ISPE REGIONAL MEETING :

SINGLE USE TECHNOLOGY : UNDERSTANDING MATERIALS RISK IN USE

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ISPE REGIONAL MEETING
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OUTLINE

- Typical bioprocesses with Single-Use Systems (SUS)
- Materials qualifications
- End to end Risk based approach to materials
- Understanding Extractables and leachables
- Summary

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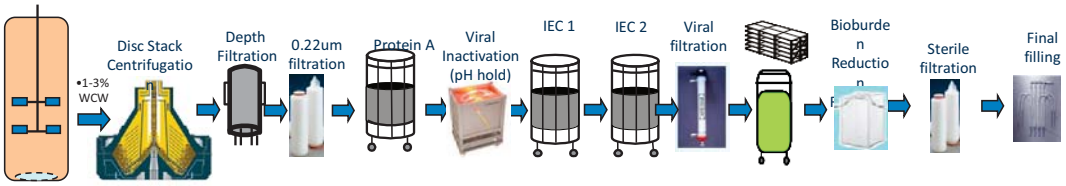
A holistic approach to risk assessment of SU Bioprocess Equipment

Typical bioprocess – Upstream, downstream and fill & finish



- Supplier data on extractables can be used as a starting point
- Risk assessments indicate that extractables are diluted and/or removed through the process
- Leachable studies confirm the absence of organic materials in storage and final product containers

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CONSIDERATIONS FOR QUALIFICATION CRITERIA:

- **Biocompatibility**
  - USP <87> and <88>
- **Mechanical Properties**
  - Tensile Strength, elongation, leak testing, seal strength
- **Gas / Vapor Transmission**
  - ASTM D3985 for oxygen and ASTM F1249 for water vapor
- **Compendial Physicochemical Properties**
  - USP <661> or EP 3.1.X
- **Extractables and Leachables**
- **Endotoxin Testing**
  - USP <85>, EP 2.6.14
- **Sterilization Validation**
  - Focuses on gamma irradiation; addresses shelf-life of PCM
- **Particulates**
- **Chemical Compatibility**
- **TSE – BSE**

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TAKE AN END-TO-END VIEW OF RISK

Supplier

- Business continuity
- Quality systems
- Technical capability

Material

- Safety
- Complexity
- Handling

Process

- Quality
- Performance
- Facility Fit

Lifecycle management by cross functional teams

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CONSIDER POINT OF USE AND COMPLEXITY TO DETERMINE RISK

Impact to Process		System Complexity: Low	System Complexity: Moderate	System Complexity: High	Impact to Process	
	Low	Buffer/Storage	UF*/DF†/ Concentration	Clarification/ Re-covery	Low	
	Moderate	Transport/ Shipping	Connectors/Mixing/ Medium Storage	Cell Culture/ Fermentation	Moderate	
	High	Freeze/Thaw	Purification/ Product Storage	Fill and Finish	High	

*UF – ultrafiltration †DF – diafiltration

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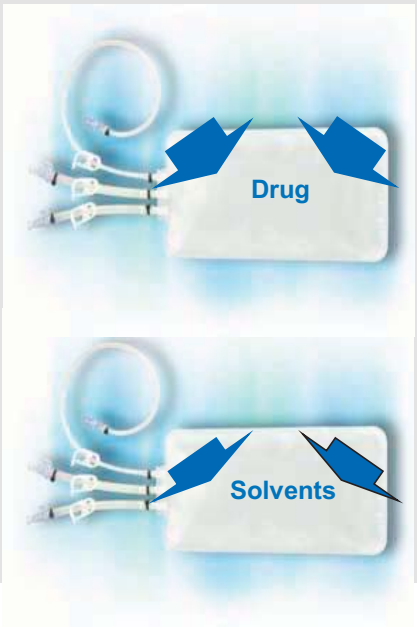
DEFINITIONS:

- **Leachables (L) - chemicals that migrate from the container into a drug formulation during normal storage/usage conditions. (Normal Condition)**
- **Extractables (E) - chemicals that migrate from the product-contact material (container) into a solvent at leveled temperatures. (Accelerated Condition)**



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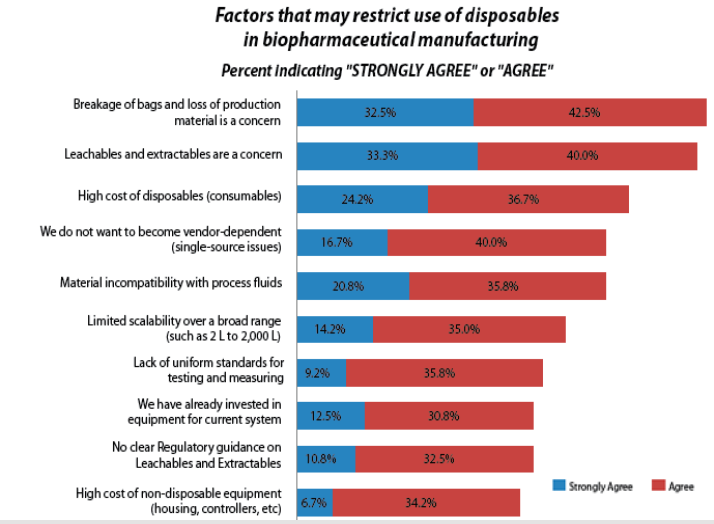
WHAT ARE THE CONCERNS?

Leachables from process equipment including SUS could

- **Affect patient safety**
- **Affect product quality**
- **Affect process performance**



BioPlan Associates, Inc., 13th Annual report and Survey of Biopharmaceutical Manufacturing Capacity and Production, 2016

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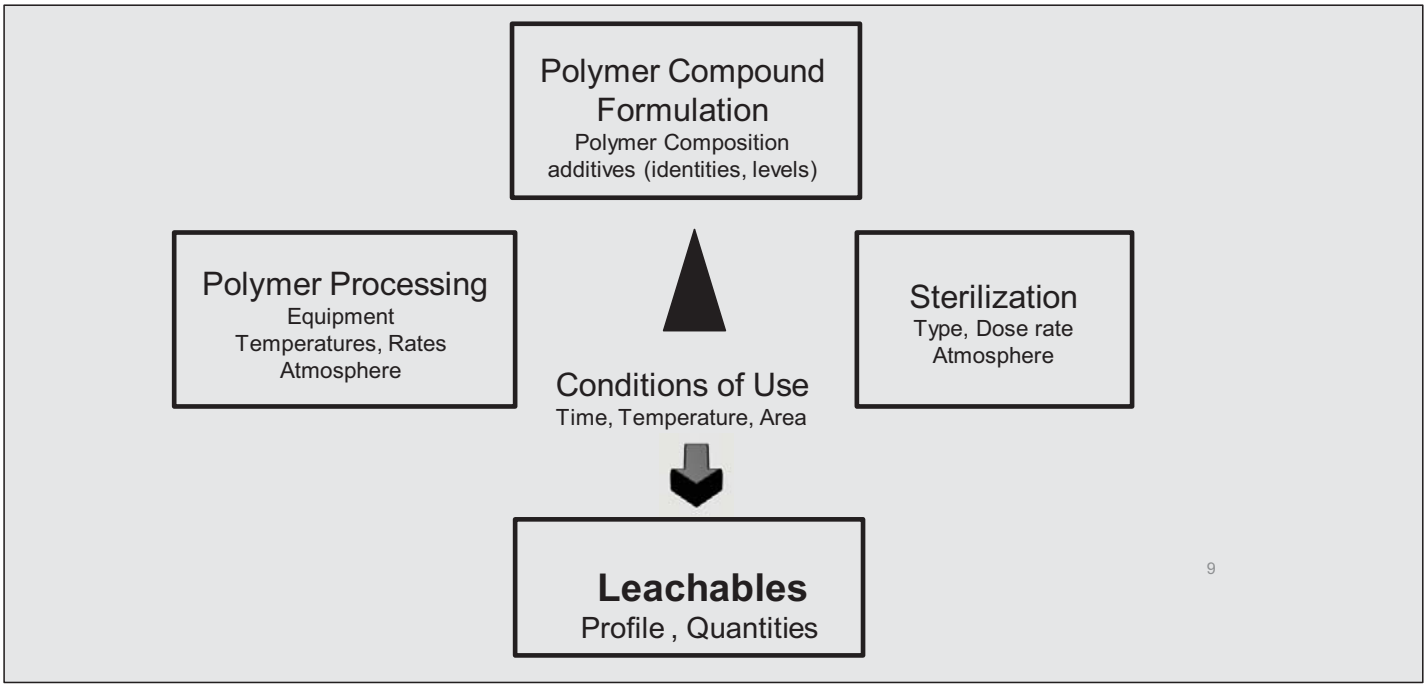
WHAT DETERMINES THE E/L'S ?



CONCLUSIONS:

- Single-use Technologies have the potential to transform the Biomanufacturing by offering cost effective solutions to flexible manufacturing and compliance challenges
- Fundamental to the successful adoption of this new technology is the need for a science based understanding of materials of constructions and the development of processes to identify and measure the risk of each material
- End user should consider a science based risk approach to material qualifications

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Thank
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