Mitigating Raw Material Risk for Supply Chain Continuity

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What's driving the focus on risk mitigation?

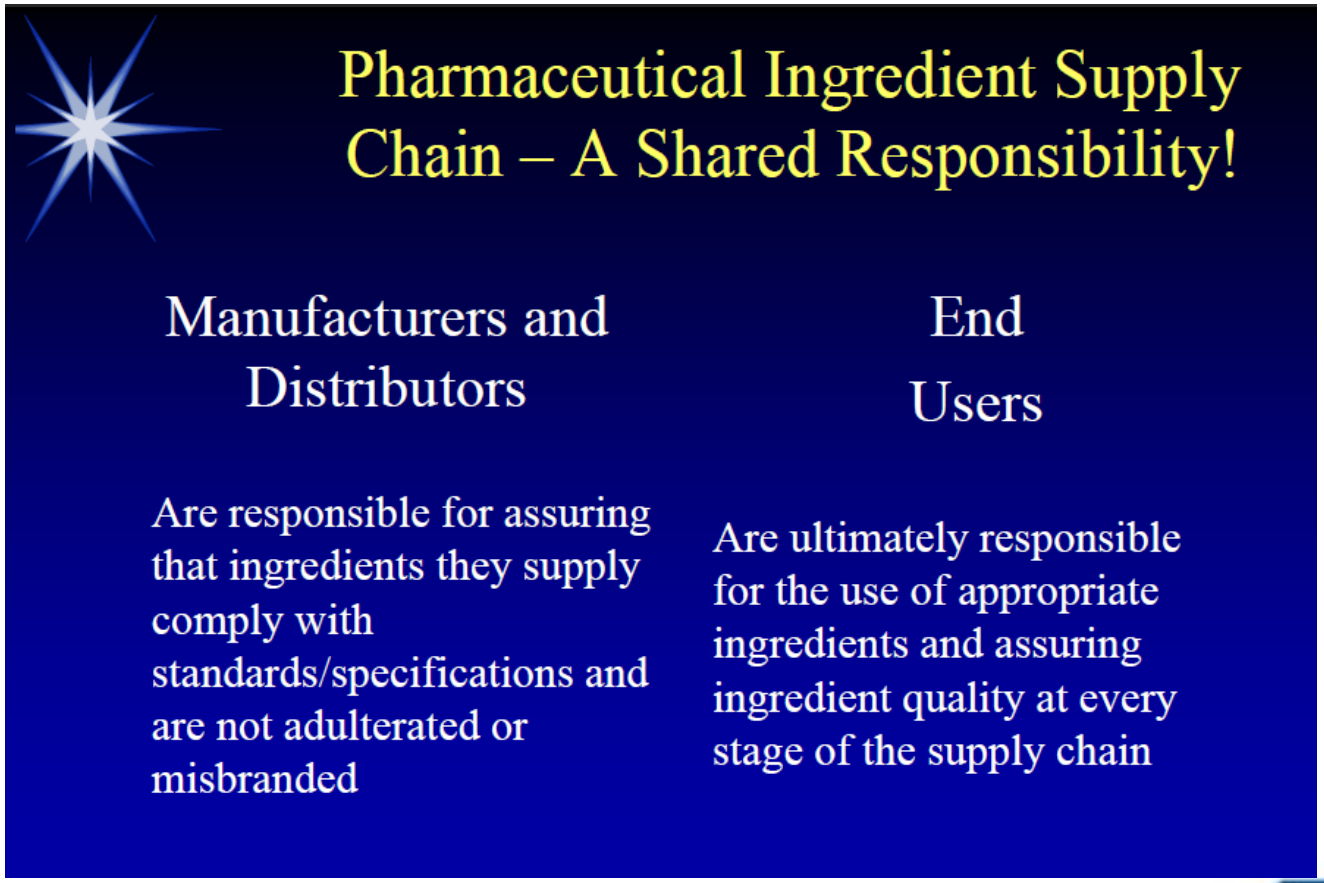
- Globalization of the supply chain
- Adverse events: e.g. heparin
- Biopharmaceutical industry is maturing
  - Lean manufacturing practices
  - Process optimization
  - Scalability considered earlier
  - Companies want to save $$
- Competing demands for raw material resources
- FDA has increased interest in risk mitigation

Slide from Deborah M. Autor, Director CDER Office of Compliance, DCAT Mar09

Conclusion

- In a global economy,
  - Pharmaceutical industry must bear clear responsibility for the integrity, quality, and safety of their products and all ingredients
  - Regulators must work together and adopt a world-wide approach
- **Complacency is NOT an Option**

Slide from Richard Friedmand, Director CDER Division Manufacturing & Product Quality, DCAT Mar09



To mitigate effectively, we need to understand **total** supply chain risk

Crude oil (or other basic source)

Industrial chemical factory

cGMP repackager

cGMP distributor

Biotech manufacturing

Systematic vs. Specific Risk

Systematic Risks: affect the majority of your raw materials. Based on market conditions.

Specific Risks: affect a segment of raw materials

Key systematic risks today: Chemical market

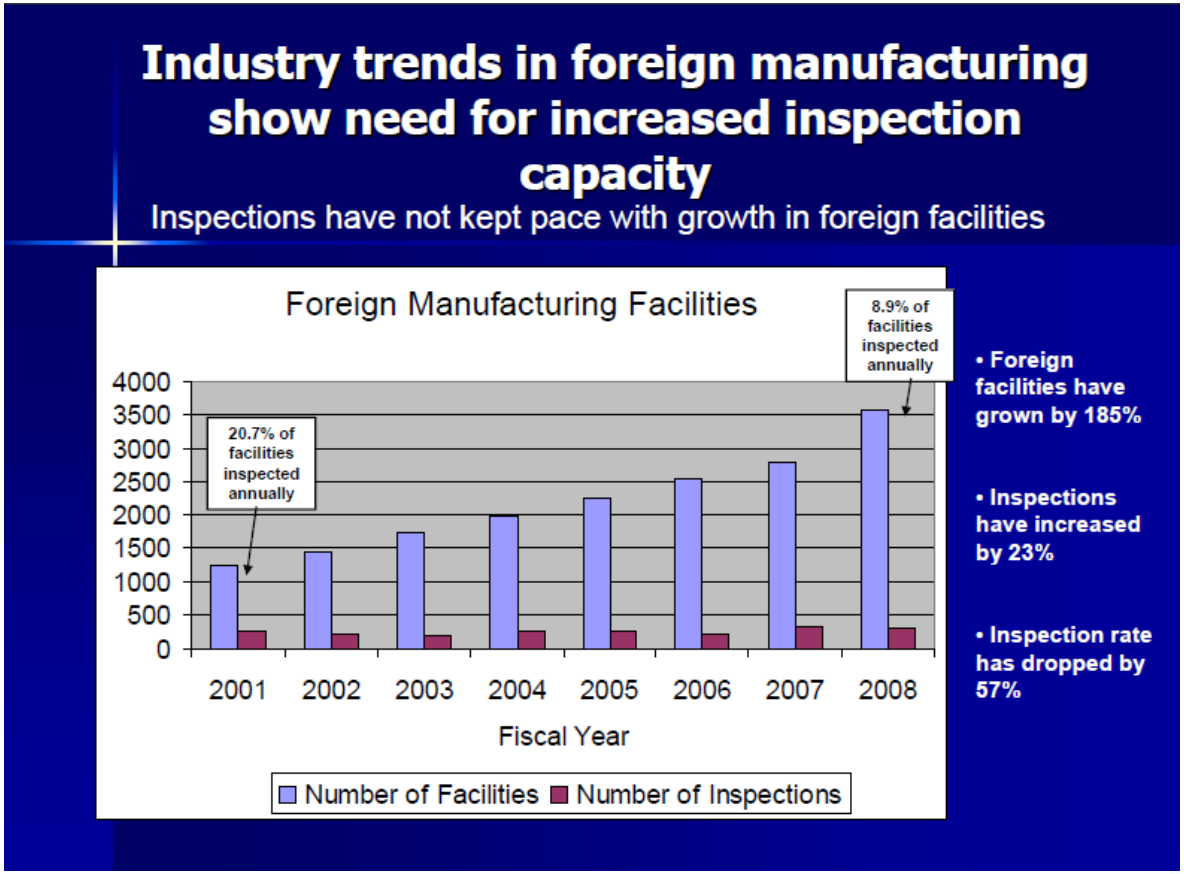
- Biotech industry is a small percentage of overall chemical market demand
- Specialty producers still upgrading facilities to meet quality standards
- Chemical industry consolidating
- Chemical industry is a mature industry
- Transparency to original source is major challenge
- Many materials still do not have compendia
- China is a net importer of many chemicals (isopropyl, benzene, acetone, methanol)

Key systematic risks today: regulatory

- Limited oversight from foreign drug regulators
  - Chemical manufacturers overseas supervised by other agencies
- Limited FDA oversight overseas
  - FDA must be invited onto foreign soil to perform inspections
  - Manufacturer “only” gets weeks advance notice of inspection
  - FDA has new and few foreign dedicated inspectors

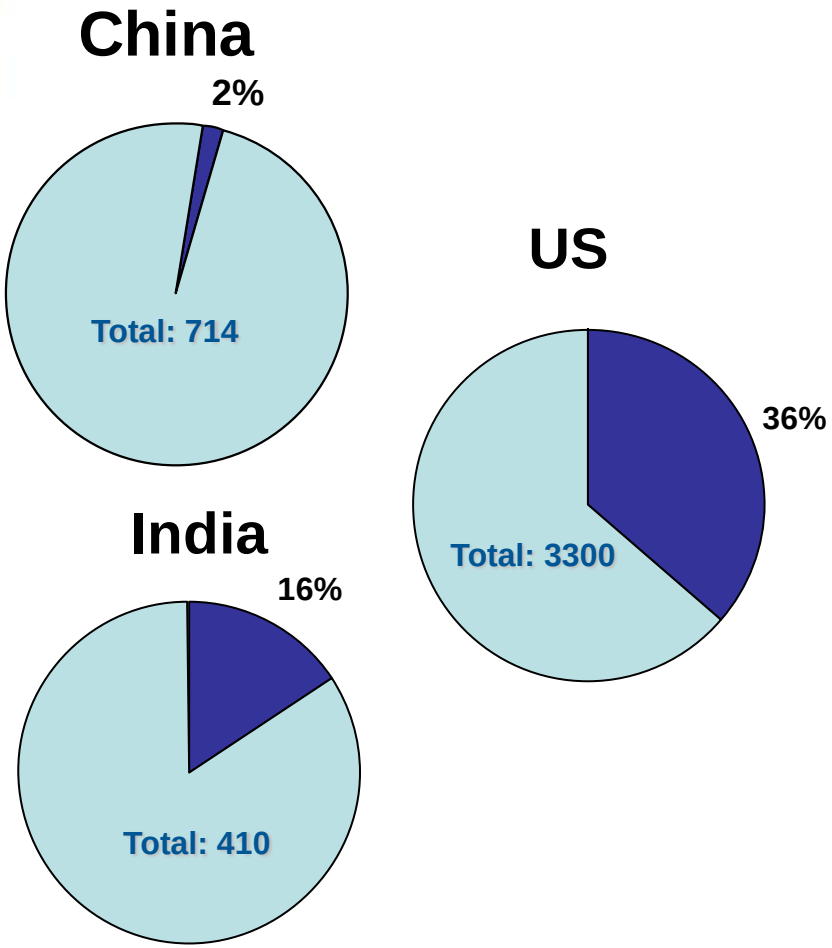
Reference: Challener/Vermont, Cynthia (2008). Inspections come under the microscope. ICIS Chemical Business. 20-21.

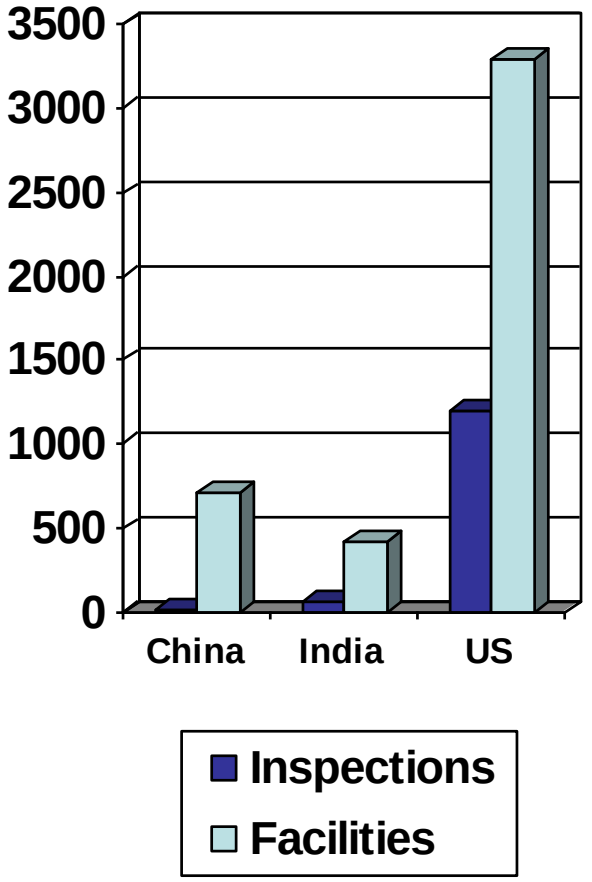
Inspection of Foreign Manufacturing Facilities: 2001 - 2008



Reference: Globalization: Challenges and Recent Case Studies, Deborah M. Autor, Esq. Director CDER Office of Compliance, excerpt from a presentation given at DCAT 18Mar2009

Limited Oversight





Source: Mansell, Pete (2008) . Supply chain globalization weighs heavily on FDA. In-Pharma Technologist.com

Example of a systematic risks we are currently facing

- Acetonitrile and it's dependence upon the automotive and housing industry
  - Co-produced with acrylonitrile
  - Acrylonitrile is driver of production

Specific risk factors—upstream supply

Risk Factor	Basic Chemical Manufacturer	cGMP Manufacturer / Repackager	Distributor
Industry Focus	X	X	X
Production Capacity	X	X	
Facility location	X	X	X
Materials source	X	X	
Product demand in all industries	X		
Environmental risk	X	X	X
Geo-political risk	X	X	X
Financial risk	X	X	X
Audited quality systems	X	X	X
Track record with governing body	X	X	
Lead time	X	X	X
Sole Sourced material	X	X	
Transparency into supply chain	X	X	X
Management of Change	X	X	X
Disaster preparedness	X	X	X
Buying power of raw materials		X	
Ability to maintain acceptable quality level	X	X	X
Leverage with suppliers			X
Alignment with suppliers and customers			X
Storage space constraints		X	X
Supply chain management expertise		X	X

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Alignment with suppliers and customers			X
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Supply chain management expertise		X	X

Recent Case Where We Have Encountered Specific Risk

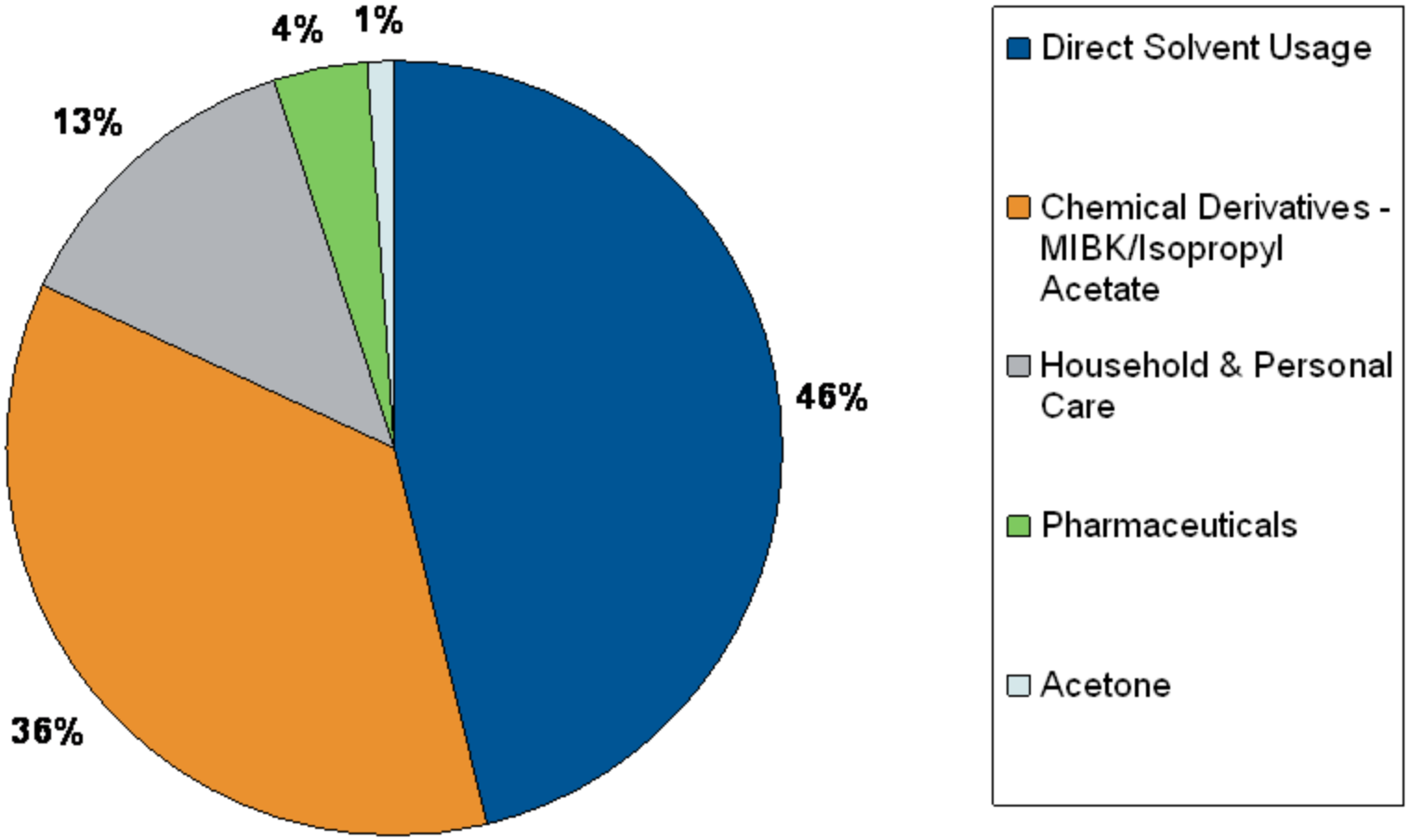
- Potash strike and the elimination of source for high quality potassium
  - Not only North American issue
  - All major chemical manufacturers purchasing starting material from Potash Co
  - Effect on Multiple Industries

Case example: IPA

- Limited number of suppliers produce 1.9 billion lbs crude IPA
  - Dow, Exxon, Shell and Equistar
  - Produced in only three U.S. locations
  - Shell is only Canadian producer of IPA
- Two different processes used to produce IPA
  - Sulfuric acid Oxidation of propylene
  - Hydrogenation crude Acetone
- Grades vary: technical, USP, ACS, semiconductor
- Importance: grade and process impact your production process and suppliers' production impacts your supply chain security

Reference: Chemical Market Reporter (2005). Chemical Profile – Isopropanol.

Usage of IPA


4%
1%
13%
46%
36%
Direct Solvent Usage
Chemical Derivatives - MIBK/Isopropyl Acetate
Household & Personal Care
Pharmaceuticals
Acetone

Counterfeiting and contamination risk

- Substitution of excipient glycerol by counterfeiters: repeat incidents in Haiti, Panama and Bangladesh
- Counterfeit Heparin supplied by a Chinese manufacturer - Changzhou SPL s

Reference: Mansell, Pete (2008). GMP an unnecessary burden for excipients. In-Pharma Technologist.com.

Environmental risk

- Hurricane Katrina exposed vulnerabilities along the gulf coast: sucrose and caustic soda producers
- Impact on transportation and logistics

Unforeseen production changes impact availability: Helium

- Many of the world's 16 helium extraction plants are not running at full capacity → supply shortages
- U.S. helium demand up > 80% in the past two decades
- Demand growing > 20% annually in developing regions such as Asia
- Up to 45% increase in cost in two years

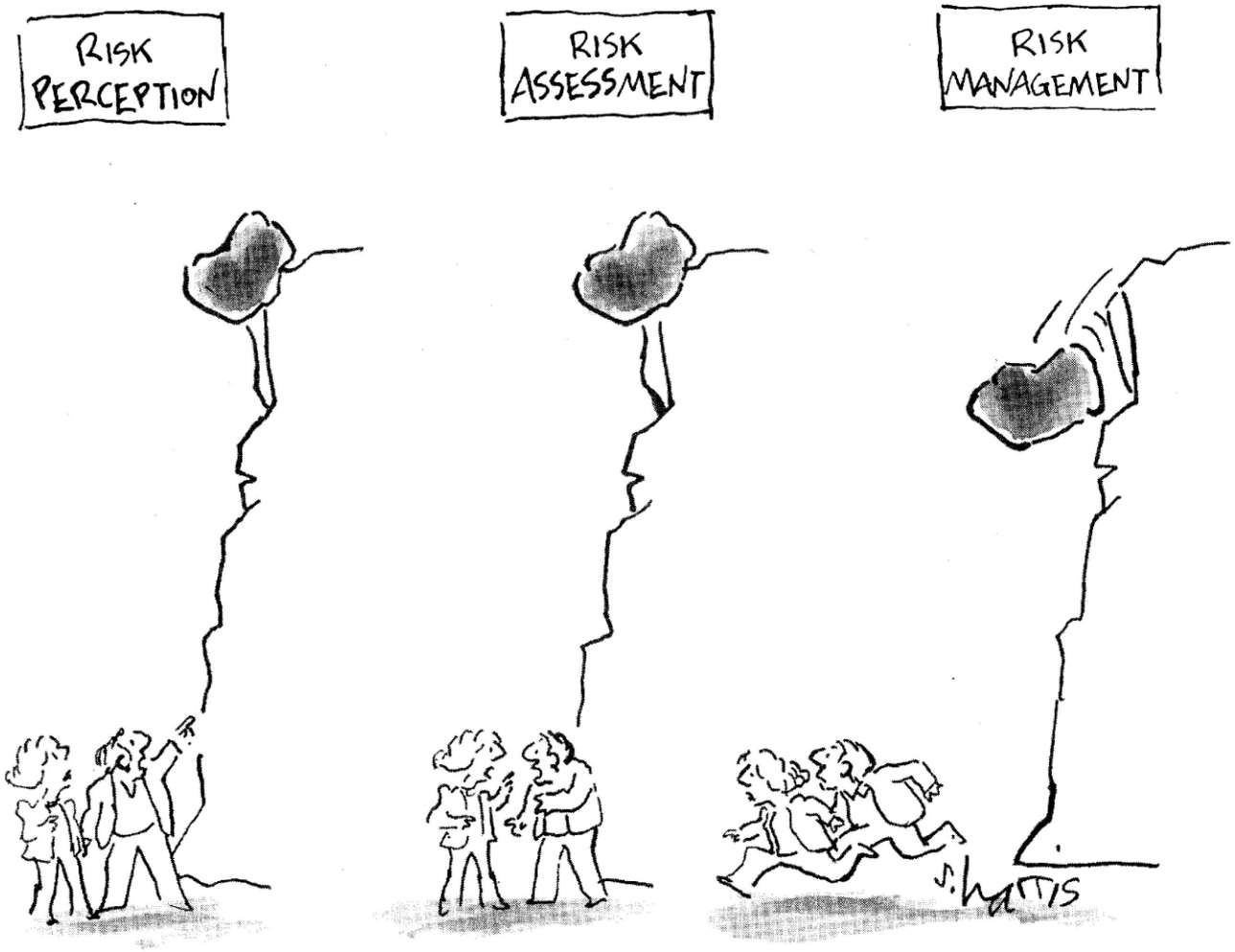
National events affecting Supply Chain logistics

- Olympics in China led to transportation and manufacturing restrictions
- The restrictions started in May … Olympics were in August
- List 257 chemicals that only authorized firms could sell and transport
- Effects felt all over the world

Financial Risk – Economic Meltdown

- Chemical factory shut downs
  - Dow consolidating manufacturing facilities
- Major chemical suppliers filling bankruptcy
  - LyondellBasell and Chemtura filling for bankruptcy
- Lack of ability to refinance debt
  - Financial concerns on balance sheets

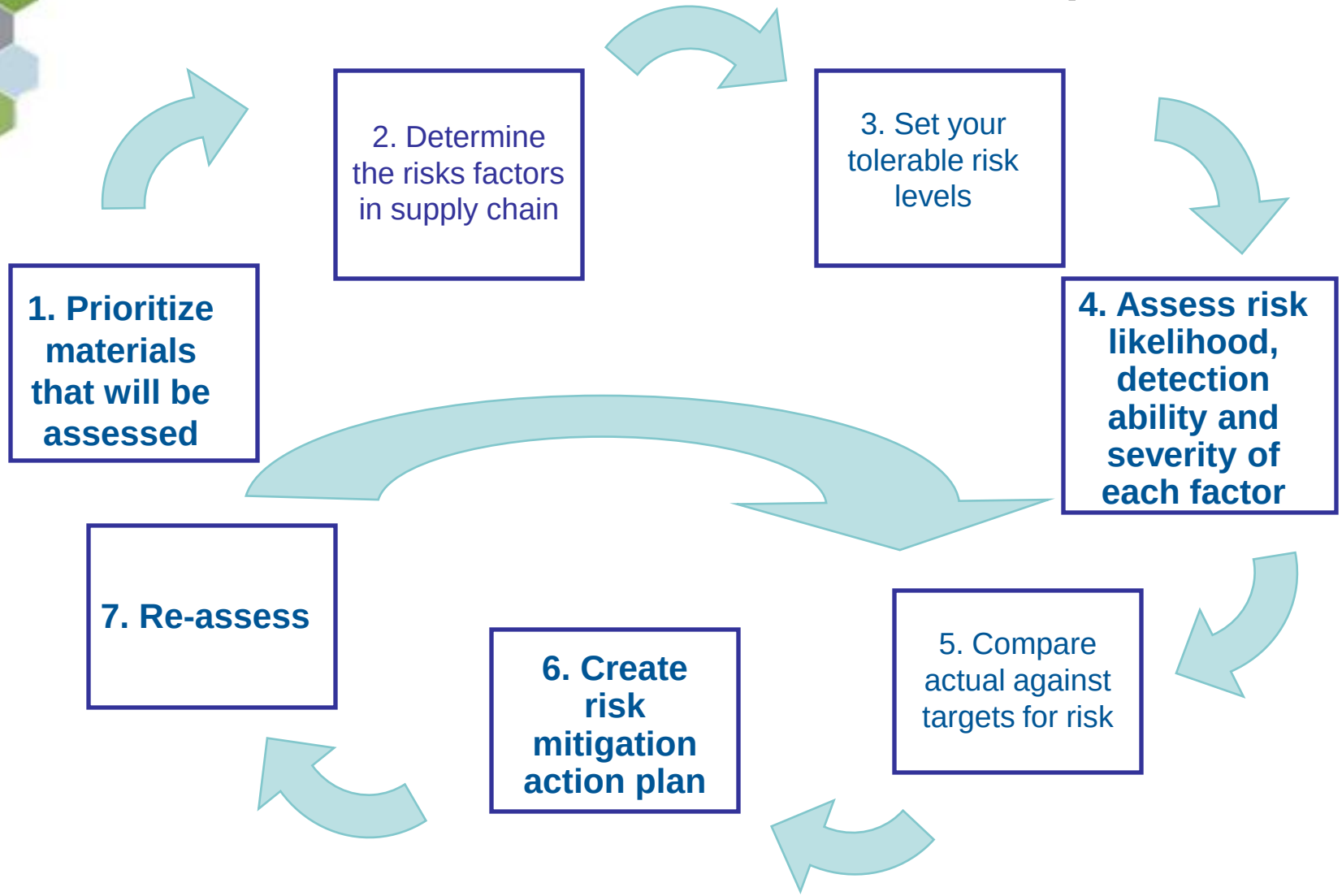
A robust procedure…



Planning a risk assessment

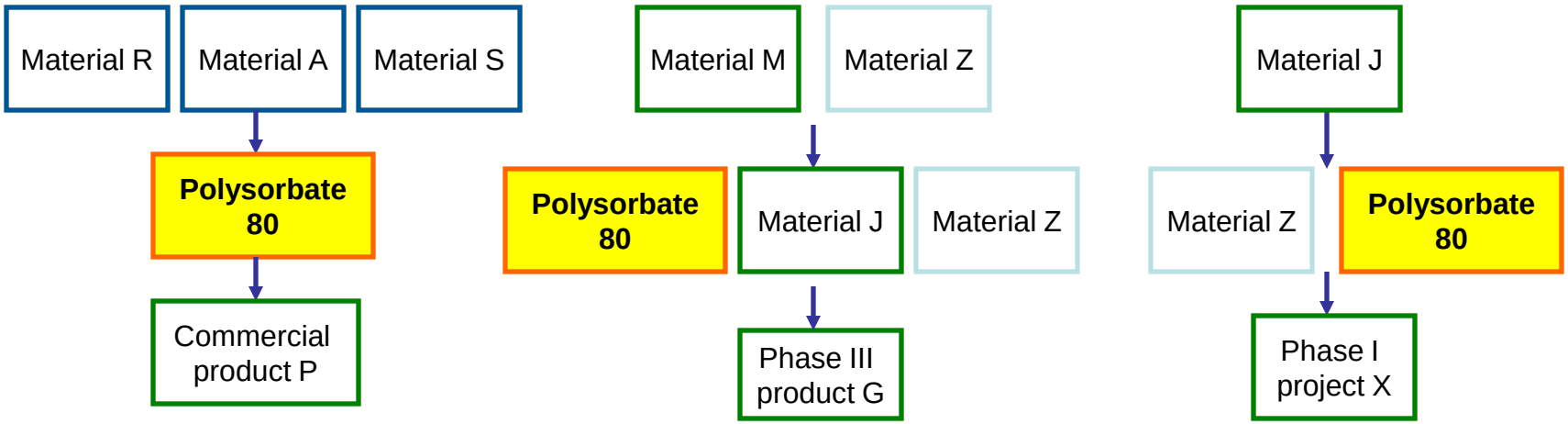
1. Attain a clear idea of your objective
2. **Decide on scope**
   - Do you plan to analyze all materials or all materials related to a particular project?
3. **Involve the appropriate people**
   - Purchasing, materials planning/management, process development, quality, company leadership, supply chain partners
4. Set a timeline
5. Set clear & concise goals

Overview of the assessment process



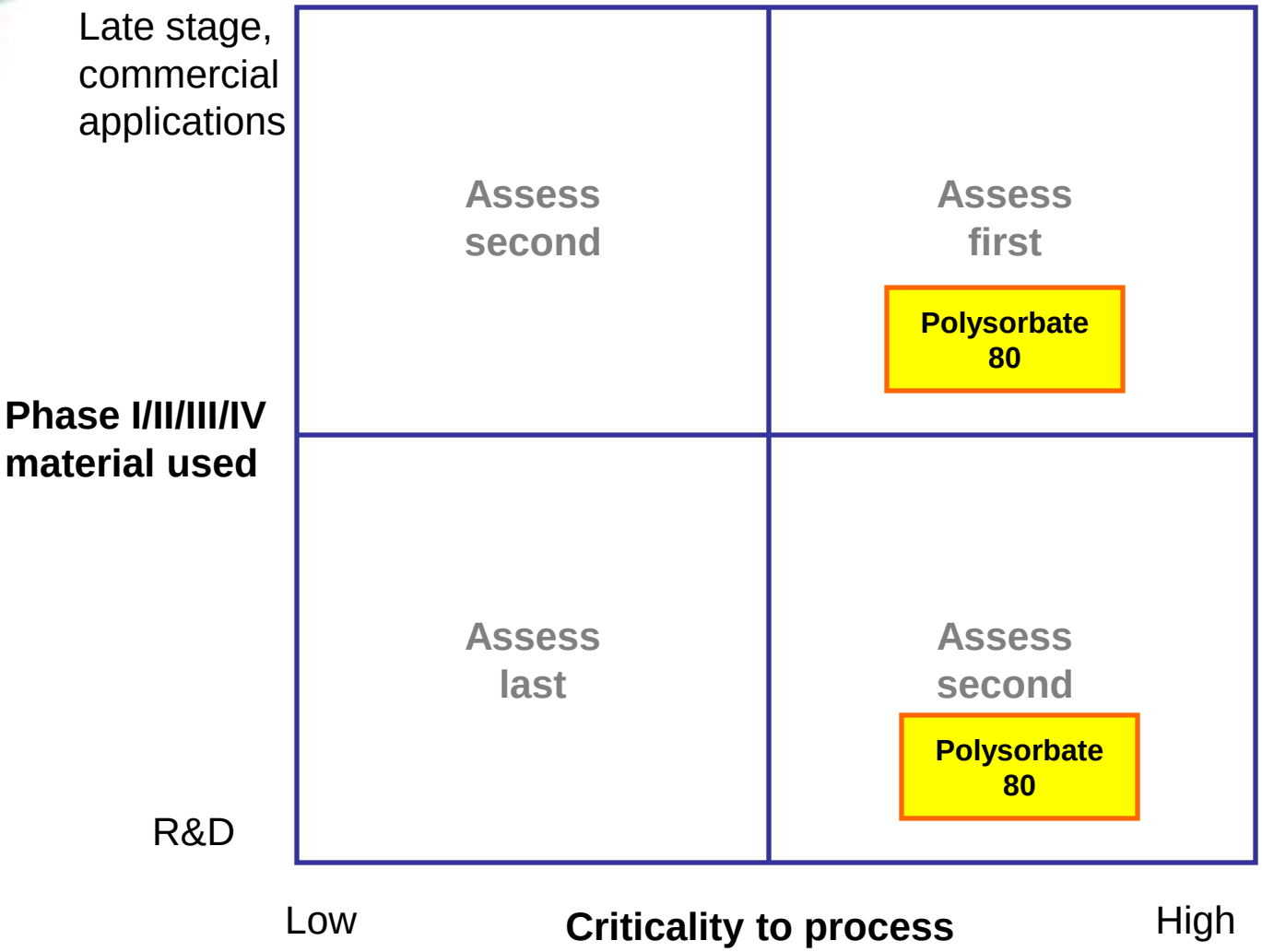
Prioritizing materials

1. Map each material to its use

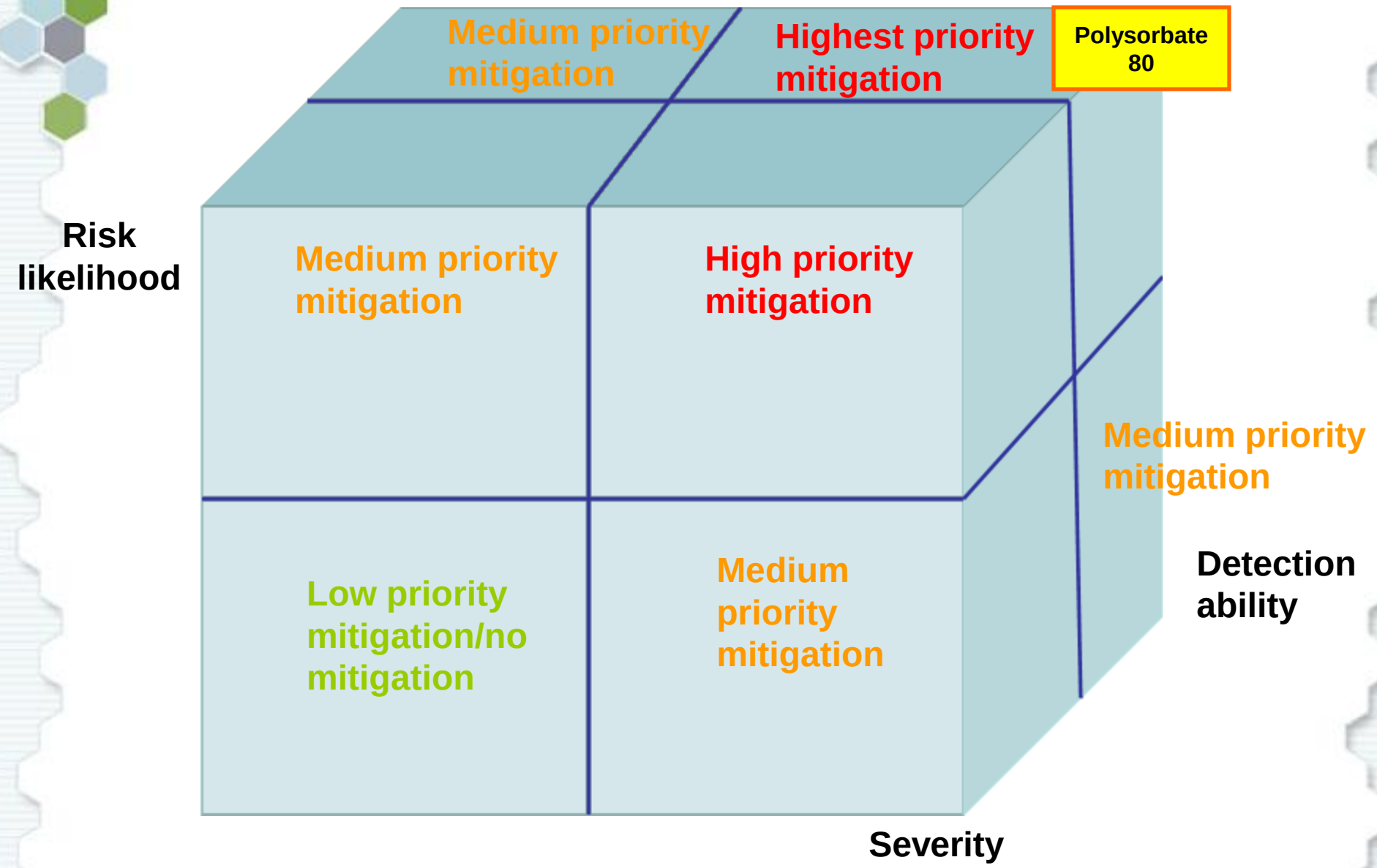


- Determine criticality of material to process
- Rank materials by priority for assessment

Prioritizing assessment



Plot materials in decision cube

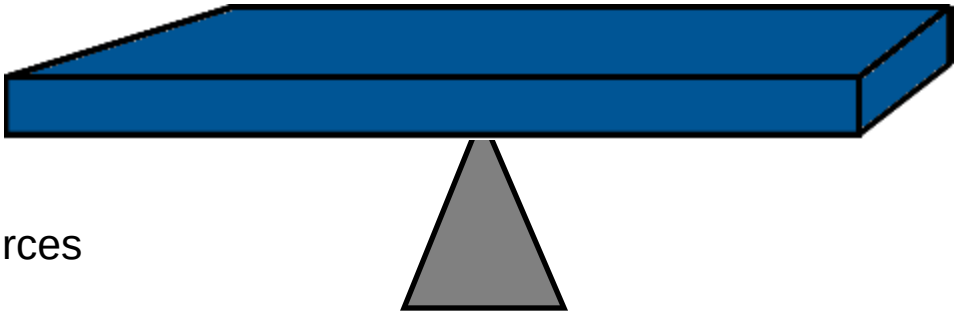


Create risk mitigation action plan

1. **Look at materials most significantly out of range first**
2. **Devise immediate actions to mitigate**
   - Risk mitigation inventory
   - Approval of alternative source
3. **Consider long-term actions to mitigate**
   - Capacity agreements
   - Supplier agreements
   - Regular audits
4. **Do a cost-benefit analysis**
   - Cost to mitigate versus cost of failure
   - Many options; pick the one with greatest ratio of benefit over cost
5. **Re-evaluate risks**
6. **Set up monitoring program**

Balancing risk mitigation and lean manufacturing

Risk **Lean**



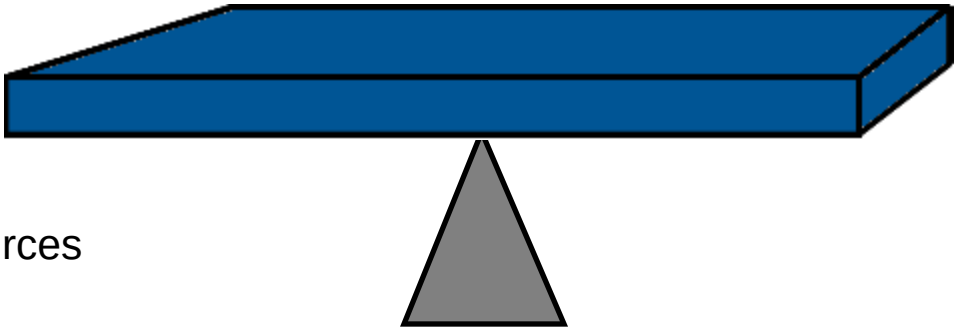
- Hold additional inventory
- Qualify smart sources
- Invest in market intelligence
- Conduct regular audits

- Minimize inventory
- Reduce redundancy
- Reduce costs
- Do the job with fewer people

Initiatives that strike the balance

- Use same raw materials for multiple products
- Initiate Kanban process
- Total chemical management program
- Use consistent set of qualified suppliers

Risk **Lean**



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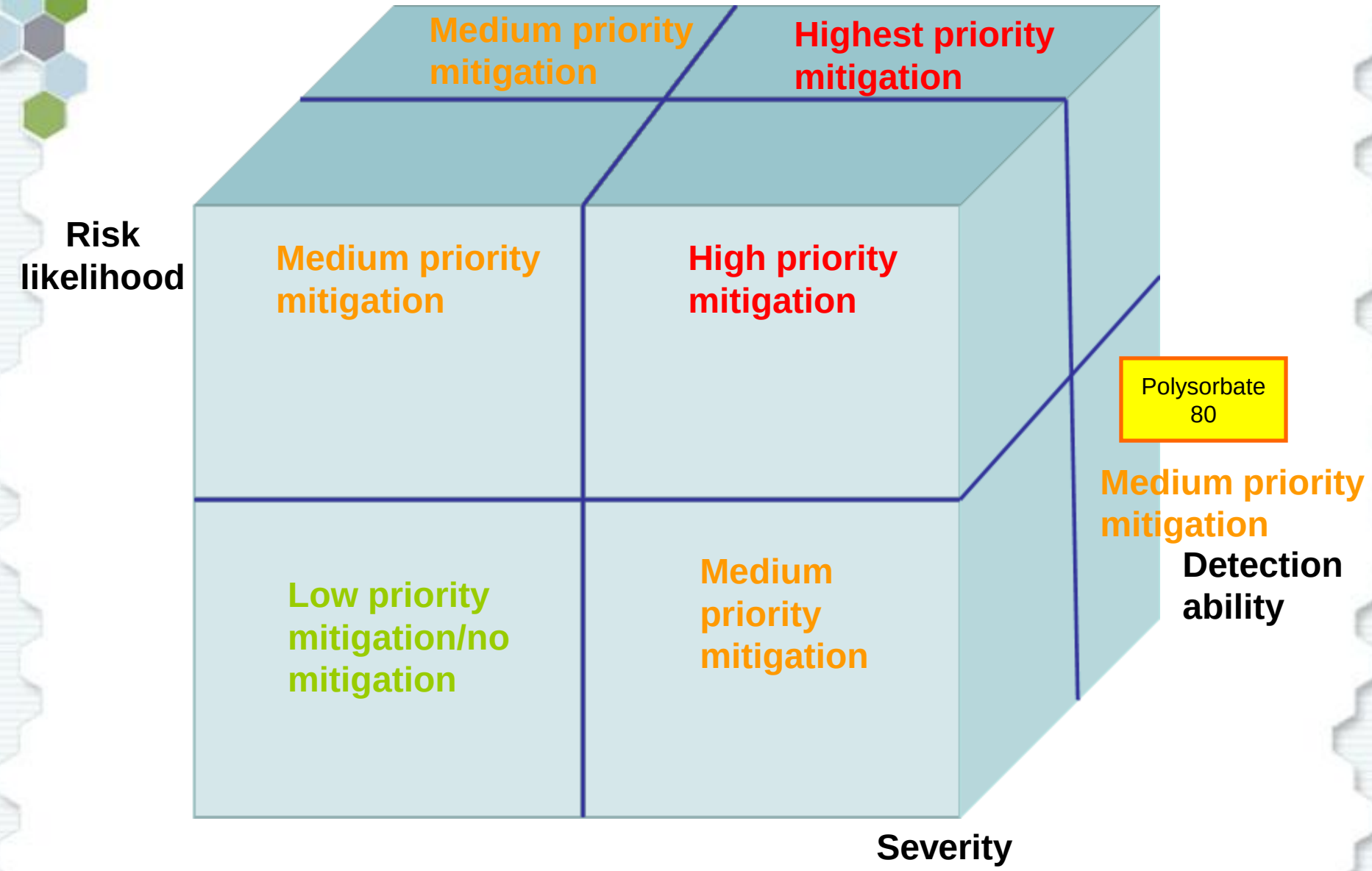
Reassess materials using decision cube



Implications of decisions made from the risk assessment

- What are the additional costs associated with your decisions for each part of your supply chain?
- Could there be alternative ways to reduce risk?
- Who should pay for the added costs?
- How does this effect the way you do business with your supply partners?
- Do your supply chain partners lose any flexibility managing their business?

Takeaways: how to secure your supply chain

- Understand complete supply chain back to basic manufacturer
- Know how decisions impact the supply chain
- Smart sourcing: best decisions start as early as PD
- Biotechnology companies require:
  - complete transparency from chemical manufacturers
  - alignment with supply chain partners with expertise, understanding and capabilities to mitigate their risks

“Efficiency is doing things right; Effectiveness is doing the right things.”

Peter Drucker

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