Identifying and Prioritizing Global Supply Chain Management Risks

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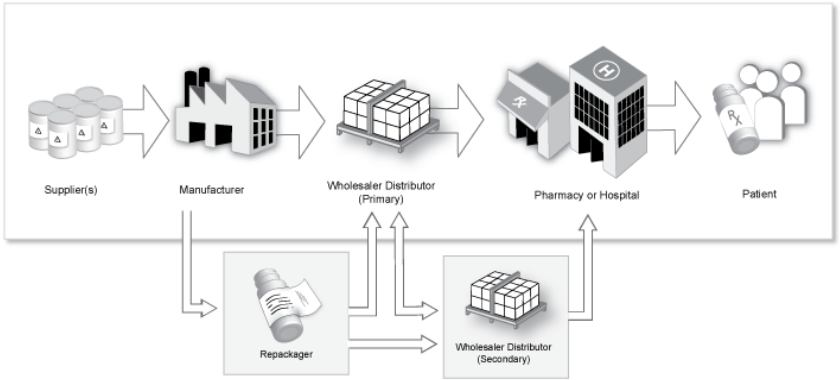
Supply Chain Integrity

- Minimizing risk at all stages of supply chain, from sourcing of raw materials through manufacturing and distribution to patient



Increasing Reliance on Outsourcing:

- Research and Development – Contract Research Organizations (CROs)
- Manufacturing – Contract Manufacturing Organizations (CMOs) and Suppliers
- Distribution – Wholesalers, Third Party Logistics Providers

Supply Chain Extends Across the Globe

Product Owner Has Ultimate Responsibility

Sponsors Responsible for CROs

- 21 CFR 312.52 - Delegation to CRO for monitoring requires written transfer agreement of obligations
- Guidance - Sponsors retain responsibility for oversight of work completed by CROs: *Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring;* https://www.fda.gov/downloads/Drugs/Guidances/UCM269919.pdf

Manufacturers Responsible for Suppliers and CMOs

- FDASIA – Section 711 explicitly includes oversight of outsourced activities as part of CGMP
- 21 CFR 210 – 211 (e.g. 21 CFR 200.10 – contract manufacturers are extension of manufacturer's own facility)
- Guidance - *Contract Manufacturing Arrangements for Drugs: Quality Agreements* https://www.fda.gov/downloads/drugs/guidances/ucm353925.pdf

Device Manufacturers Responsible for Outsourced Suppliers and Manufacturing

- 21 CFR 820.50 - Purchasing Controls - manufacturers required to establish and maintain quality requirements for suppliers
- ISO 13485:2016 - revised to be more consistent with FDA's purchasing controls requirement

Tissue Manufacturers Responsible for Outsourced Manufacturing

- 21 CFR 1271.150 - manufacturing arrangements
- Must ensure compliance with GCTP before entering contract
- If become aware of information suggesting non-compliance, must take reasonable steps to ensure compliance
- Must terminate contract if establishment not in compliance

What tools do you use?

- Quality Agreement
- Comprehensive Risk Assessment
- Supplier Audit
- Performance Monitoring
- Implementing Controls to Ensure Quality
- Change Control Procedures
- Documentation

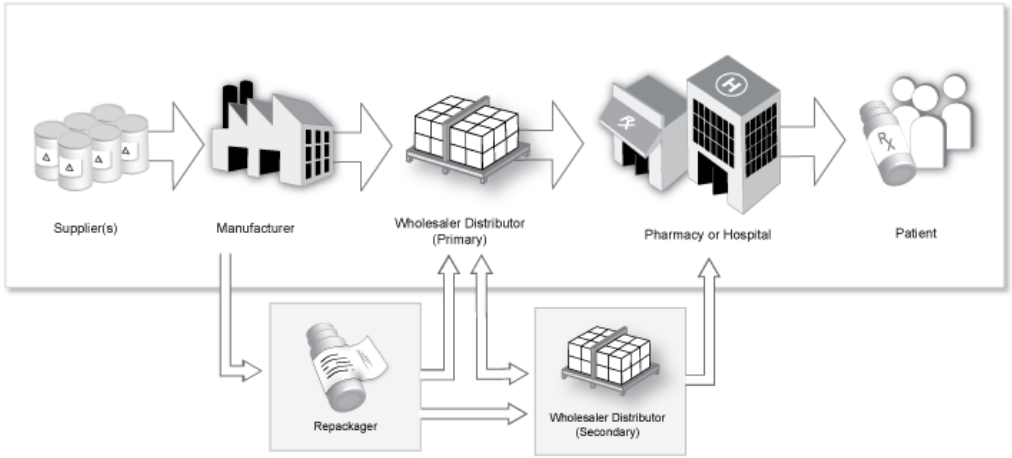
Due Diligence – What questions should you be asking?

- Roles and responsibilities defined?
- Access allowed for oversight?
- Clear change control procedures?
- Involved in investigations and CAPAs?
- Clearly defined criteria for accepting product?
- Performance metrics that can be measured over time?
- Dispute resolution process?
- Verifying the accuracy and completeness of testing results in the COA?

What can go wrong?

- For cause inspection of facility
- 483/WL to CRO/CMO/Supplier
- Rejection of data
- Import Alert
- Delay of pending NDA or ANDA
- Observation or WL to product owner
- Seizure
- Consent Decree
- Injunction

Enhanced Responsibilities for Distribution Chain



Drug Supply Chain Security Act (DSCSA)

- Creation of an electronic, interoperable system to identify and trace certain specific drugs as they are distributed in the United States
- To be fully implemented by 2023
- Are you ready? https://www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/DrugSupplyChainSecurityAct/ucm427033.htm

Unique Device Identification System

- Unique device identification system designed to adequately identify devices through distribution and use
- Unique Device Identifier (UDI) on label and packaging
- Implementation in stages
- UDI basics: https://www.fda.gov/medicaldevices/deviceregulationandguidance/uniquedeviceidentification/udibasics/default.htm

Economically Motivated Adulteration Risks in Global Food Supply Chains

FDLI Annual Conference, Washington DC, May 5, 2017

Massachusetts Institute of Technology

FDLI

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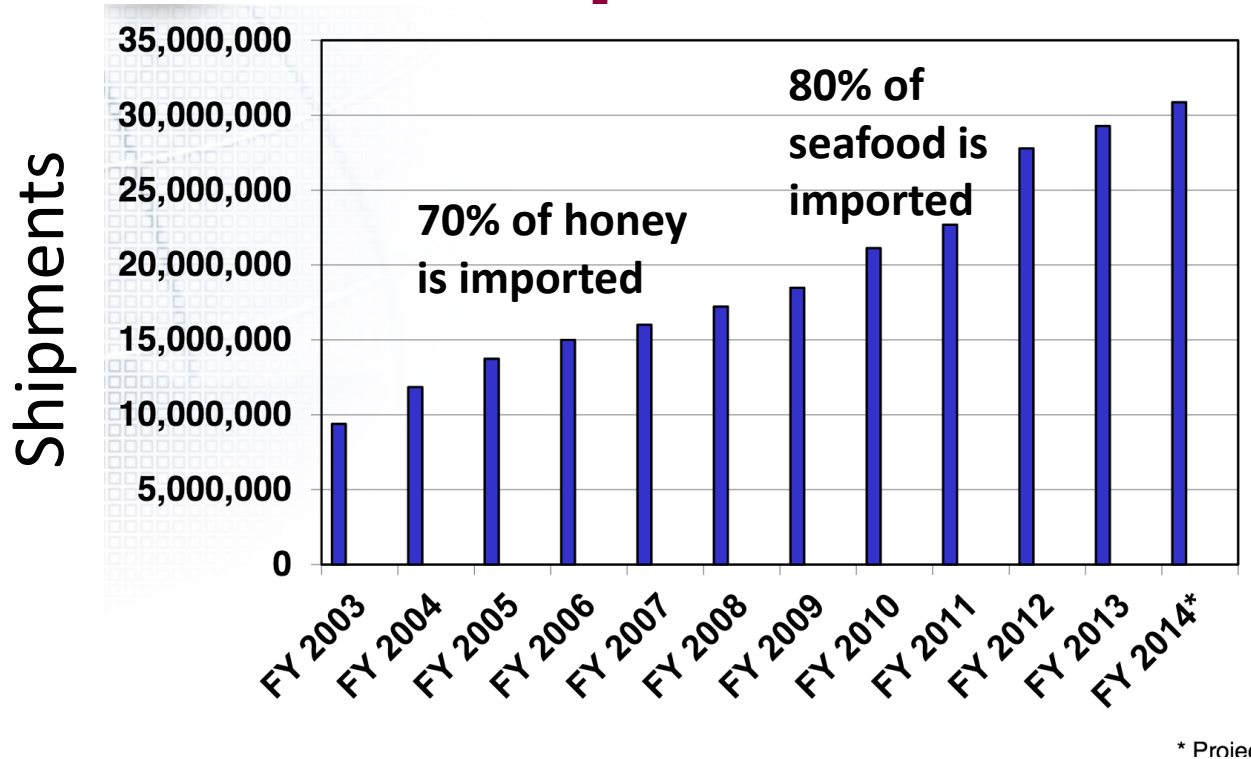
Food Imports to US



* Projected

Types of Food Adulteration

How does the structure of food supply chains impact the risk of economically motivated adulteration?

FDLI

Challenges in Regulating Food

- **Adopted approach from drugs & devices:**

  Heavy testing of final products (develop testing protocols)

- **However, unlike drugs there is a lack of a ‘recipe’:**

  Too many things can penetrate the supply chains

- **Very complex and opaque supply chains**:

  Many problems start at the invisible upstream parts

- **Extremely targeted testing methods**:

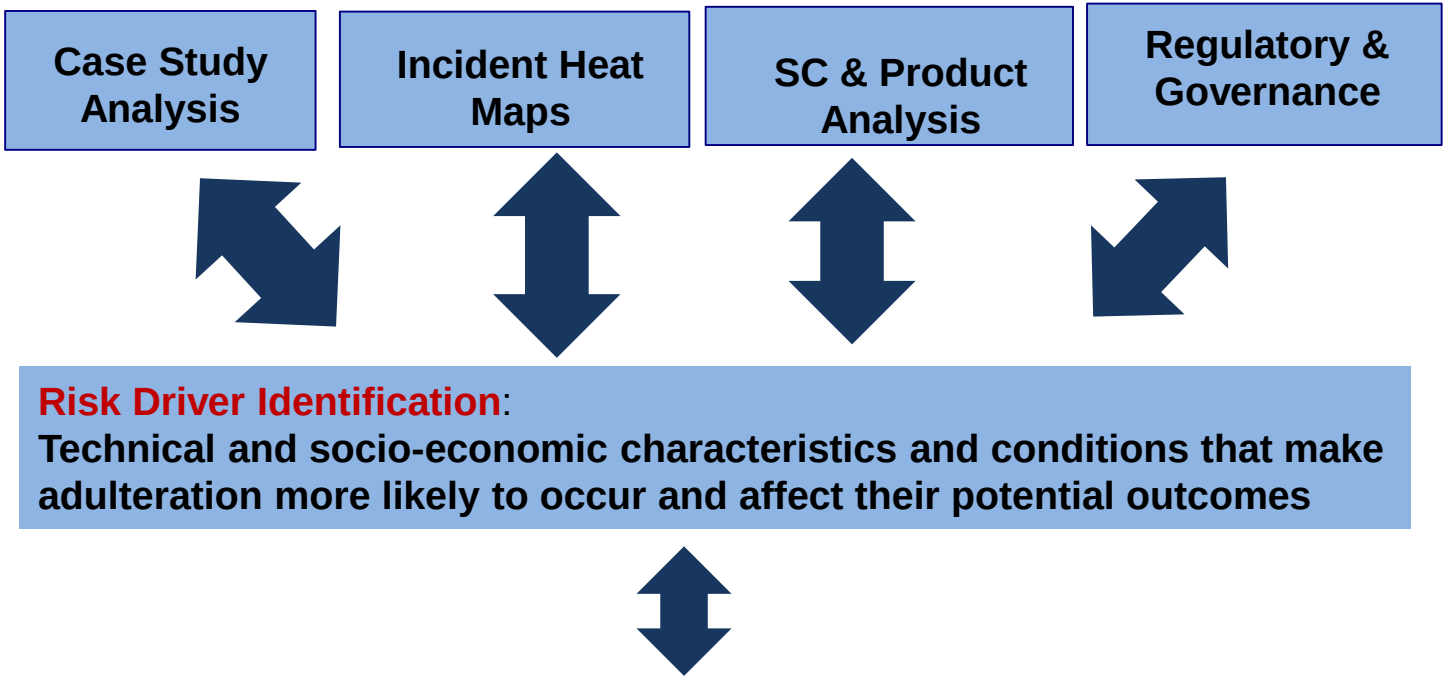
  Problematic economics that leads to sparse monitoring!

Federal Response

- Response needed to large number of food-borne illnesses in the 2000s
- FDA Food Safety Modernization Act is signed into law in 2011

- Focuses on ***preventing*** food safety problems rather than ***reacting*** to them
- Responsibility and accountability of the industry

MIT Effort Domains



The MIT Team

Team expertise in risk management, operations research, intelligence, Chinese socio-economic and regulatory environment, food manufacturing, adulteration testing, supply chain tracing, and machine learning

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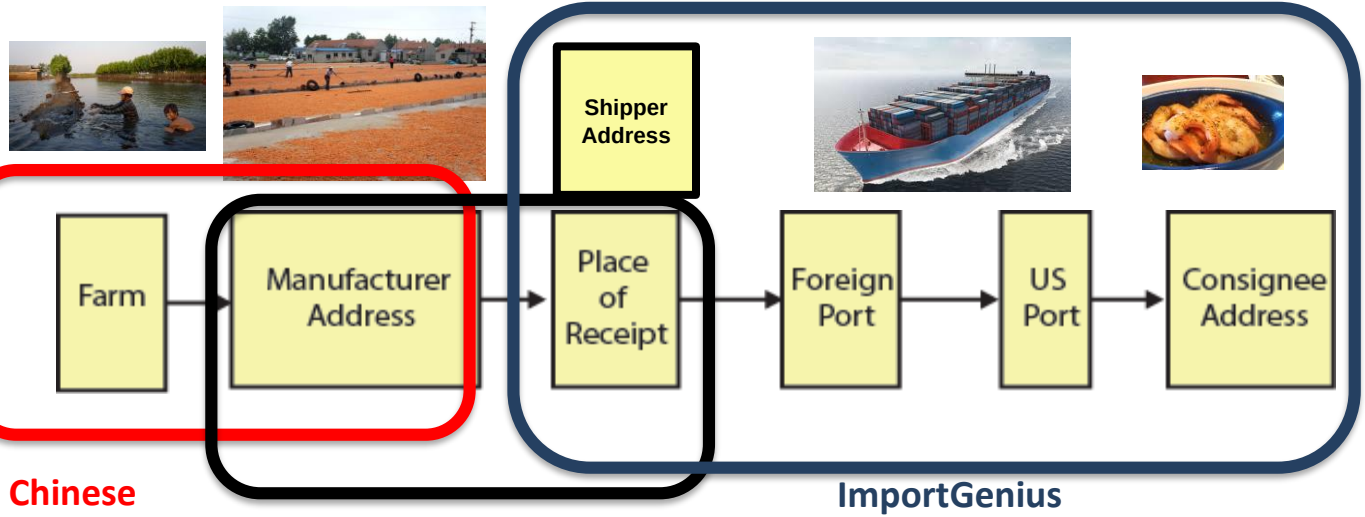
Food Supply Chains Data

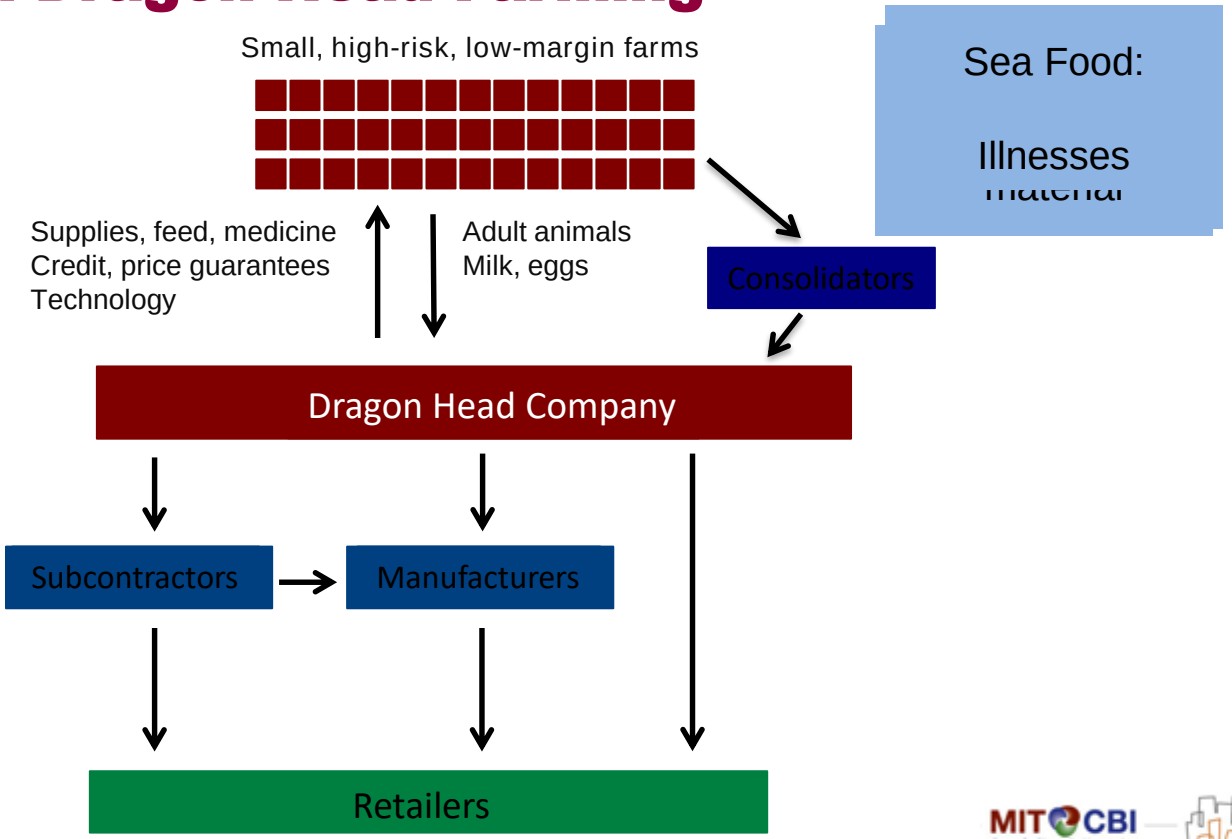


Chinese sources

- FDA shipment data
- FDA Alerts and Refusals for manufacturers
- Sampling information

ImportGenius (Database of bills of lading)

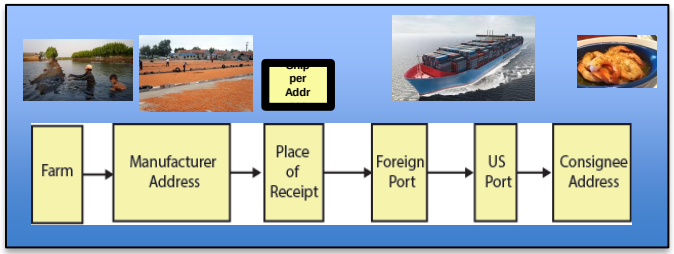
Example I: Dragon Head Farming



Example II: Risk Analytics

- Use shipment data to identify SC patterns of food adulteration and develop predictive risk models

- Leverage predictive models into decision support tools



A model will be developed and validated per product category!

Decisions

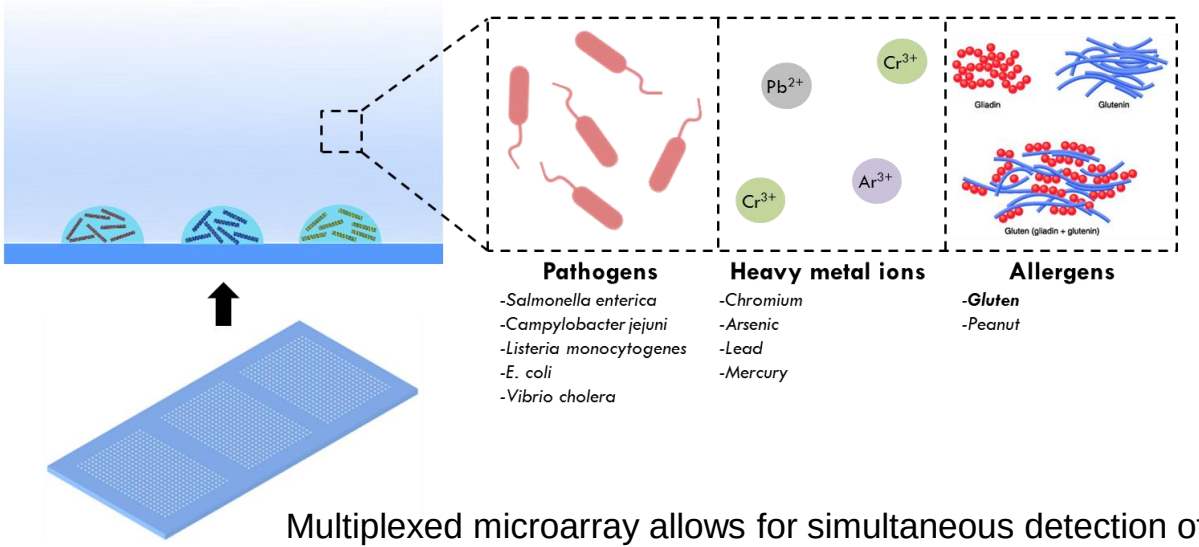
- Sample Shipments
- Inspect Sites
- Raise Alerts for Products, Manufacturers, or Countries

Example III: Multipurpose Ingredients

- SCs of ingredients that feed into a wide range of products (industrial applications, food, pharmaceuticals and/or cosmetics)
- Different grades and prices/costs
- SCs that are highly distributed and opaque
- SCs that are exposed to major price differences and have unused capacity
- SCs that are exposed to a variety of contaminants (hard to test)
- Examples: Glycerin, Gelatin

Example IV: Innovative Testing

Our goal: Develop a portable platform of carbon nanotube sensors capable of rapid, versatile and multiplexed detection of many harmful food and water-borne contaminants



Multiplexed microarray allows for simultaneous detection of various classes of contaminants

Concluding Comments

- Supply chains matter! Testing will not suffice without deep understanding and monitoring of the supply chains
- Food supply chain risk drivers (structure, visibility, socioeconomic environment, dual use)
- Supply chain analytics could help prioritizing risk at the product level, firm level and shipment level
- Need to develop new systematic testing capabilities
- Changing the economics of monitoring food SCs
- Many takeaways to drugs & devices