CDER Priorities for 2009

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Backdrop: FY 2008

- 2008 was an eventful year
- Abrupt change in Center leadership:
  - JW acting Center Director 10/07-
  - Permanent Center Director 3/08
- Passage of FDA Amendments Act
- Heparin contamination crisis
- Large hiring surge for CDER: over 600 hires
- Developing new Amendment Act procedures, policies and documents

2008 Priorities

- CDER management team set immediate priorities for 2008/early 2009 in the face of overwhelming demands on people's time
- Overarching priority: restore credibility of drug regulatory process
- Many other of the priorities reactive: required to respond to PDUFA reauthorization, multiple sections of FDA AA, IOM report on drug safety, etc.
- Organized priorities around "lines of business" model

CDER “Lines of Business”

- Organizing framework for “what we do” at CDER

- Three lines of business
  - Oversee drug development: new drugs; OTC drugs; generic drugs
  - Oversee postmarket safety and promotion
  - Oversee drug quality throughout lifecycle

Multiple essential crosscutting activities support these

Overseeing Drug Development: Selected 2008 Priorities

- Implement FDAAA premarket provisions
- Address skepticism about generics
- Implement good review management practices (GRMP)
- Conduct Safety First Initiative

Safety First

- Make sure drug safety is our first priority
- Organized implementation of FDAAA safety provisions
- Identify and track drug safety issues: manage timelines as we do PDUFA goals
- Appointed Deputy Director for safety in each new drug division, also safety project manager
- Develop and refine tracking application

Safety First: "Equal Voice"

- OSE/OND signed MOU about roles and responsibilities
- ALL disciplines, not just OSE and OND, have role in assuring drug safety and efficacy
- Equal voice= disciplines have equal voice
- Being implemented now
- Essential as other sources of scientific knowledge need to be incorporated into our evaluation of drugs

Oversee Postmarket Safety and Performance: 2008 Priorities

- Strengthen Office of Surveillance and Epidemiology
- Launch Safe Use Initiative
- Implement MedWatch Plus
- Develop Sentinel
- Take action on pediatric monographed cough and cold products

Strengthening Office of Surveillance and Epidemiology

- Goal: world leader in phamacovigilance and pharmaceutical risk management
- Large staff buildup with appropriations and PDUFA
- Assume lead on certain activities as gain capacity
- Improve procedures and business practices
- Build up scientific capacity

Safe Use Initiative

- Vast majority of harm from approved drugs comes from misuse, inappropriate use, abuse, medical mixups, etc.
- Come from interaction of inherent properties of drug with characteristics of our healthcare system
- FDA does not control the healthcare system
- Improving use of marketed drugs involves influence rather than control

Safe Use

- Plan to start in January 09
- Implement public-private partnership around "safe use" of medical products
- Why PPP? Venue to share best practices and problems in non formal setting. Shared responsibility, not FDA's alone
- Multiple candidate drug safety issues being surfaced in CDER

Overseeing Safety of Marketed Drugs: FDAAA Implementation

- FDAAA provided new resources for postmarket safety activities
- FDA 2008 supplemental also provided funding for IT investment in drug safety
- FDAAA called for establishment of “active surveillance” system using health care databases

Safety Surveillance Enhancements

- Plan to replace old AERS system with MedWatch Plus system
- Have let multiple contracts with database sources and with expert groups to enhance surveillance capacity
- Announced Sentinel initiative

MedWatch Plus

- Two separate, connected projects
- Easy online AE reporting for healthcare professionals and patients
  - Project ongoing
  - Partnering with NIH
  - NIH plans to use for clinical trial AE reports
- Purchase new pharmacovigilance system for Agency, install
  - Will need customization for various product types
  - Will use common report format

Ongoing Active Surveillance Pilot Projects

- OMOP (Observational Medical Outcomes Pilot): FNIH, FDA, PhRMA, large methodologic evaluation pilot
- FDA-CMS-ASPE pilot
  - Part D and other Medicare data
  - Evaluate ability to find signals
- eHealth Initiative Pilot: "Connecting Communities for Drug Safety Collaboration
  - Methodologic pilot
  - FDA serving in advisory role

Sentinel Initiative

- Use large claims databases and e-HRs for analysis of drug outcomes
- Link in “distributed network”
- Patient data stays behind firewalls
- Results of analysis shared
- “Network” is enabling infrastructure
- FDAAA call for access to:
  - 25M patient records by 2010
  - 100M patient records by 2012

Sentinel Initiative: Progress

- FDA has held 9 stakeholder meetings
- Solicitation for work on 8 topics
  - Developing a governance and operations structure
  - Engagement of patients, consumers and healthcare professionals
  - Defining and evaluating possible database models

2008 Priorities: Oversight of Drug Quality

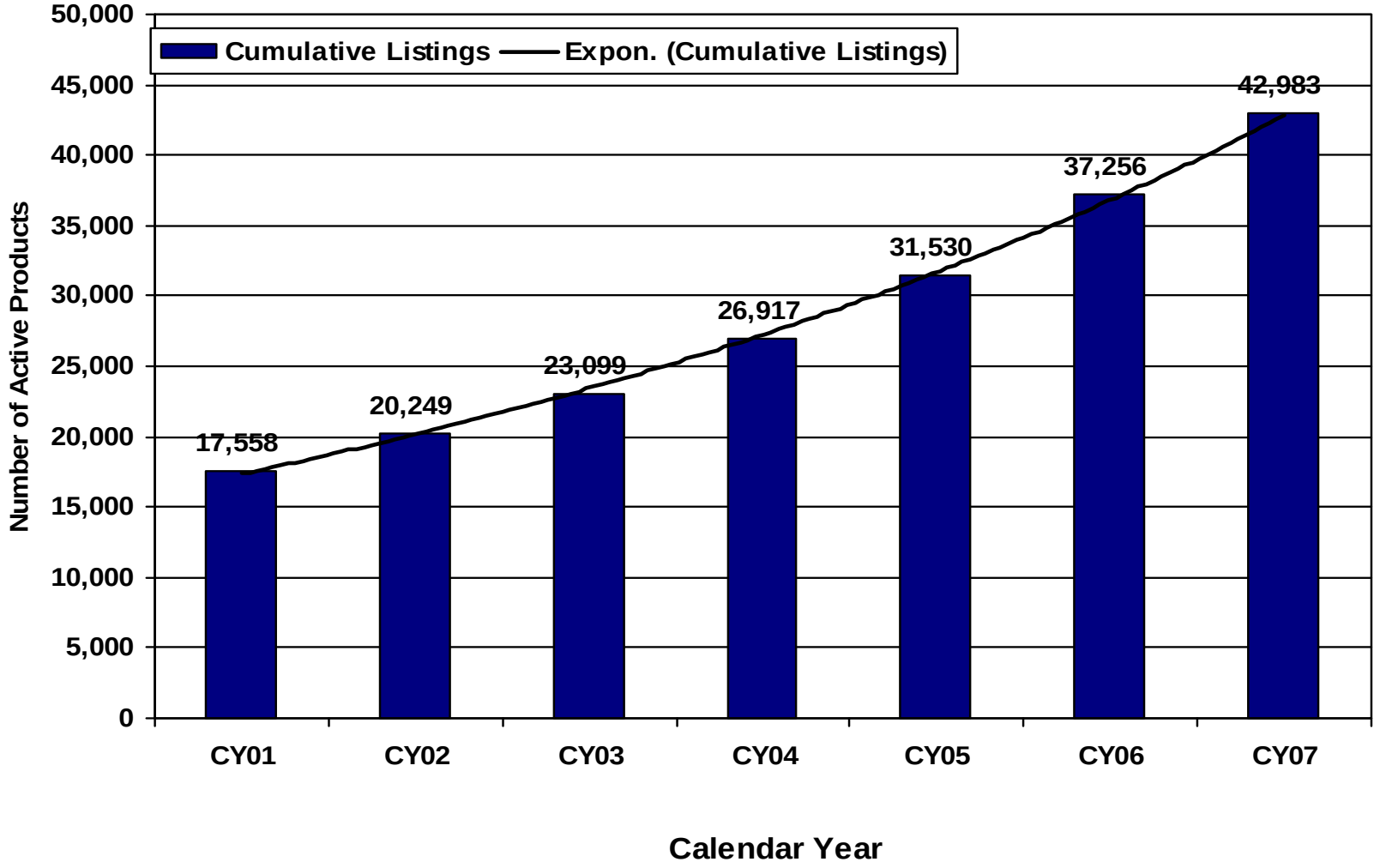
- Perform rigorous evaluation of future needs for assuring drug quality in the global environment
- Reinvigorate “Pharmaceutical Quality for the 21st Century” Initiative
- Push forward on “Unapproved Drugs” initiative

Evaluation of Needs for Oversight of Drug Quality in a Global Environment

- Heparin incident was a wake-up call
- Drug containing a large amount (wt/wt) of contaminant passed acceptance testing for API and finished product and entered drug supply
- Not detected until severe reactions occurred in patients

Number of Drug Products* Manufactured at Foreign Sites Has More Than Doubled Since 2001

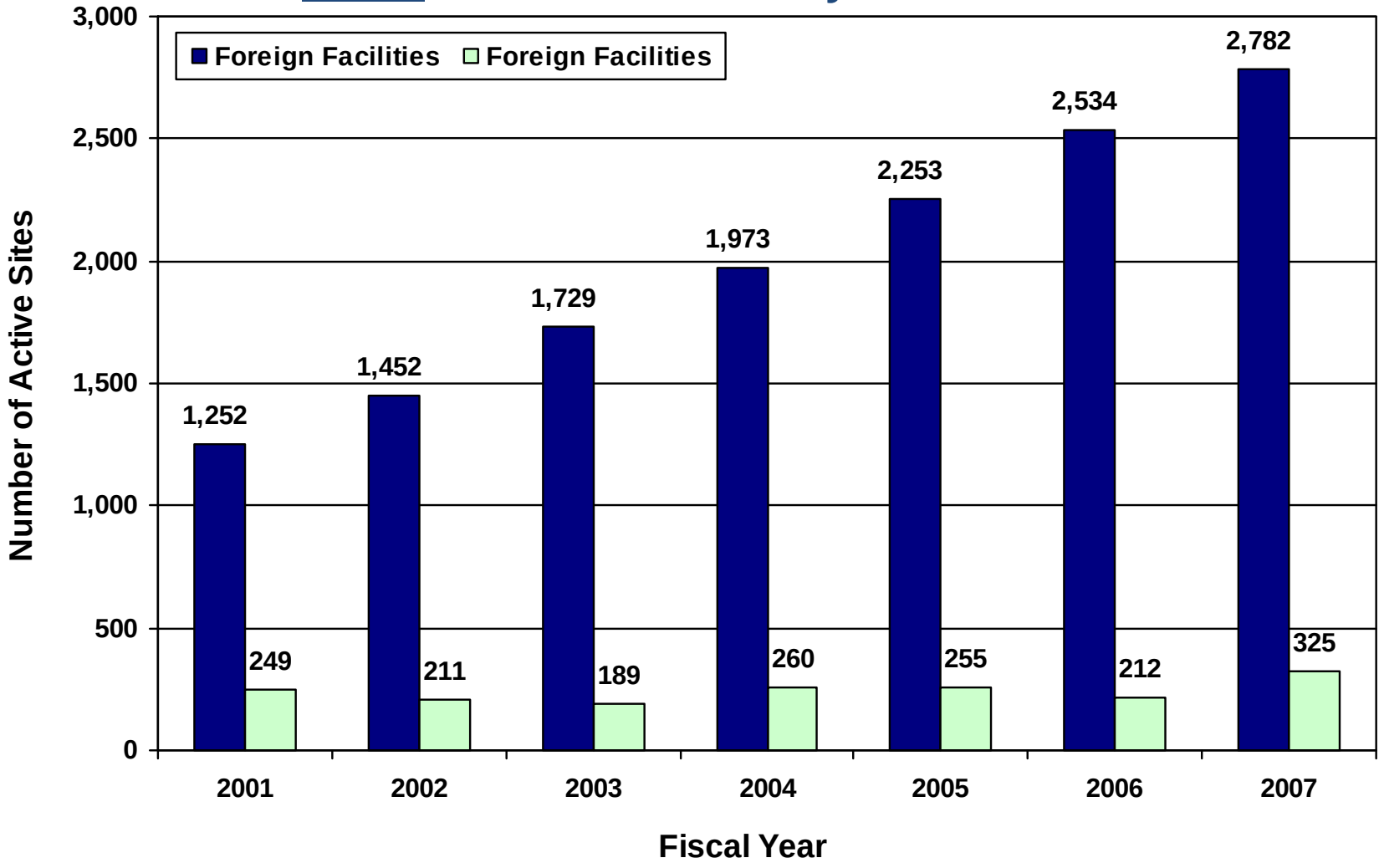
Listed by Registered Manufacturing Sites



Data Source: FDA/CDER Drug Registration and Listing System

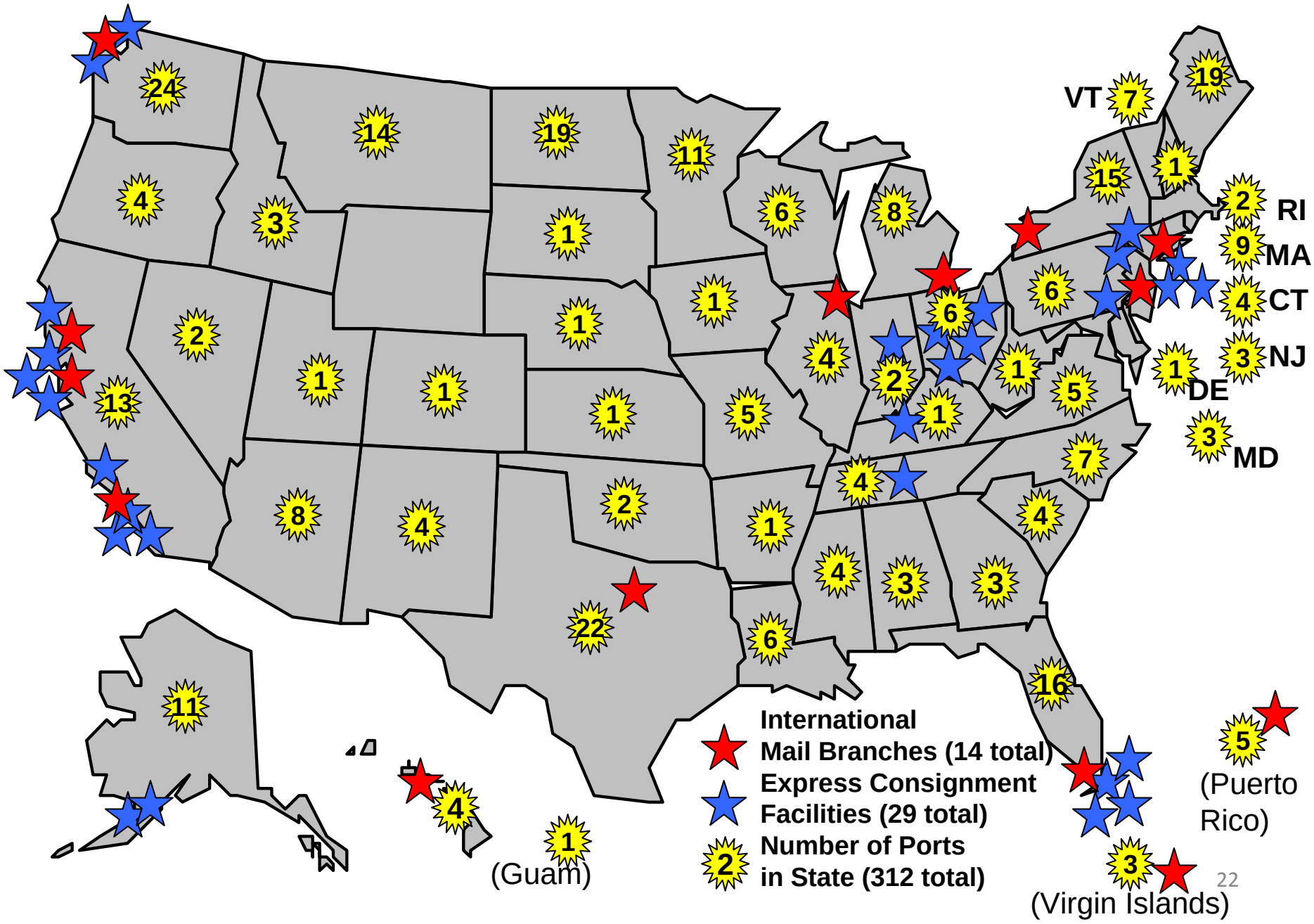
* Finished drugs, intermediates and APIs; Products active on 3/18/2007

Number of Foreign Sites Making FDA-Regulated Drug Products Has More Than Doubled Since 2001. Number of Inspections Has Increased but Inspection Rate has Declined by 41 Percent



* Data Source: FDA Drug Registration and Listing. Sites active on 3/18/2008

For Drug Imports, Many Possible "Points of Entry"



Significant Challenges

- Explosion of globalized manufacturing
- Increased complexity of supply chains
- Greater potential for exploitation (e.g., counterfeits, terrorism)
- Global regulatory system still fragmented
- Erosion of inspectional coverage over last several decades
- Lack of modern IT (e.g., registration and listing systems, inspection tracking, imports)

Dealing with the Reality of Globalization

- FDA cannot inspect quality into the global drug supply: inspection is only one important component
- Manufacturers, importers, brokers and distributors must take primary responsibility for maintaining the quality of pharmaceuticals throughout the supply chain
- Legislators and the public will increasingly hold all involved parties responsible

Electronic Drug Registration and Listing

- Required under FDAAA by end of 2009
- FDA has issued draft guidance and is operating a pilot for firms to register and list electronically
- We will issue a final guidance and start officially registering in June 09
- Piloting DUNS number voluntarily
- Will need to issue a final regulation on registration and listing as well

Pharmaceutical Quality for the 21st Century: Next Steps 09

- Quality by Design: "Regulatory Agreement Guidance"
- Guidance on Filing status for various types of manufacturing supplements
- Re-invigorate pharmaceutical inspectorate
- Continue to develop risk-based approaches to review and inspection

Unapproved Drugs Initiative

- Many non-FDA approved drugs marketed in the US
- Some very old drugs; some opportunistic marketing
- Frequent legal battles
- FDA taking a risk-based approach to removal of unapproved drugs/urging firms to seek FDA approval

So How Will 2009 Look?

- Many of the above priorities will continue
- 2009: longer-term planning
- Expect additional CDER hiring to achieve full staffing of programs
- Transition of administration may bring additional or different priorities

2009 CDER Focus

- Develop and execute a rigorous plan to get to fully electronic submission and review as quickly as possible
- Build advanced computational capacity

2009 CDER Focus

- Operational excellence

2009 CDER Focus

- Build the science of drug regulation

2009 CDER Focus

- Continue our workplace culture initiative

CDER 2009 Focus

- Strengthen our external relationships

Summary

- 2008 brought many challenges
- Focus on priorities enabled significant accomplishments, even in the face of crises such as contaminated heparin
- In 2009 CDER will
  - Continue to complete short term, tactical priorities
  - Develop longer term priorities and work plans for accomplishing them