Supply Chain Security Workshop
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GREENLEAF HEALTH IS A FULL-SERVICE REGULATORY CONSULTING FIRM GUIDING COMPANIES THROUGH THE CHANGING FDA LANDSCAPE.
INTRODUCTION

This workshop and presentation will focus on approaches to enhancing global supply chain security. Specifically, it will:

• Create awareness to threats targeting the global pharmaceutical supply chain;

• Provide insight into world-wide regulatory trends related to securing the supply chain; and

• Provide insight on processes, procedures, tools, and resources that can be used to enhance supply chain security.
OVERVIEW

Reality of Globalization – Increasing Threat to Pharmaceutical Quality, Safety, Reliability, and Accessibility

Globalization’s Impact on Global Product Quality has implications for health, medicine, the role of industry, and the role of regulators

FDA and other regulatory bodies had to retool their efforts in many ways including:

• Expanding their International Presence - Global Solutions and Global Collaboration
• Refining Strategic Initiatives
• Realigning Resources
• Focusing on “Quality” as the basis of medical product regulation
• Emphasizing Global Prevention, Global Detection, and Global Response

We will discuss these efforts in more detail throughout the workshop
THREATS TO THE GLOBAL PHARMACEUTICAL SUPPLY CHAIN
Incidents involving Counterfeit and Substandard Products:

- Xeplion – Schizophrenia
- Avastin – Cancer/Eye Disease
- Altuzan – Cancer
- Vicodin – Pain
- Medication
- Adderall – ADD
- Anti-Malarial Drugs
- HIV medications
- Meningitis Vaccines
- Antibiotics
- Heparin – Blood thinner
- Lipitor – Cholesterol
CHALLENGES RELATED TO GLOBAL PRODUCT QUALITY

Global Supply Chain Risks:

• Larger more complex global supply chains – product mobility
• Increasing number of individuals, producers, and companies – geographically dispersed
• Availability of alternate distribution channels for products (e.g., Internet)
• Reliability/Availability issues – drug shortages, recalls, counterfeits, and substandard products
• Criminal activity – diversion, cargo theft, and counterfeiting
• Lack of common indicators of quality across industry
• Quality regulations are dated – compliance with regulations does not ensure optimal quality
• Outdated manufacturing technology
• Availability of resources
TIMELINE OF EVENTS

Some Seminal Regulatory Events in FDA’s Transformation to a Globalized Regulatory Agency that focused on Global Pharmaceutical Quality and Supply Chain Security

1998 – GAO reports relating to Foreign Drug Inspections and Counterfeit Drugs
1999 – Internet Drug Sales Initiative
2002 – Pharmaceutical Good Manufacturing practices for the 21st Century Initiative
2004 – Counterfeit Drug Task Force Report
2011 – Pathway to Global Product Safety & Drug Shortage Executive Order
2012 – Global Engagement Report, The Food and Drug Safety and Innovation Act (Title VII and GDUFA), and the Establishment of the Office of Drug Security, Integrity, and Recalls
2013 – Drug Quality and Security Act & Program Alignment Group
2014 – 21st Century Cures – Grants for Continuous Manufacturing
2015 – Establishment of the Office of Pharmaceutical Quality (OPQ)
2017 – Mutual Reliance Agreement and ORA’s Implementation of Program Alignment
FDA’S GOALS: REGULATING PHARMACEUTICAL QUALITY

• Ensure the availability of authorized/approved products
• Ensure that all US marketed medical products are of the requisite quality and reliability
• Enhance understanding of product development, raw material sourcing, manufacturing controls, and import export operations
• Ensure that beneficial medical products are available, substandard products are not
• Identify meaningful risk assessment tools for product quality
• Strengthen connection between science and risk based quality standards and regulatory oversight
• Expedite the availability of new beneficial medical products
• Harmonize with International Regulatory Counterparts
• Broaden Global Presence/Global partnerships and collaborations
• Educate patients and healthcare professionals
REGULATORY TRENDS RELATED TO GLOBAL PHARMACEUTICAL QUALITY AND SECURITY
In response to the Challenges of Globalization, FDA’s regulatory goals did not change but its regulatory approach did.

Meeting the challenges of globalization required a fundamental shift in its regulatory approach. Both unilaterally, and in conjunction with its regulatory partners and stakeholders.

FDA had to transform from a domestic agency operating in a globalized world to an agency that is fully prepared for a rapidly changing global environment.

- Border could no longer be the primary line of defense
- Need preventive controls throughout the supply chain
- Need to partner with others to achieve greater levels of safety and security with fewer, more targeted resources
ONGOING TRANSFORMATIVE EFFECTS

As part of FDA’s transformative efforts, the Agency adjusted and broadened its Comprehensive Approach to Global Pharmaceutical Quality and Security.

It was crucial to develop new programmatic strategies that continued to focus on product quality, safety, reliability, and accessibility and address the continuing global threats noted below:

- Counterfeit products
- Intentional adulteration
- Substandard products
- Poorly manufactured products
- Product diversion
- Cargo thefts
- Product tampering
ENHANCED FOCUS ON THE PRODUCT LIFECYCLE

End to end supply chain solutions are necessary to combat these threats and strengthen supply chain security.

Strategies had to be incorporated into a comprehensive plan in order to cover the entire supply chain and life cycle of the product – from raw materials to use by patients.
PROCESSES, PROCEDURES, TOOLS, AND RESOURCES THAT CAN BE USED TO ENHANCE PHARMACEUTICAL QUALITY AND SECURITY
FDA’S EFFORTS TO STRENGTHEN GLOBAL PHARMACEUTICAL QUALITY

As part of FDA’s comprehensive and transformative efforts to strengthen Global Pharmaceutical Quality and Security, FDA has identified several strategic areas that should be addressed by regulators and industry stakeholders.

• Best Practices for Identifying Areas of Vulnerability
• Good Manufacturing Practices
• Good Distribution Practices
• Good Import/Export Practices
• Clinical and Retail Pharmacy Practices
• Product Security
• Detection tools
• Monitoring Internet Sales
• Adopting Track and Trace Technology
• Improving Surveillance and Monitoring
• Establishing Points of Contact
FDA’S EFFORTS TO STRENGTHEN GLOBAL PHARMACEUTICAL QUALITY

To properly address the identified strategic areas, FDA has adopted a comprehensive multilayer approach to strengthening Global Pharmaceutical Quality and Security.

The current multilayered approach focuses on strategies that help regulators and stakeholders prevent, detect, and respond to breaches in the supply chain and the presence of substandard products.

As an important partner in the collective effort to ensure Pharmaceutical Quality and Security it is also important for individual industry stakeholders to establish a similar plan.

The consequences of a breach in quality/security can be devastating from a public health, financial and reputational perspective.
STAKEHOLDERS’ TRANSFORMATIVE EFFORT

However, the risk of a breach can be mitigated by developing a comprehensive corporate good management system that ensures, among other things, the establishment of:

• Robust quality standards and procedures and other approaches to ensure that products are manufactured with optimal quality
• Steps to control inappropriate access to products
• Employer training
• Procedures for the selection of suppliers and distributors
• Tools to manage upstream supply chain threats
• Processes and procedures to utilize audits
• Processes to help assess vulnerabilities and monitor marketplace threats to the supply chain
• Procedures for detecting and rapidly responding to supply chain security breaches
• Points of contact for regulatory and law enforcement officials
• Procedures for notifying regulators and law enforcement officials, patients and other stakeholders
• Processes to measure the effectiveness of efforts to secure the supply chain
REGULATORS’ EXPECTATIONS REGARDING STAKEHOLDERS’ STRATEGIC PLAN

From the regulator’s perspective, a strong comprehensive corporate plan should contain the elements below:

• Prevention – preventing problematic products from entering the supply chain
  • Strengthen standards/procedures for ensuring compliance with current good manufacturing, distribution, and pharmacy practices
  • Implement track and trace and end to end product security and supply chain solutions
  • Establish strong import and export practices

• Detection – identifying problematic products in the supply chain
  • Incorporate detection technologies – strengthen surveillance and monitoring
  • Strengthen investigations and actions against breaches and suspect products
REGULATORS’ EXPECTATIONS REGARDING STAKEHOLDERS’ STRATEGIC PLAN

Elements continued below:

- Response – responding to breaches in the supply chain or problematic products
  - Develop relationships and points of contacts with regulatory, law enforcement, and medical officials
  - Develop processes and procedures to facilitate coordination, communication and information regarding incidents with suspect medical products
  - Improve communications about incidents by reporting to regulators and global surveillance and monitoring programs
TOOLS AVAILABLE TO ASSIST STAKEHOLDERS EFFORTS TO ENGAGE IN COMPREHENSIVE PLANNING

- Drug Supply Chain Security Act – Overview and implementation [www.fda.gov](http://www.fda.gov)
- BeSafeRx: Know Your Online Pharmacy [www.fda.gov/BeSafeRx](http://www.fda.gov/BeSafeRx)
- Office of Criminal Investigations at [www.fda.gov/oci](http://www.fda.gov/oci)
- Partnership for Safe Medicine – [www.safemedicines.org](http://www.safemedicines.org)
- International Federation of Pharmaceutical Manufacturers and Association (IFPMA) – [www.ifpma.org](http://www.ifpma.org)
TOOLS AVAILABLE TO ASSIST STAKEHOLDERS EFFORTS TO ENGAGE IN COMPREHENSIVE PLANNING

- FDA’s Pathway to Global Product Safety and Quality Report – www.fda.gov
- Interpol – Pharmaceutical Crimes and Operation Pangea Reports – www.interpol.int
- Pharmaceutical Inspection Cooperation Scheme (PIC/S)– https://www.picscheme.org
- National Association of Boards of Pharmacy – https://nabp.pharmacy
- FDA’s Medwatch Safety Information and Adverse Event Reporting – https://www.fda.gov/safety/medwatch
DISCUSSION QUESTIONS

• What steps can we continue to take to ensure greater cooperation between regulators and industry in regards to addressing pharmaceutical quality and security?

• To date, have the DSCSA notification provisions worked well?
  • Regulator perspective?
  • Industry perspective?

• What more can or should be done to better quantify the scope and challenges of pharmaceutical quality and security?

• Is there adequate guidance to help stakeholders identify a potentially problematic product and then make a determination as to whether a product is a suspect product?

• What steps might increase the possibility that a suspect product will enter the supply chain?

• What are some best practices for determining whether a product might be a suspect product?
BACKGROUND
SCOPE OF FDASIA – TITLE VII: WHAT IT DOES

Increases FDA’s ability to:

- Collect and analyze data to enable risk-informed decision-making
- Advance risk-based approach to facility oversight – part of broader shift towards more strategic, risk-based approach to regulation and enforcement
- Partner with foreign regulatory authorities to leverage resources through information-sharing and recognition of foreign inspections
- Drive safety and quality throughout the supply chain through strengthened tools

Source: Overview of Title VII and FDA’s Approach to Implementation, Susan S. de Mars, July 12, 2013
OVERVIEW OF THE DSCSA

Title II: Drug Supply Chain Security Act (DSCSA) adds new sections in the Federal FD&C Act

- 581 – Definitions
- 582 – Requirements (product tracing, product identification, verification)
- 583 – Standards for licensure of WDs
- 584 – Standards for licensure of 3PLs
- 585 – Uniform national policy

Source: Drug Supply Chain Security Act (Title II of the Drug Quality and Security Act), US FDA, September 2015
DSCSA MAJOR PROVISIONS

• Product tracing (by 2015 lot-level, by 2023 package-level)

• Product verification
  - Quarantine and investigation (steps for detection and response)
  - Notification, record keeping

• Product identification (applied to product beginning 2017)

• Wholesale distributor and Third-party logistics provider standards for licensure

• Enhanced system (electronic, interoperable system to trace products at the package-level by 2023)

• Penalties

• National uniform policy

Source: Drug Supply Chain Security Act (Title II of the Drug Quality and Security Act), US FDA, September 2015
DSCSA REQUIREMENTS: IDENTIFICATION OF SUSPECT PRODUCT AND NOTIFICATION

Trading partners (manufacturers, repackagers, wholesale distributors, dispensers) must have systems:

- To quarantine and conduct investigations of suspect products;
- To notify FDA and immediate trading partners within 24 hours, if a product is illegitimate; and
- To terminate notifications without illegitimate product in consultation with FDA

DEFINITIONS
[SECTION 581(21) OF THE FD&C ACT]

Suspect product – there is reason to believe it:

A. Is potentially counterfeit, diverted or stolen;
B. Is potentially intentionally adulterated such that the product would result in serious adverse health consequences or death to humans;
C. Is potentially the subject of a fraudulent transaction; or
D. Appears otherwise unfit for distribution such that the product would result in serious adverse health consequences or death to humans.

DEFINITIONS
[SECTION 581(8) OF THE FD&C ACT]

Illegitimate Product – credible evidence shows that the product is:

A. Counterfeit, diverted, or stolen;
B. Intentionally adulterated such that the product would result in serious adverse health consequences or death to humans;
C. Subject of a fraudulent transaction; or
D. Appears otherwise unfit for distribution such that it would be reasonable likely to result in serious adverse health consequences or death to humans.

NOTIFICATIONS TO FDA

1) Trading partners should access FDA’s Drug Notification Web page to make notifications:
   http://www.accessdata.fda.gov/scripts/cder/email/drugnotification.cfm

2) Trading partners should follow the instructions on the Web page for accessing Form FDA 3911 and to provide information.

3) Form FDA 3911 should be submitted by using the method provided in the form.

TERMINATION OF NOTIFICATIONS TO FDA

1) Trading partners must follow the instructions on the Web page for accessing Form FDA 3911 and provide information.

2) This form must be submitted by using the method provided in the form.

3) FDA will review the request and consult with the trading partner.
