FDA Recommendations to Industry Regarding Outsourcing

Marlène G. Swider, MHSA
American Society for Quality (ASQ) Orange Empire
Anaheim, California
February 12, 2013

Personal Claim

This presentation is based on journal articles written by the author and does not reflect a position, official or unofficial, of the FDA.

Past

Previously one or two firms were responsible for the entire manufacturing of a product including its development, testing, labeling, packaging and distribution to the markets.

History

Then, the complexity and highly specialized technology and equipment fostered the emergence of companies capable of performing only limited aspects of manufacturing process. Consequently, firms were interested in sharing or contracting to facilitate product development.

Currently,

Today, the increasing demand for the products along with innovation is fostering specialization of manufacturing by firms. This, along the pressure to reduce cost and increase productivity will make companies moving manufacturing activities to new and different locations.

Nevertheless,

- All imported products are required to meet the same standards as domestic goods – must be pure, produced under sanitary conditions and contain informative and truthful labeling in English.

Cooperative Manufacturing Arrangements recognized by FDA

- Short Supply
- Divided Manufacturing
- Shared Manufacturing
- Contract Manufacturing

Who is a manufacturer

License applicant and contractors legally engaged in the manufacture of a product subject to license under the FD&C Act, are defined as “manufacturers” under the Law.

License Holder's Responsibilities

- Assure compliance with product and establishment standards
- Report changes to production and facilities
- Identify all contractors manufacturers responsible for the manufacture of the product

Contractor's Responsibilities

- Inform applicant of all deviations in manufacturing methods, and adverse events
- Inform applicant of all tests and investigations regarding or possibly impacting the product
- Inform proposed changes to production and facilities (including introduction of new products)

Information regarding a change

When contractor notifies the license holder about a recent change, they have the options to provide the information as a supplement or provide the license holder with an authorization letter to review their DMF.

This letter should be part of the supplement submitted to FDA by the license holder regarding the given change.

Applicant and Contractors

Compliance with applicable provisions of the FD&C Act (21 USC 301) and applicable regulations: CFR and FDA's current guidance.

Interplay of 3 Powerful Forces

- Growing demand
- Constrained supplies
- Increased regulatory and social scrutiny

Outsourcing Complexity for FDA

- Increased number of inspections without commensurate resources
- Inspection obligation sites are dispersed
- Complex oversight of compliance with good manufacturing practice in firms

Complications for FDA

- More travel time
- More resources requirements
- More country clearances
- Multi-language in control documentation
- Travel Restrictions

More complications

- Different modalities of communications (compatibility of systems)
- More regulatory requirements
- Different compliance expectations
- Increased opportunity of substitution of components

Trends being seeing now

- Companies will be producing more products abroad.
- Products will follow a complex paths through multi-step supply chains to reach the U.S.
- More parties involved in end-to-end production and distribution of a single product.

Complications affecting you!

More parties involved in the supply chain

Great increase on the risk of unknown drug quality and integrity

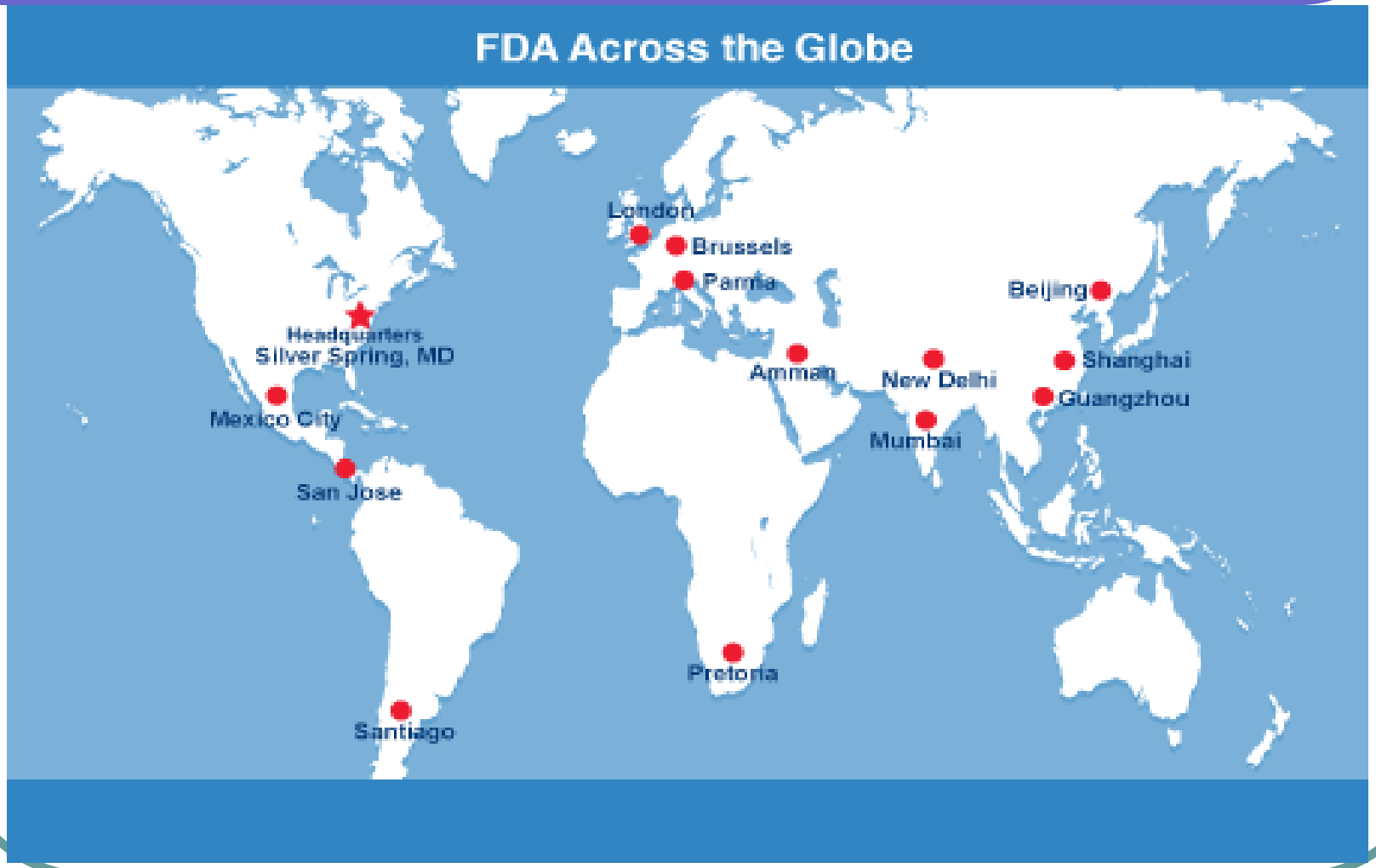
Harder to oversee the lifecycle of the drug

Greater need for a secure supply chain

How is FDA helping you?

- Implementing mechanisms to contrarrest these events including Import Alerts
- Opening offices around the world
- Increasing the number of foreign inspections
- Collaborating with counterparts
- Engaging in harmonization
- Joining the Pharmaceutical Inspection Cooperation/Scheme (PIC/S)

FDA helping you.



More ways FDA is helping you.

- Implementing innovative ways to do business
- Providing timely information
- Establishing state-of-the art technology
- Cooperating with other Federal Agencies
- Regulations/compliance/surveillance

Remember…

Every company with products or activities under FDA's jurisdiction has a duty to comply with the law… (Remarks by Margaret A. Hamburg, MD., Commissioner of FDA – FDLI August 6, 2009)

FDA Recommends

Having a signed, written agreement with contractors to identify:

- Locations to be used for manufacture
- Responsibilities of each participant
- Product shipped to contract facility
- Manners and conditions of shipment
- Product segregation SOPs
- Commitment to inform errors and deviations
- How and when contract facility will be audited

References

Guidance for Industry:

FDA's Policy Statement Concerning Cooperative Manufacturing Arrangements for Licensed Biologics, November 25, 1992 (57 FR 55544)

(Current 1999 draft is being circulated for approval – www.fda.gov/cber/gdlns/coopmfr)

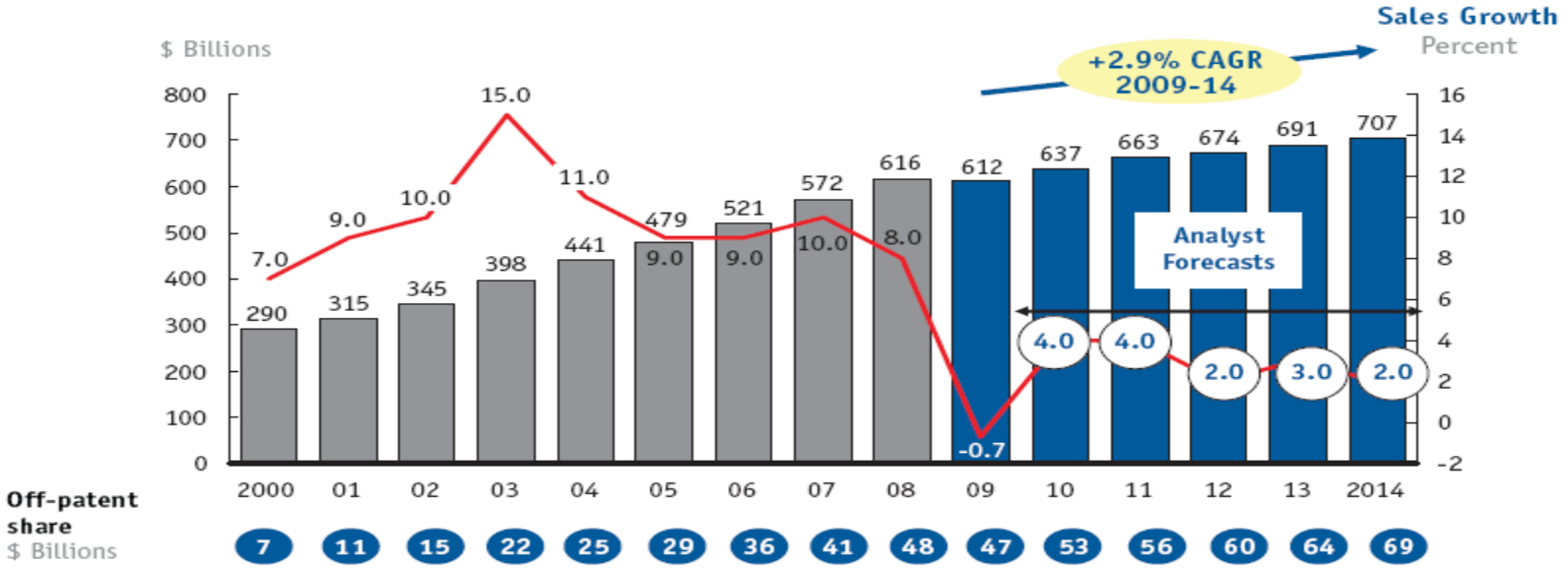
Other events affecting you

- Unapproved Drugs Purchased Outside the United States
- Imported Drugs

Cost pressures facing pharmaceutical companies

Pharmaceutical company revenues are under pressure and unlikely to regain historical levels of growth.

Worldwide total prescription drug sales 2000-14



1 EvaluatePharma focuses on manufacturer's selling price for Top 500 pharma and biotech companies (IMS traditionally higher since it includes all retail/wholesale invoices and excludes rebates).

2 Majority of industry estimates more conservative in early 2009; IMS revised in late 2009 to project 4-7% CAGR growth through 2013.

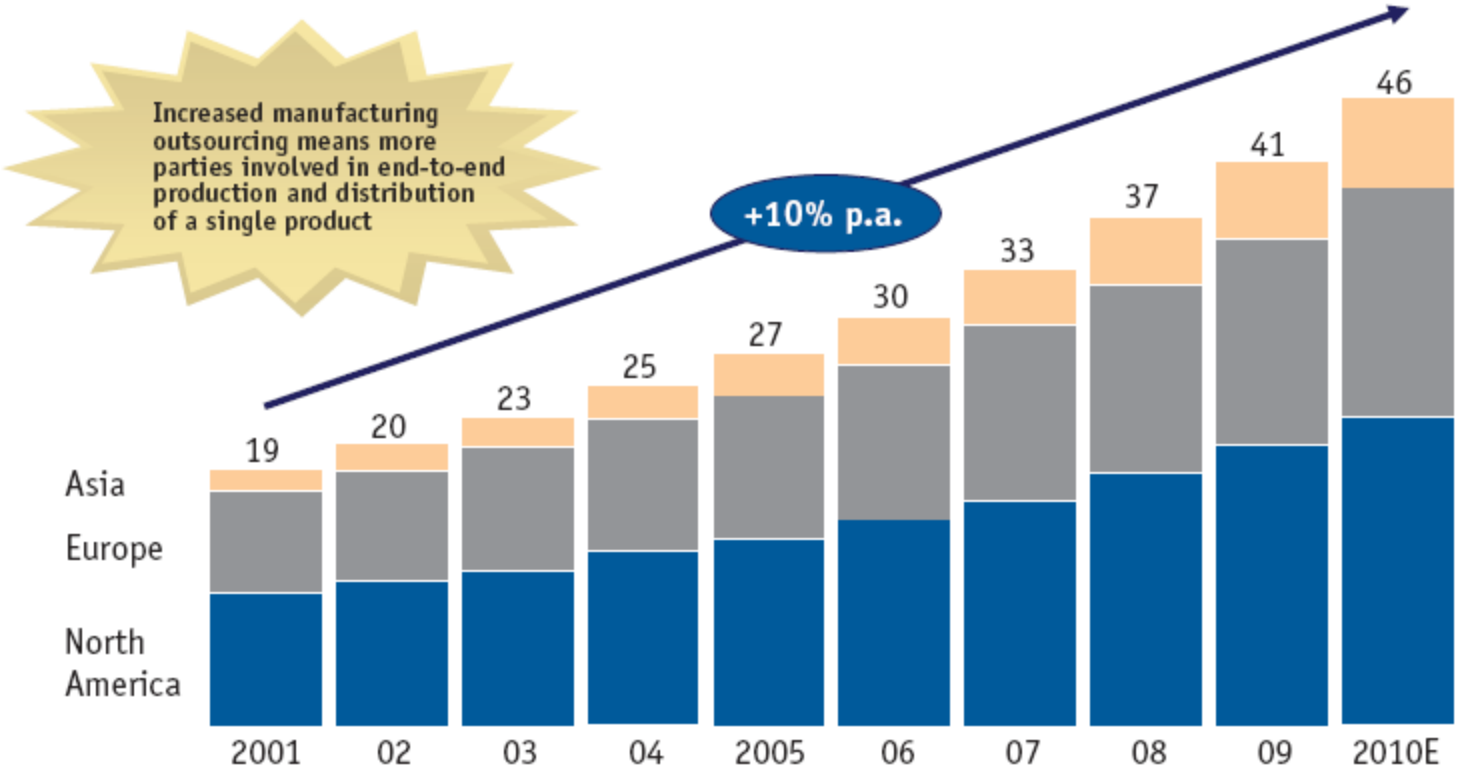
Source: EvaluatePharma April 2009; team analysis

Market for Contract Manufacturing Outsourcing

Increased fragmentation of regulated producers adds a new challenge to the FDA's safety assurance efforts both domestically and abroad.

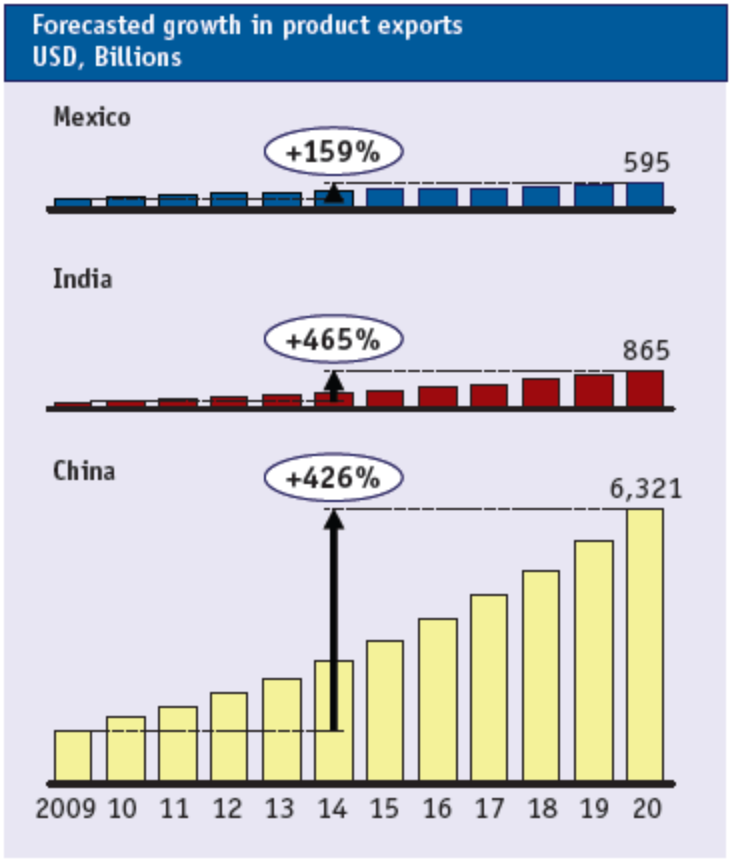
Pharmaceutical contract manufacturing outsourcing market

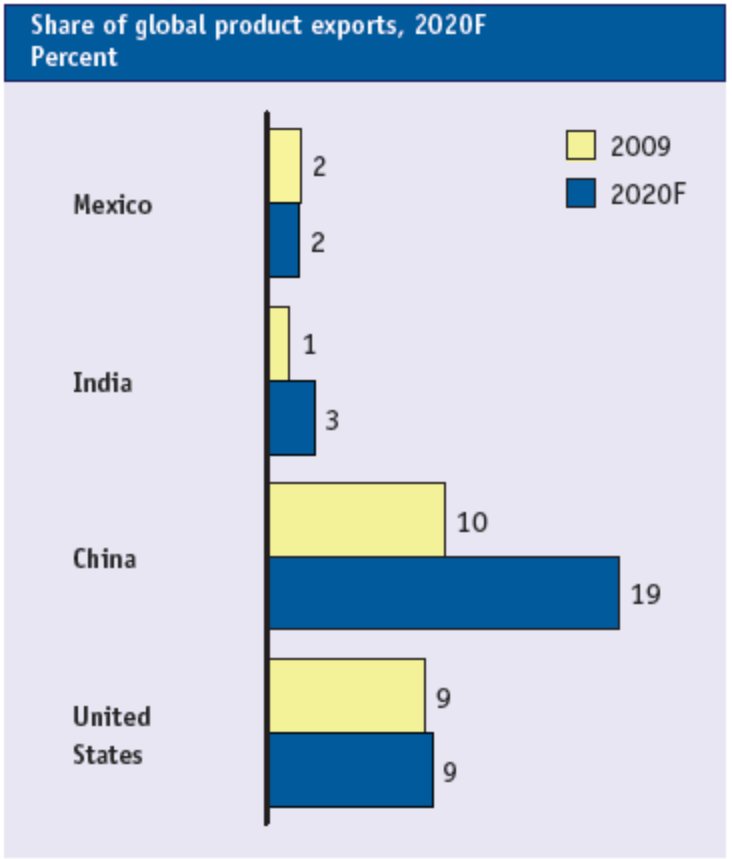
USD Billions



Increase in total foreign exports

A significant portion of the increase in foreign products will come from developing countries.





Source: McKinsey Global Insights

Unapproved Drugs Purchased Outside the United States

- FDA cannot provide assurance to the American public that these drugs are of the same quality and are as safe as the products approved by FDA.

Imported Drugs & FDA's Concerns

- Quality Assurance
- Counterfeit Potential
- Presence of Untested Substances
- Risks of Unsupervised Use
- Labeling and Language
- Lack of Information

In Conclusion

FDA wants to facilitate product development and manufacturing flexibility so it supports advancement of new and innovative ways that will lower the Cost of Drug Development and advance the Pathway to Global Product Safety and Quality.

Contacts

Outsourcing Guidance

Leonard Wilson (CBER) 301-827-0373

Globalization issues at
global@fda.hhs.gov or at
(301) 796-4600