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Determining the Value of Re-Shoring Drug Ingredient Manufacturing

Richard Mutchler
President

Dora Meissner / Director of Regulatory Affairs

Sarah DeMaio / General Manager

Agenda

- Introduction
- When to Consider Re-Shoring
- Decision Process
- Return on Supply Chain Investment
- Why Re-Shore?
- Case Studies

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Introduction: BioSpectra History

1993	Improvement of Supply Chains for Buffers
1994	Research and Development
1995	Established Commercial Paths for Legacy Products
1996	First Manufacturing Facility in Sciota, PA (10,000 sq ft)
2000	Stroudsburg, PA Manufacturing Facility (25,000 sq ft)
2012	Bangor, PA Corporate and Manufacturing Facility (150,000 sq ft)
2017	Currently Expanding for API and Solvent Manufacturing

Introduction: BioSpectra's Goal

To ***support*** those drug product manufacturers who strive for:

The safest and most consistent therapeutic effect from each and every dose of medicine to each and every patient.

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Introduction: BioSpectra's Responsibility

To ***supply*** those drug product manufacturers who support our goal with:

Pharmaceutical Ingredients that are designed and manufactured in accordance with regulatory guidelines, guaranteed in writing to be suitable for use in drug product manufacturing, insured as such and offered at competitive prices.

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Introduction: Supply Chain History

1950 – 1970's	Drug Manufacturing in the US
1980 – 2000's	"Not In My Back Yard" Movement
2010 – present	Renewed focus on Compliance, Efficacy, and Quality

When to Consider Re-Shoring?

- Re-Shored material vs. Off-Shore material
  - Hidden Cost of Off-Shore Manufacturing
    - Translation
    - Impurity
    - Sampling
  - Cost of Poor Quality
    - Supply Chain Insecurity
    - Additional Supplier Management Resources

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Hidden Cost of Off-Shore Manufacturing

- Translation
  - Validated language translation certification programs
  - Cross translating documents from site audits
  - Verification of Translation with Manufacturing Tests
  - Failed Translation Validation Programs
  - Third Party Auditor Translations
- Change Control
  - Cost of failure to notify of changes
- Sampling
  - Cost of Increased Sampling Plans for product uniformity assurance

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Costs of Poor Quality

- Supply Chain Insecurity
  - Inability to Comply with procedures
  - Unverifiable Quality Systems / Traceability
  - Absence of Change Notification
  - Intended End Use
- Additional Supplier Management Resources
  - Supplier Corrective Actions
  - Outreach Programs

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Improving Existing Manufacturer

Pros	Cons
History of Supply	Increased Manufacturer Resources
Existing Relationship	Established History of Non-Compliance
Potential Limited Requalification	Negative Quality Culture Norms
Reduced Regulatory Impact	Systemic vs. Isolated Incidents

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Re-Shoring Decision Process

- Effects of Re-Shoring
  - Obstacles
  - Opportunities
- Financial Impacts of Re-Shoring
  - Costs
  - Risks
- Benefits to End Patients and Shareholders

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Effects of Re-Shoring: Obstacles

- Obscuring Supply Chain
  - Increased Complexity of Supply Chain
  - Risk of Repackaging non-pharma materials in a controlled environment
- Audit Practices of Non-GMP Manufacturers
  - Repackaging and Retesting vs. GMP
    - “GMP Lite”
    - “elements of GMP used in manufacturing”

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Effects of Re-Shoring: Opportunities

- Create Partnerships with the Manufacturer
  - Long Term Supply Agreements
    - Dispersion of Cost
  - Create Legitimate Systems
    - To support Intended End Use
  - Written Declarations of Intended End Use
    - Shared risk with Supply Chain

Critical Raw Materials should be supported by a Drug Master File

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Financial Impacts of Re-Shoring

Costs and Risks associated with Off-Shoring	
Validation of Translations	Risk Management for Compliance in accordance with Intended End Use
Implied liability for inherent language and cultural inconsistencies	Increased Sampling Plan and testing costs
Staff	Raw Material Usage Changes
Travel	Specification Changes
Additional Systems and Procedures	Process Changes
Investigations, Corrective Actions, Preventative Actions	Trace Impurity Analysis
On-Site Staffing and Training	Impact Assessment to Final Product efficacy
Manufacturer Costs	Third Party Translator Validation
Plans and procedures to avoid, explain, justify, or shift responsibility for these events and maintain liability coverage for the significant occurrences of each of these at each manufacturer	

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Or…

- Establish a Supply Agreement with a USFDA registered and inspected facility and ask for a Letter of Authorization to reference the DMF for the Excipient or API being used.

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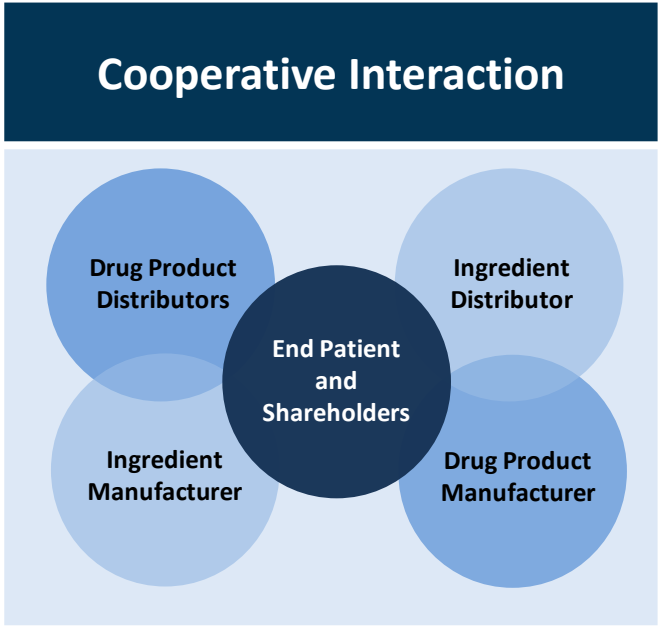
Benefits to End Patients and Shareholders

- Ensuring Supply Chain Decision is Beneficial to End Patients and Shareholders
  - Regulatory and Quality benefits
  - Return on Investment
    - Short Term
    - Long Term



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Regulatory and Quality Benefits of Re-Shoring

Advantages to Regulatory and Quality in Re-Shoring	
Utilizing US Manufactured Ingredient	USFDA Registered and Inspected
	Validated Processes
	Validated Analytical Methods
	Drug Master Files
Positive Impact	Share Holders
	Corporate Officers
	Board of Directors
	Regulatory Agencies
	Risk Partners
	Customers
	End Patient

Disadvantages to Regulatory and Quality in Off-Shoring	
Utilizing an Off-Shore Manufactured Ingredient	Poor Translation of Quality Documents
	Lack of Quality Compliance
	Limited Regulatory Support
	Reduced Process Capabilities
Negative Impact	Share Holders
	Corporate Officers
	Board of Directors
	Regulatory Agencies
	Risk Partners
	Customers
	End Patient

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Return on Investment (Adverse)

- Intended End Use
  - Risk to Quality based on perceived cost
  - Risk of departmental objective not matching corporate objective
  - Risk partner impact / Ability to support intent
- Cooperate with existing manufacturer
  - Opportunities for Improvement
  - Long Term ROI

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Return on Investment (Favorable)

- Materials of Correct Intended End Use
  - Consistent Therapeutic Effect
  - Allows Regulatory team to focus on growth
  - Shows clear commitment to patient safety
- US Manufacturer
  - Accountable to USFDA
  - Improved access to information and inventory

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Supply Chain Deficiencies are not Country Specific

- Drug Product Manufacturers:
  - Know your supplier
  - Demand adequate evidence of compliance
  - Clearly communicate expectations
  - Require clear (non-ambiguous) Intended End Use Statements for every batch of every Raw Material
- Drug Ingredient Manufacturers:
  - Limit Regulatory support to the Grade requested and purchased
  - Make sure you are prepared to support the Drug Product Manufacturers Intended End Use.

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Re-Shoring – Case Studies
Industrial Chemicals

Company	Initial Off-Shoring	Concerns with Off-Shoring	Re-Shoring Benefits	Success Rate
Dow	Product R & D	➢ Skilled Labor ➢ Product costs	➢ Direct economy impacts ➢ Skilled/Trained Labor	➢ Re-Shored in 2016 with continued cost improvement

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Re-Shoring – Case Studies Appliances

Company	Initial Off-Shoring	Concerns with Off-Shoring	Re-Shoring Benefits	Success Rate
General Electric	Outsourced Manufacturing of specific Products	➢ Price ➢ Inventory Management ➢ Wage ➢ Freight Cost ➢ Personnel Risks	➢ Direct communication ➢ Government Incentives ➢ Lean process improvement ➢ Reduction in Total costs	➢ Re-Shored in 2012 with continued cost improvement

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Re-Shoring – Case Studies
Food

Company	Initial Off-Shoring	Concerns with Off-Shoring	Re-Shoring Benefits	Success Rate
Heinz	Manufacturing	➢ Process Techniques ➢ General lack of financial Benefit ➢ Business Improvements	➢ Government Incentives ➢ Business Improvement Techniques	➢ Long Term Results

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Re-Shoring – Case Studies Automotive

Company	Initial Off-Shoring	Concerns with Off-Shoring	Re-Shoring Benefits	Success Rate
General Motors	Outsourced Manufacturing and R&D	➢ Price ➢ Inventory Management ➢ Wage ➢ Freight Cost ➢ Personnel Risks	➢ Innovation ➢ Image/Brand ➢ Lean Process Improvement ➢ Skilled workforce ➢ Higher Productivity	➢ Re-Shoring in 2015-2017 with continued process/cost improvement

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Re-Shoring – Case Studies
Active Pharmaceutical Ingredient

Company	Initial Off-Shoring	Concerns with Off-Shoring	Re-Shoring Benefits	Success Rate
BSI Customer	Sourced API from China	➢ Consistency ➢ Inventory Management ➢ Difficulty of Access ➢ Gaps in Quality Systems	➢ Traceability ➢ Regulatory Support ➢ Full access to manufacturing site and Inventory	➢ Re-Shored in 2015 with Three new API's in Development at BSI

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Questions?