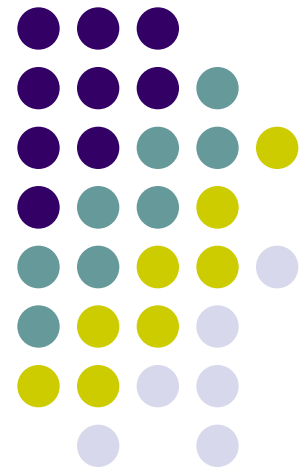


FDA Foreign Inspections

Susan Laska
Deputy Director Foreign Field
Investigations





Today's Objectives

Multi-tiered approach toward pharmaceutical quality and oversight

- Inspections
 - Foreign
 - Domestic
- Import activities
- International Collaboration
 - Agreements
 - Foreign offices
- Industry responsibility

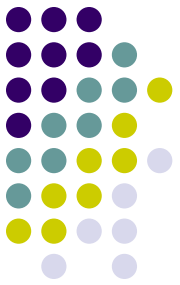
PROGRAM OBJECTIVES



- Coordinate foreign travel for ORA
- To accomplish over 2,800 FDA International Inspections in FY-11
- To ensure the most efficient use of budget and human resources.



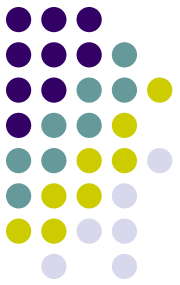
FDA Changes



“Globalization has multiplied the scale of our responsibility and the challenges we face..... Although my duty as FDA Commissioner is to protect the health of the American people... public health protection is a global endeavor.”

Dr. Margaret Hamburg
FDA Commissioner
February 4th, 2010

Globalization Trends



- More foreign facilities supplying the U.S.
- Increasing volume of imported products
- More outsourcing of manufacturing
- Greater complexity in manufacture and supply
- Imports involving countries with less developed regulatory systems

International Inspection Program



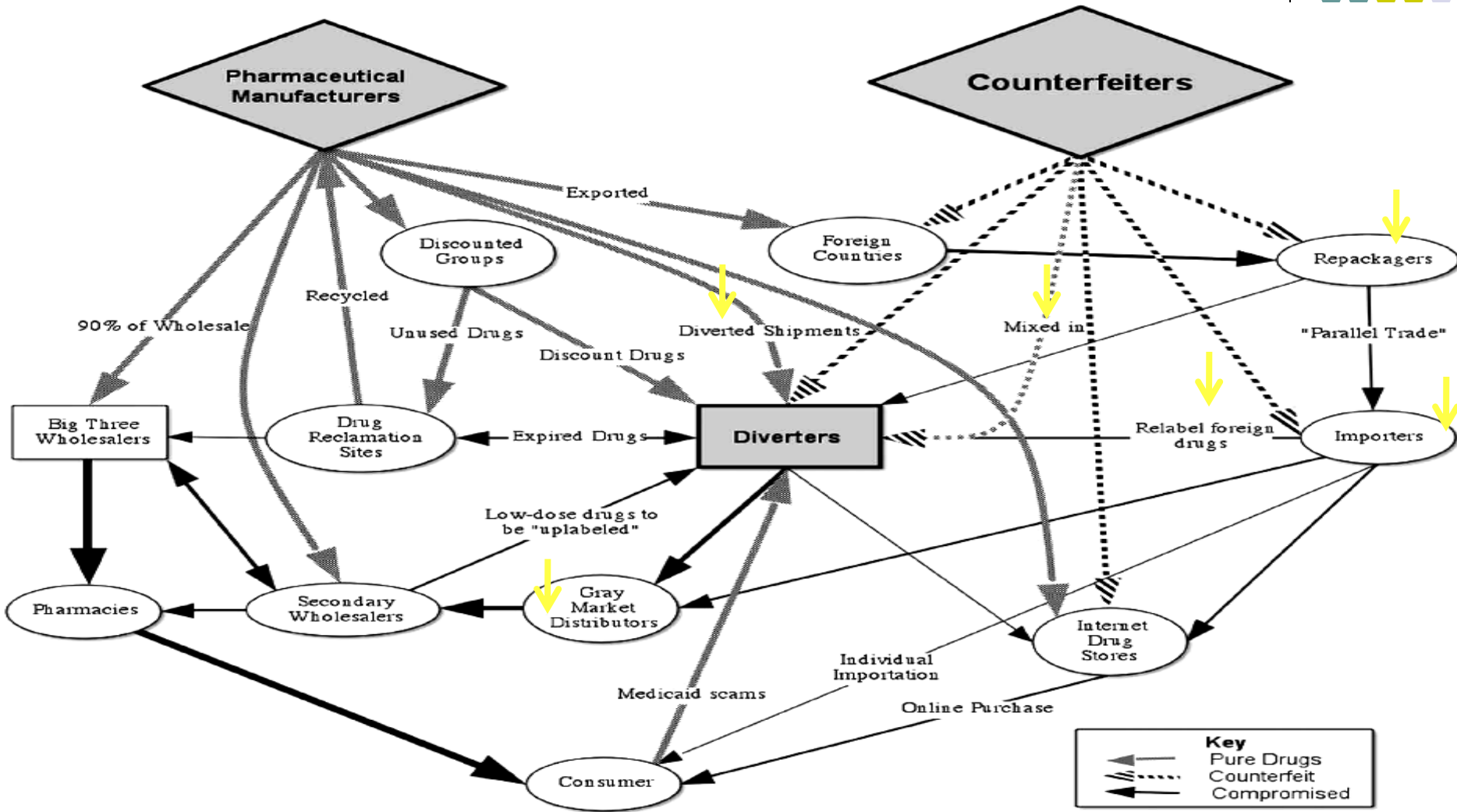
- Historically
 - Approximately 1300 CSOs
 - International Inspection Cadre
 - Over 500 CSOs/Analysts in the Cadre
 - Nomination process and type of people in the cadre
- Current state we have @ 1500 CSO's in Field
 - Approximately 400 CSO capable of foreign inspections
 - Approximately 150 analysts capable of foreign inspections
- Inspection Trip
 - 3 weeks in length
 - 1-2 inspections per week
 - Travel between cities on weekday or weekend

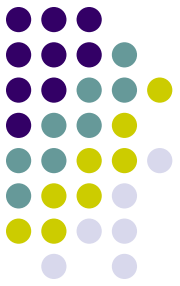
Related Trends



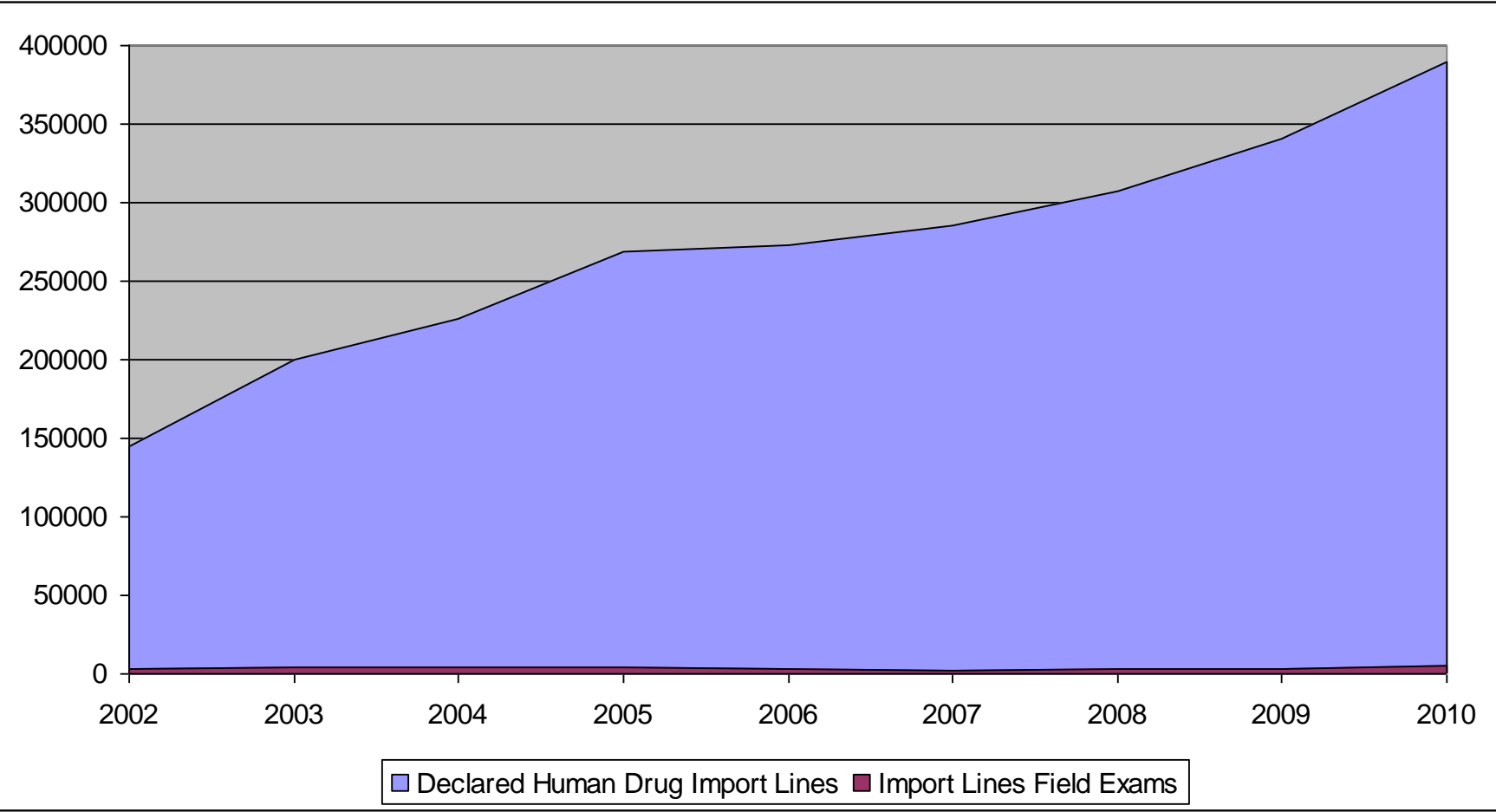
- Distribution chains are more complex
 - ‘upstream’ and ‘downstream’ of product mfg
- More attacks on distribution chains
 - Cargo theft
 - Marketing of counterfeits
- Technology is more complex

Drug Supply Chain: Complexity & Hazards





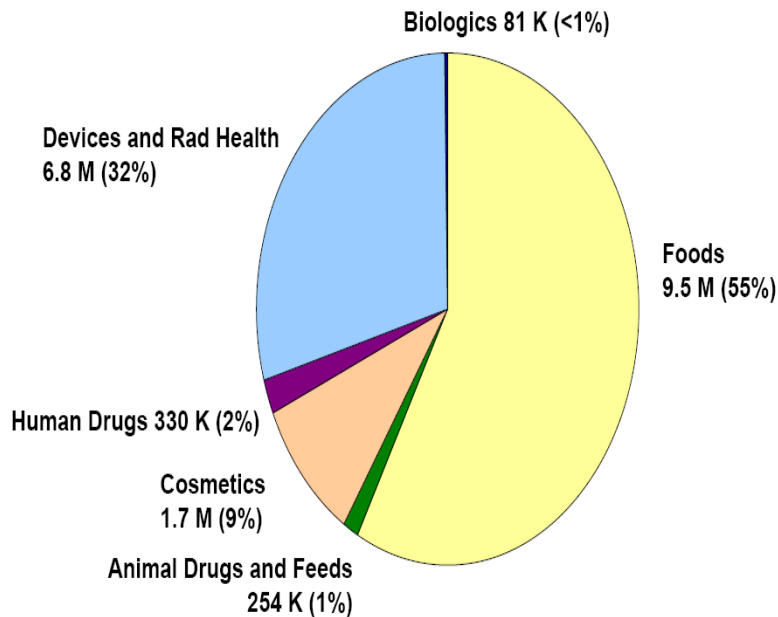
Human Drug Imported Products



Volume of Imports

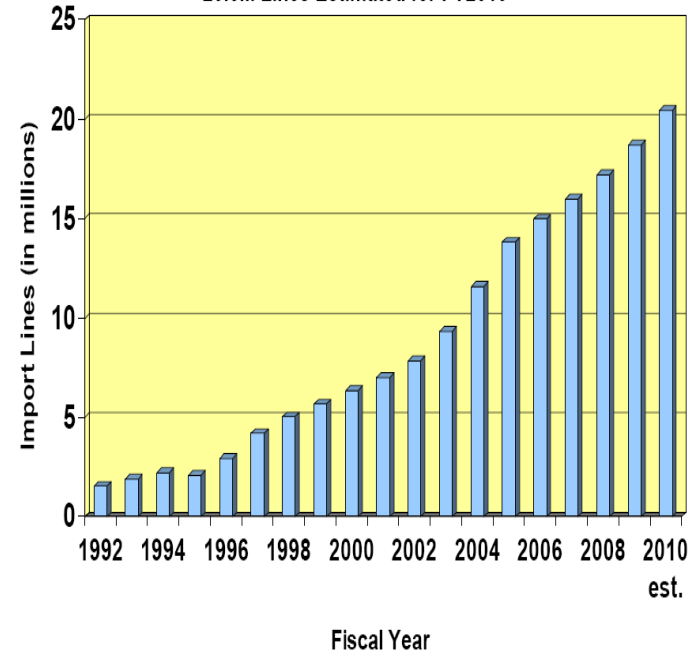


FY 2009 Estimated Import Lines By Program Area Total: 18.7 Million Lines

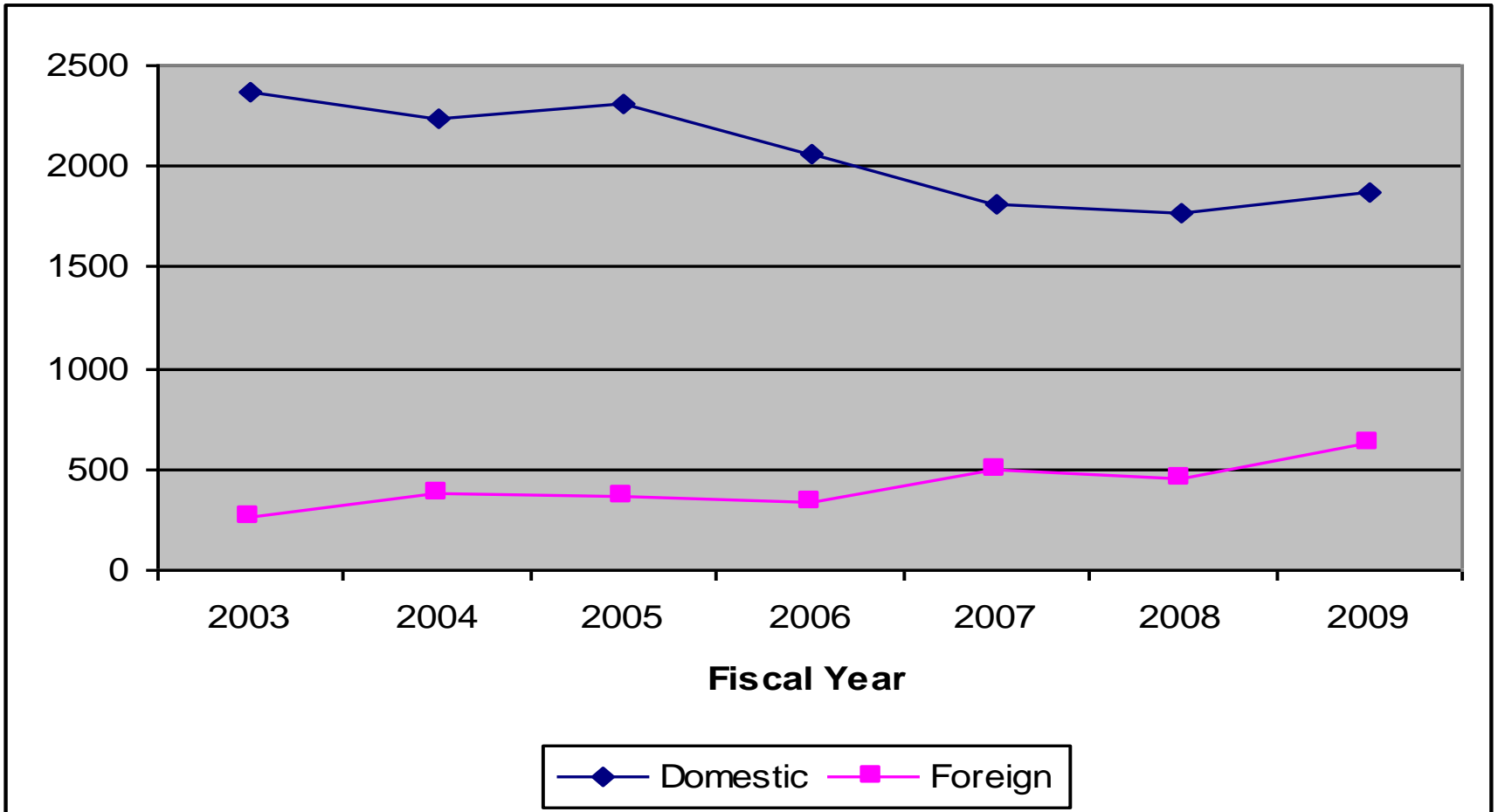
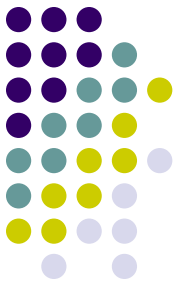


Import Volume History

17.2M Lines Actual for FY2008
18.7M Lines Estimated for FY2009
20.5M Lines Estimated for FY2010



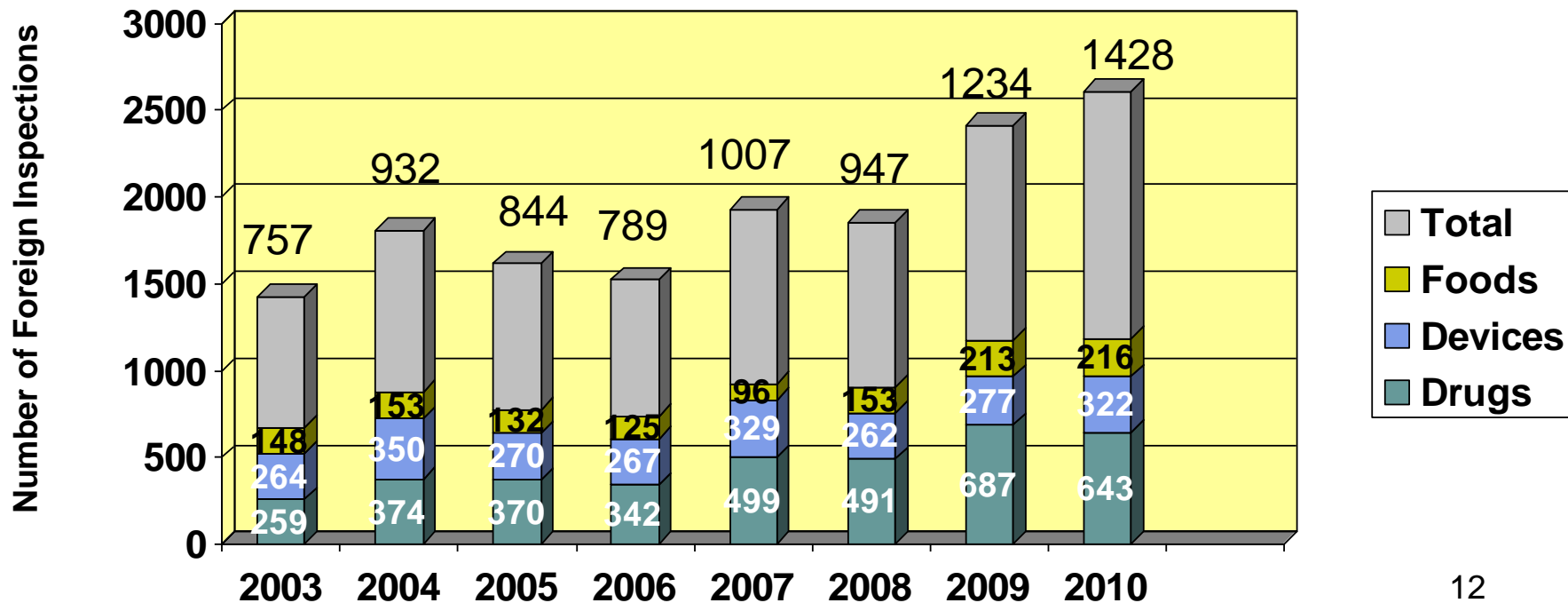
Human Drug Inspections





FDA's Foreign Inspection Accomplishments

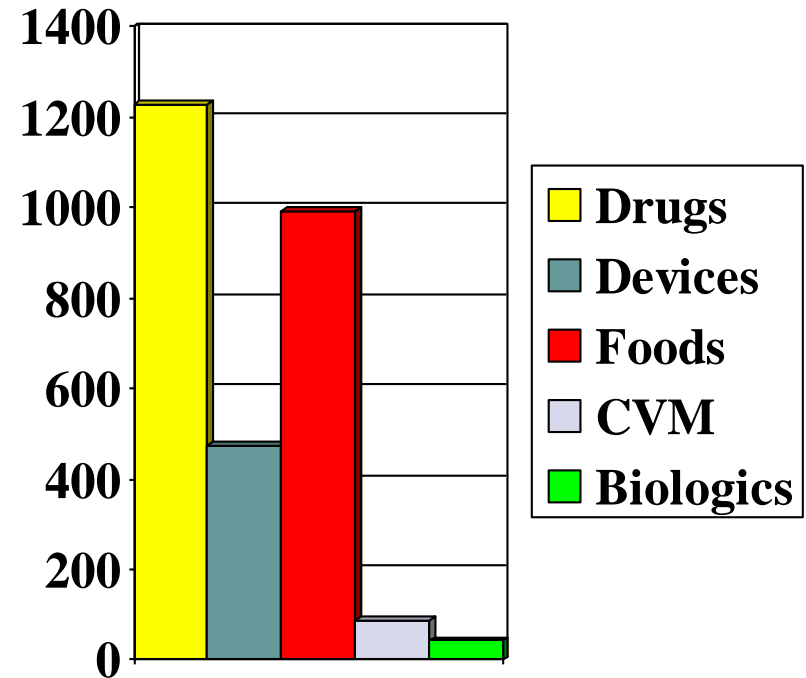
- FDA accomplished more foreign inspections in FY10 than at any other time in our history.



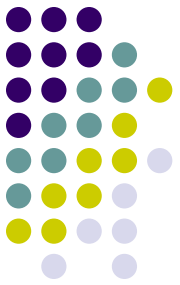
FY 11 International Inspection Obligation Per Program Area



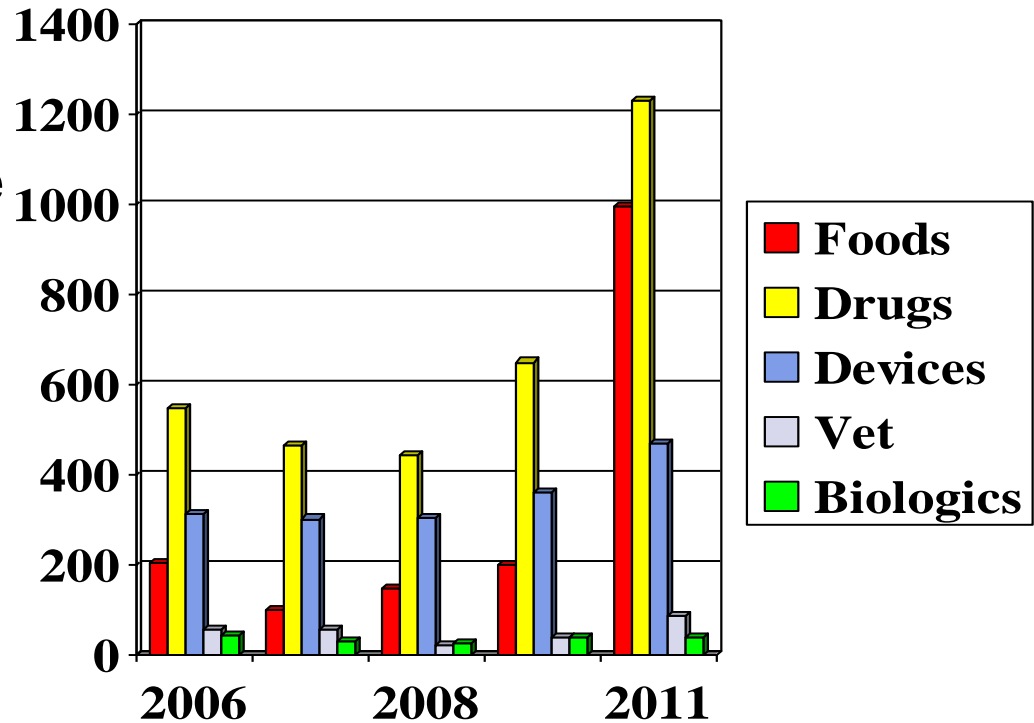
- Drugs – 1249
- Devices - 472
- Foods - 994
- CVM - 88
- Biologics - 42
- TOTAL – 2825*



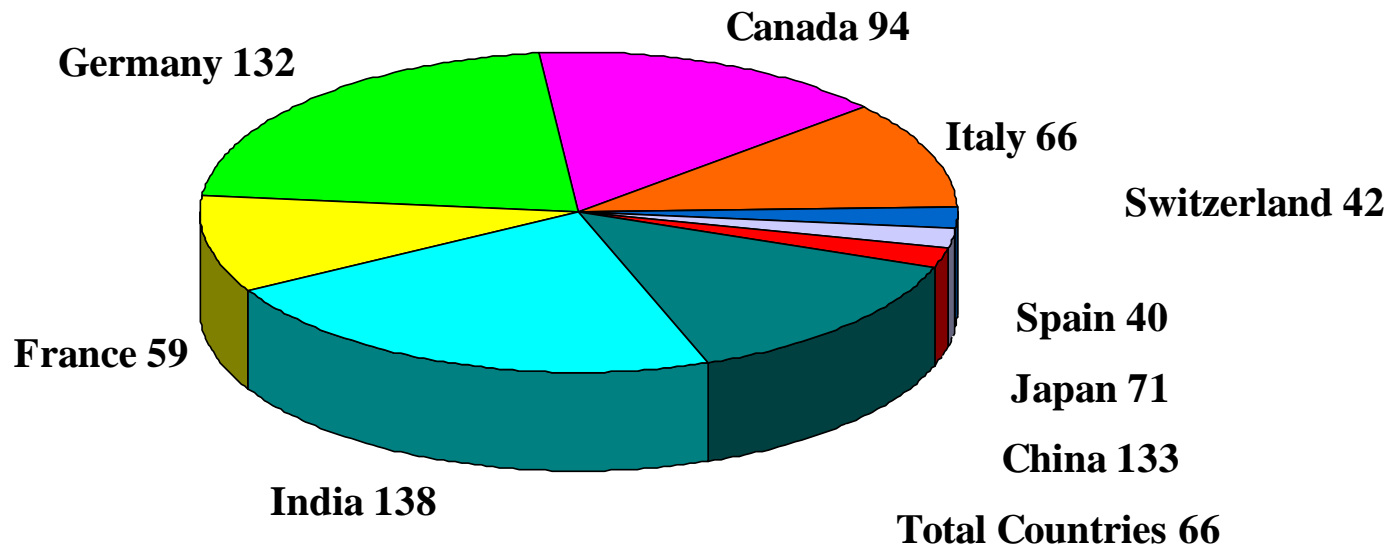
International Inspection Numbers



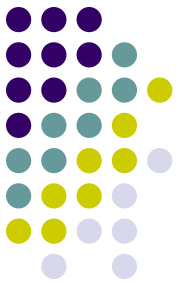
- Factors which result in inspections
 - Pre-Approval Submissions (PEPFAR)
 - Routine surveillance
 - Post approvals
 - F/U
 - Food assessments
 - MOUs/international agreements
 - Import issues
 - Emergencies



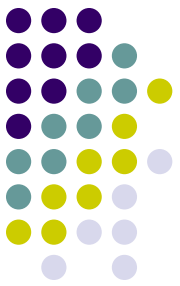
FDA's International Inspections By Country, FY 2010



Challenges in Foreign Inspection Coordination

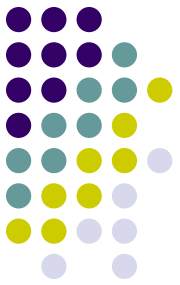


- Short deadlines – outbreak follow-up
- Multiple priorities within different Centers
- Information provided by different sources
- Availability of travelers
 - Domestic vs. international work plan
- Availability of firms
 - Time difference
 - Communication
- Natural disasters (i.e. Japan, floods in SA, State department restrictions)



What is to be done?

- Corporate responsibility
- Quality systems in place
- Working with regulatory partners
- Supply chain security
- Information to deploy resources effectively
- Swift enforcement, if necessary



Approaches to Corporate Responsibility

Assure preventive controls

- With suppliers and their suppliers
- With contractors and subcontractors

Investigate and act on nonconformities

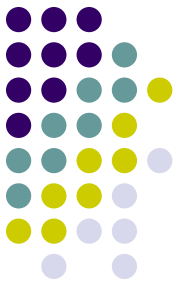


FDA's 'Guiding' Role in Corporate Responsibility

Help industry be responsible through the development of standards and best practices

- Work with industry to set standards
- Inform industry of risks and ways to address them
- Where possible, ease the burden of responsible firms

Regulatory Challenges: Supply Chain Safety

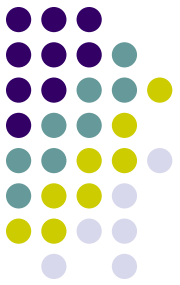


- Incomplete information about supply chains, including participants and vulnerabilities
- Gaps in regulatory standards needed to increase corporate responsibility/accountability to prevent risks
- Complex system of foreign, Federal, and State oversight of product safety
- Incomplete set of enforcement tools
- Resources not aligned with workload or public expectations



Multi-layer national strategies for enhanced supply chain security

- Greater stakeholder responsibility, diligence, & vigilance
 - Sourcing
 - Product security: transport, packaging/product features
 - Business practices
- Increase supply chain transparency/accountability
- Aggressive enforcement strategies....risk-based
- Find ways to leverage resources and trusted partners



What this means for the Importing Company

- Promote adoption of Quality Management Systems
- Encourage Industry Consortia to set standards for technologies and practices
- Swift, Aggressive Enforcement
 - Expectation of rapid and broad investigation into product defect and adverse event reports to identify scope and containment of problems



■ Initiatives past two years

- Global offices
- Dedicated Cadre

Global Offices



- Agreements with foreign governments (Example: China)
- Improve cooperation and info exchange
- More easily facilitate inspections or changes to inspections/schedules
- Quicker inspections during emergency
- Work with private and government agencies to ensure quality standards

FDA Global Presence: Location and Status & Accomplishments

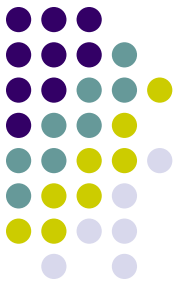


- China: Locations in Beijing (main), Guangzhou, and Shanghai opened in November, 2008.
- Europe: Main location in Brussels opened in December, 2008;. Staff located at European Medicines Agency in London, and to be located at the European Food Safety Agency in Parma.
- Latin America: Main location in San José, Costa Rica opened in January, 2009. Staff is also located in Mexico City, and, Santiago, Chile.
- India: Main location in New Delhi opened January 14, 2009. Staff is also located in Mumbai.
- Middle East: Main location in FDA Rockville headquarters. Locations under discussion with U.S. State Department.

- 1) Working with counterpart agencies in-country; and gathering better knowledge about industry practices.
- (2) Engaging with trusted counterpart agencies overseas to leverage scientific, inspectional, and other resources.
- (3) When requested, engaging with *developing* counterpart agencies to help build their capacity.
- (4) Engaging private- and public-sector *trusted third parties* to provide helpful information about regulated industry compliance with FDA standards.
- (5) Engaging with *regulated industry* to provide greater information about expectations and standards for their products to be admitted to the USA.
- (6) Engaging with other *USG agencies already in-country* with complementary missions
- (7) Performing *more overseas inspections of high risk facilities*

RESULT: To assure that products shipped to the U.S. meet FDA standards

Dedicated Cadre

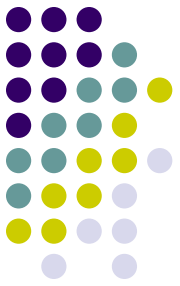


- First trips started in 2/09
- Currently
 - Drug, Device and Food
- 1 Year term – options to renew



- Initiatives with foreign regulatory bodies
 - PICs
 - EMEA
 - TGA

Recent Program Enhancements

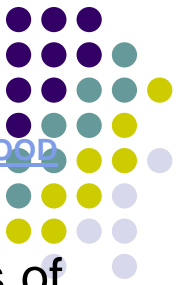


- Dedicated Drug Cadre
- Improved risk-based targeting & firm validation
- OAI follow-up and Agency response.

TITLE 21--FOOD AND DRUGS

CHAPTER I--FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES SUBCHAPTER C--DRUGS: GENERAL PART 211 -- CURRENT GOOD MANUFACTURING PRACTICE FOR FINISHED PHARMACEUTICALS



- Subpart B--Organization and Personnel Sec. 211.22 Responsibilities of quality control unit.
 - (a) There shall be a quality control unit that shall have the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging material, labeling, and drug products, and the authority to review production records to assure that no errors have occurred or, if errors have occurred, that they have been fully investigated. The quality control unit shall be responsible for approving or rejecting drug products manufactured, processed, packed, or held under contract by another company.
 - (b) Adequate laboratory facilities for the testing and approval (or rejection) of components, drug product containers, closures, packaging materials, in-process materials, and drug products shall be available to the quality control unit.
 - (c) The quality control unit shall have the responsibility for approving or rejecting all procedures or specifications impacting on the identity, strength, quality, and purity of the drug product.
 - (d) The responsibilities and procedures applicable to the quality control unit shall be in writing; such written procedures shall be followed.

Ingredient Adulteration: Health Hazard



Question for Industry/Regulators: *What went wrong here? What is, and should be industry's responsibility?*

Some Notable Worldwide Examples:

- 2008-2009 DEG-Contaminated glycerin used in Teething Gel
- 2008 Melamine contamination of milk products (low qty in foods in US) and Infant Formula (in China)
- 2008 Heparin – OSCS contaminant
- 2007 DEG contamination in toothpaste
- 2007 Melamine contamination in wheat gluten (pet foods)
- 2006 DEG-contaminated Glycerin in Panama, Bangladesh
- 1999 Gentamicin Pyrogenic reactions
- 1990-2006 Recurring incidents of DEG-contaminated Glycerin (India, Haiti, Argentina, Bangladesh, and Nigeria)



All parties who manufacture (includes testing), process, pack, or hold an *ingredient* or *drug product* are responsible for meeting CGMPs.

Adulterated Ingredient = Adulterated Drug Product



Guidance for Industry

Testing of Glycerin for Diethylene Glycol

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
May 2007

Compliance

Guidance for Industry

Pharmaceutical Components at Risk for Melamine Contamination

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Veterinary Medicine (CVM)
August 2009

Current Good Manufacturing Practice (CGMP)



Inspections
• Domestic
• Foreign

Industry
Responsibility

Import
Activities

Pharmaceutical
Quality

International
Collaboration

Foreign
Offices

