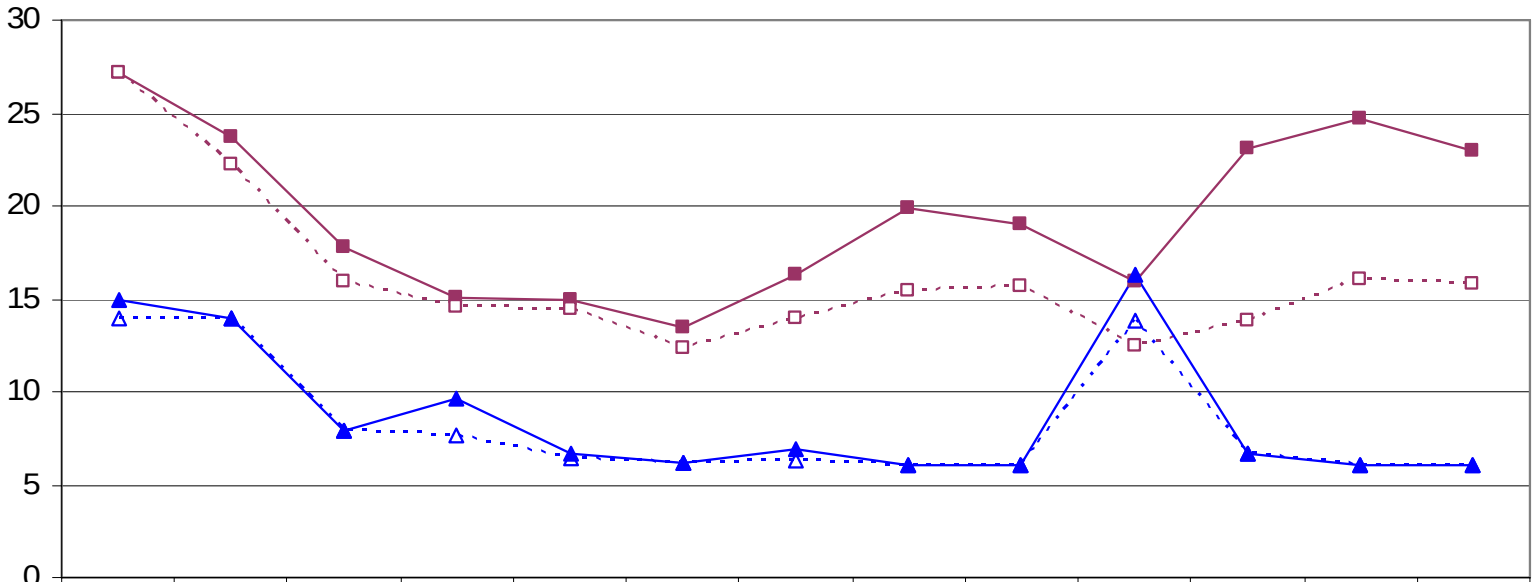
CDER New Molecular Entity and New Biologic Approvals by Calendar Year*



*Beginning in 2004, these figures include new BLAs for therapeutic biologic products transferred from CBER to CDER effective 10/1/2003.

CDER Standard and Priority NME and New BLA Approval Times*

Median of FDA Review Time and Total Approval Times (months)



	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004*	2005*
Standard Total AP Time	27.2	23.7	17.8	15.1	15.0	13.4	16.3	19.9	19.0	15.9	23.1	24.7	23.0
Standard FDA Time	27.2	22.2	15.9	14.6	14.4	12.3	14.0	15.4	15.7	12.5	13.8	16.0	15.8
Priority Total AP Time	14.9	14.0	7.9	9.6	6.7	6.2	6.9	6.0	6.0	16.3	6.7	6.0	6.0
Priority FDA Time	13.9	13.9	7.9	7.7	6.4	6.2	6.3	6.0	6.0	13.8	6.7	6.0	6.0

*Beginning in 2004, these figures include new BLAs for therapeutic biologic products transferred from CBER to CDER effective 10/1/2003.

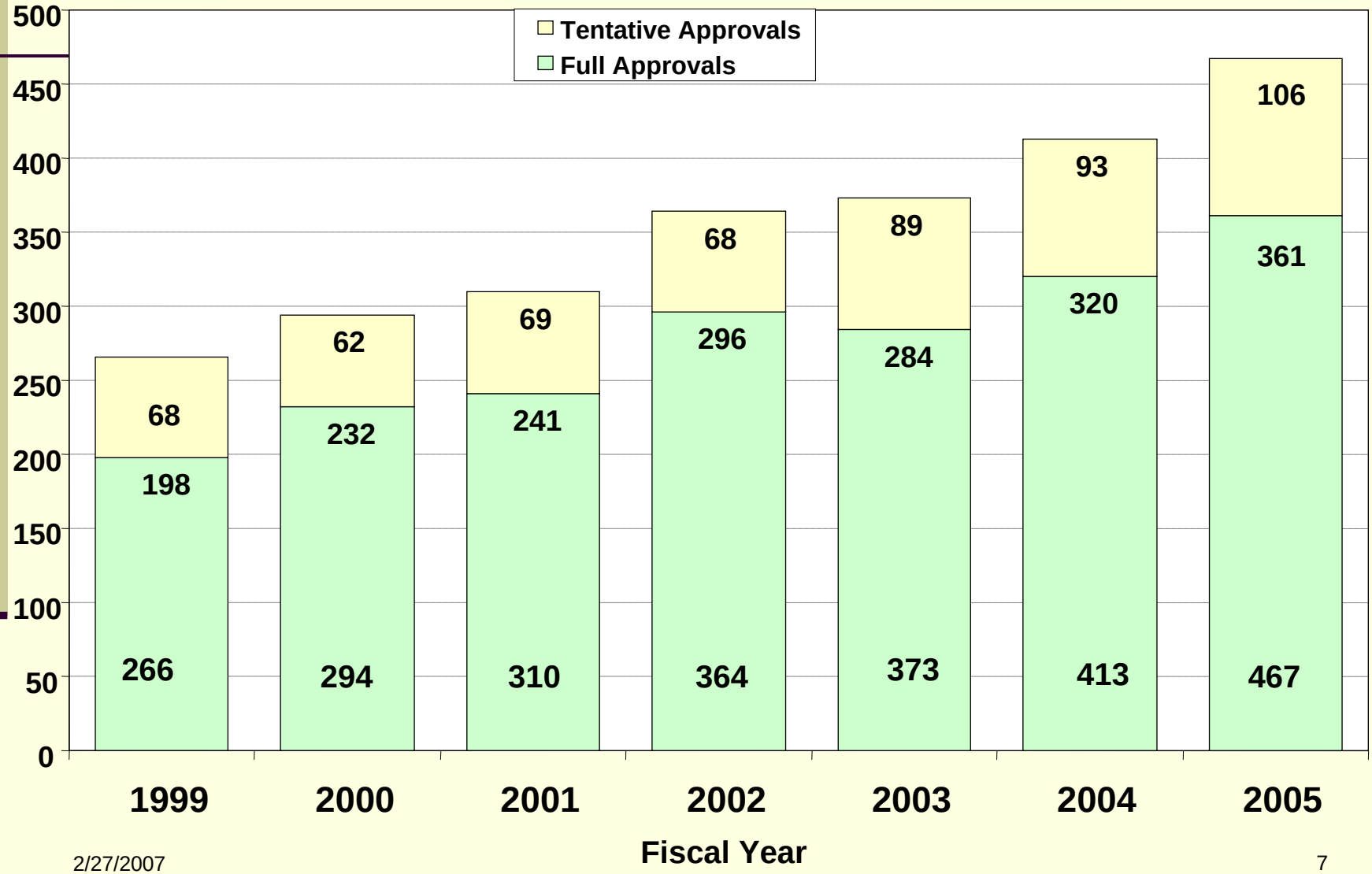
Fewer NMEs in 2005…

- Agency processes for approving new drugs unchanged; companies submitting fewer applications
  - Good news: Interaction with fda reviewers becoming more intense but may be detracting from speed of standard reviews
- Drug development not keeping pace with drug discovery
  - Industry investment in research continues to grow – now at ~$38 billion
  - Making progress in the laboratory – e.g., genomics
- Looking for new ways to speed development of new treatments
  - Critical Path Initiative
    - C-Path Institute, CP Opportunities List

Notable Approvals in 2005

- *Baraclude (entecavir)* – hepatitis B
- *Increlex (mecasermin)* – growth failure in children
- *Velcade (bortezomib)* – multiple myeloma
- *BiDil (hydralazine/isosorbide dinitrate)* – heart failure
- *Aptivus (tipranivir)* – antiretroviral/HIV1
- *Orencia (abatacept)* – active rheumatoid arthritis
- *Exjade (deferasirox)* – chronic iron overload due to transfusions
- *Revlimid (lenalidomide)* – transfusion dependent anemia
- *Nexavar (sorafenib)* – advanced renal cell carcinoma

Generic Drug Approvals



Issues in Generic Drug Review

- Increasingly important to controlling US healthcare costs
- Workload outpacing available FDA resources
- Scientific progress needed to determine bioequivalence for certain products, ie inhaled and topical drugs
- Solutions needed to head off slow-down

Drug Safety Initiatives

Update

Drug safety initiatives will…

- Give patients, healthcare professionals and other consumers quick and easy access to the most up-to-date and accurate information on medicines
- Make FDA's drug review, approval, and monitoring programs as transparent as possible

FDA Response on Drug Safety

Progress on Announcement in 2004

- Institute of Medicine (IOM) Study of the Drug Safety System – ongoing, summer completion
- Implement a Program for Adjudicating Differences of Professional Opinion - completed
- Appoint Director, Office of Drug Safety - completed
- Conduct Drug Safety/Risk Management Consultations - ongoing
- Publish Risk Management Guidance - completed

FDA Response on Drug Safety

HHS Secretary Leavitt's announcement in February, 2005

- Get more outside expert consultations
  - 27 Advisory Committee meetings
  - Risk communication, Direct-To-Consumer promotion Part 15 Hearings
- Improve how drug safety is managed at the FDA – DSOB, 5 meetings
- Improve FDA communication about emerging drug risks to give patients, healthcare professionals and other consumers access to emerging safety data earlier
  - 63 Health Care Provider and 59 Patient info sheets
- Continue our work to improve scientific methods of safety signal detection – drug safety contracts

External studies/Investigations Underway

- Institute of Medicine
- General Accounting Office/ US Congress
- HHS Inspector General
- Open Congressional Investigations

IOM Study

- Study began in January 2005
- Committee has had three meetings (June, July, October); fourth scheduled for January 17-19, 2006
- Detailed information about each of the meetings http://www.iom.edu/CMS/3793/26341.aspx
- Have interviewed large number of stakeholders, including many FDA staff
- IOM hopes to issue a final report in July 2006

Drug Safety Oversight Board
Progress in 2005

- Established the Board
- Held five meetings
- Organizing and refining procedures and deliberations
- Focusing on critical and pressing safety issues
- Planning underway for applying a quality management system approach

Themes from meetings

- Informative sessions on drug safety
- Oversight of CDER safety issues
  - Pre-decisional
    - Make recommendations for ongoing CDER activities
  - Post-decisional
    - Review of decisions about safety communications
- Policy development
- Commercial confidential nature of the data used in many of the discussions

Proposed Drug Watch Draft Guidance

- Many comments
- Support for early communication but unfavorable comments about Watch concept itself
- Collating/ summarizing
- Policy to be revised, as appropriate

Surveillance Contracts

- Epidemiologic Studies of Adverse Effects of Marketed Drugs
  - Conduct drug safety analyses proactively
  - Respond to urgent public safety concerns
- 4 new contracts:
  - Kaiser Foundation Research Institute (Oakland, CA)
  - Vanderbilt University (Nashville, TN)
  - Harvard Pilgrim Health Care (Wellesley, MA)
  - Ingenix, Inc (Auburndale, MA)

Key Points on Safety

- 50 % of CDER resources spent on drug safety – every office, most activities
- Many new initiatives underway to improve: pre and post-market analysis & communication
- Fundamental progress in drug safety will be made only with continued scientific investments and scientific progress (key component of Critical Path)
- Separating pre and post- marketing functions and communication wasteful and potentially hazardous
- No objective evidence of hypothesized conflict-of-interest within CDER

Improvements in Drug Regulation/Review

Physician Labeling Rule (PLR) – promulgated last week

Physician Labeling Rule

- Final rule, titled *"Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products"*
- Requires prescribing information of new and recently approved products
  - Highlights of the prescribing information
  - Table of contents
  - Reordering and minor content changes
  - Minimum graphical requirements

PLR (cont'd)

- Benefits
  - Easier for healthcare professionals to access and use information
  - Increase extent to which professionals rely on labels to obtain information
  - Enhance safe and effective use of prescription drug products
  - Reduce number of adverse reactions resulting from medication errors due to misunderstood or incorrectly applied drug information

Improvements in Drug Regulation/Review

cGMP Initiative

Status of cGMPs for the 21st Century Initiative

- September 2004 “Final Report” **not the end**, but the beginning of the next phase
  - Completed 2-year *assessment* initiative
  - Released with 6 guidance documents and 6 white papers and similar documents
  - Reaffirms and expands upon the vision of the initiative

cGMPs for Investigational New Drug Applications (INDs) – one example of ongoing efforts

- Making earliest stages
  Of drug development more efficient
- Modernize existing cGMP regulations to streamline clinical development

INDs – Guidance

- *Exploratory IND Studies* and *INDs—Approaches to Complying with CGMP During Phase 1*
  - specific approaches for
    - researchers planning to conduct very early clinical studies in people
    - performing appropriate safety testing
    - producing small amounts of drugs safely

INDs – Guidance (cont'd)

- *Approaches to Complying with CGMP During Phase 1*
  - Formally recognize specific standards for manufacture of small amounts of drug product for phase 1 studies
  - Provides guidance on formulating an approach to cGMP compliance appropriate for the particular stage of drug development
    - Formerly, companies were required to comply with same GMP for companies mass producing drugs

Improvements in Drug Regulation/Review

Pharmacogenomics

Development: VGDS

- Voluntary Pharmacogenomics Data Submissions
  - Informal format for exchange of scientific information and ideas
  - Separate from formal regulatory advice tied to individual drug development
- Genomics information included in labeling:
  - Erbitux
  - Herceptin
  - Strattera
  - 6-Mercaptopurine (6-MP)

Pharmacogenomics (PGx)

- Received 25 requests for VGDS PGx Meetings
  - Four requests for FDA-EMEA VGDS joint bilateral briefings
- Held 13 VGDS meetings in 2005
  - Including 2 FDA-EMEA joint briefings
  - Covered following therapeutic areas:
    - Cancer (multiple types)
    - Alzheimer's Disease
    - Hypertension
    - Hypoglycemia
    - Depression
    - Obesity
    - Rheumatoid Arthritis

Pharmacogenomics (cont'd)

- Held two FDA/PhRMA/BIO/DIA public workshops and an FDA Advisory Committee meeting on pharmacogenomics
  - Pharmacogenomics Workshop #3, Optimizing the Benefit/Risk of Drug Development and Therapy, May 2005
  - Application and Validation of Genomic Biomarkers for Use in Drug Development and Regulatory Submissions, October 2005
- FDA Advisory Committee for Pharmaceutical Science, Clinical Pharmacology Subcommittee, November 2005

Pharmacogenomics (cont'd)

- Finalized the Guidance for Industry: Pharmacogenomic Data Submissions, March 2005
- Published the Pharmacogenomic Drug Device Co-development Concept Paper, April 2005
- Co-developed with the American Medical Association and Online Course: Personalized Medicine Online Course: Personalized Medicine

FDA Genomics Website

www.fda.gov/cder/genomics

Improvements in Drug Regulation/Review

CDER Reorganizations

2005 Reorganizations

- CDER Office of New Drugs reorganization completed 10/11/05
  - Merger of therapeutic biologics with relevant Divisions
    - Promote best practices
    - Unite subject-specific expertise in a single division
  - Reorganization of review divisions
    - Workload distribution
    - Balance sizes
    - Promote logical grouping
  - Creation of the Office of Nonprescription Products
    - Review responsibility for NDA products
    - Continue important monograph work
- 1500 CDER staff relocated to the White Oak campus
  - From 20 buildings to 1

2006 Proposed Reorganization
Goals

- Reflect the commitment of CDER to sustained, multi-disciplinary, cross-Center approach to drug safety
  - Placement in organization must reflect level of commitment
  - Need focus and consistency and improvement in communication about drug risks and benefits
  - Need focus for cross-center policy development
- Locus for Critical Path Activities

2006 Reorganization
Proposal

- New Associate Center Director – drug safety policy and risk communication focus
  - Consolidate certain communications activities
- Elevated organizational status unit responsible for epidemiology and surveillance (current Office of Drug Safety)
  - Report to Center Director
- New “super-office” combining OCPB, OB, responsible for CP projects and other cross-cuttting science activities

Overall Summary

- Pipeline challenges continue as agency enters PDUFA IV discussions
- While outside evaluations on drug safety underway, CDER is making important process improvements.
- Pharmacogenomics initiative and efforts to improve efficiency and consistency of new drug review program represent important incremental improvements.

Questions?

Steven.Galson@fda.gov