Innovative Drug and Device Technologies and their impact on Quality Systems, Control Strategies and Risk Management (Part I)

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Agenda

- Leveraging the streamlined QMS approach
- Quality by Design and Design Controls synergies (including Risk Management)
- Essential Performance Requirements
- Design/Tech Transfer and Developing Control Strategies

Streamlined Approach

Software Driven Electromechanical Device

- Cybersecurity
- Electrical Safety
- Software Validation

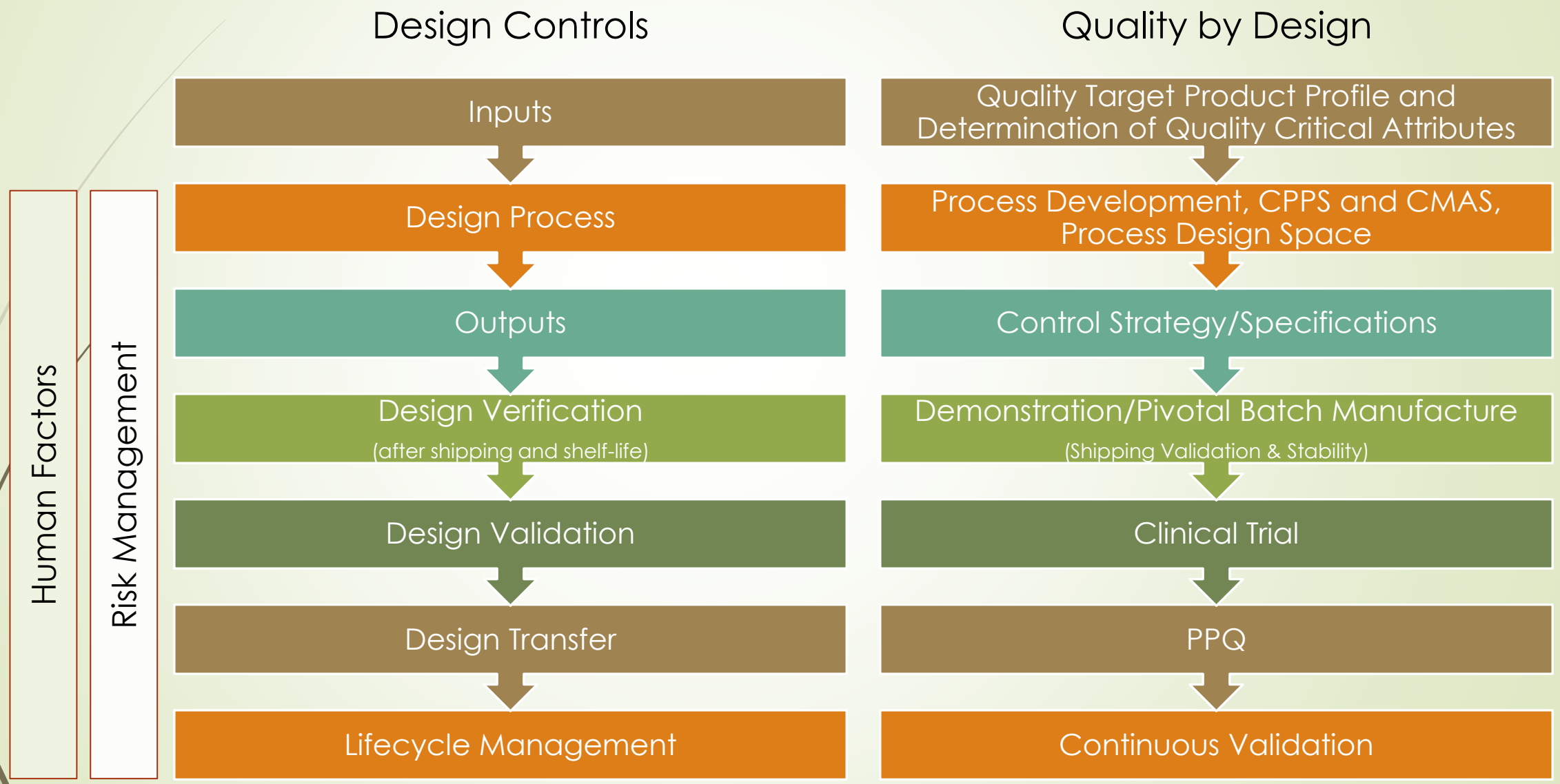
Europe (MDR)

- Technical File
- General Safety and Performance Requirements (GSPR)

FDA 21 CFR Part 4 – cGMP Requirements for Combination Products Quality Systems.

21 CFR Part 210/211 Quality System (Pharma Companies)	21 CFR Part 820 Quality System (Device Companies)
If a manufacturer chooses to demonstrate compliance with the drug CGMPs, that manufacture must also demonstrate compliance with the following provisions of the QS regulation to demonstrate compliance with both sets of regulations:	If a manufacturer chooses to demonstrate compliance with the Quality System regulations, that manufacturer must also demonstrate compliance with the following provisions of the drug CGMPs to demonstrate compliance with both sets of regulations:
§ 820.20. Management responsibility. § 820.30. Design controls. § 820.50. Purchasing controls. § 820.100. Corrective and preventive action. § 820.170. Installation. § 820.200. Servicing.	§ 211.84. Testing and approval or rejection of components, drug product containers, and closures. § 211.103. Calculation of yield. § 211.132. Tamper-evident packaging requirements for over the counter (OTC) human drug products. § 211.137. Expiration dating. § 211.165. Testing and release for distribution. § 211.166. Stability testing. § 211.167. Special testing requirements. § 211.170. Reserve samples

Parallel Development Structures



EPR FDA Communication Keywords

- In FDA communications Essential Performance Requirements have been linked to the following keywords
  - Reliability
  - Shelf-life
  - Release
  - Verification
  - Validation
  - Shipping
  - Side by side (interchangeability)
  - Control strategy

"Essential Performance – Identify essential performance requirements (EPR) for
the device.

For each identified essential performance requirement, your marketing application should include verification and validation information of EPR specifications. While the final set of essential performance requirements should be based on your design control process, we are providing the following example EPRs for your device type. This is not an exhaustive list and product specific factors should influence your EPR selection."

"Control Strategy – Provide a control strategy that ensures that the final finished combination product maintains its essential performance requirements. The control strategy may consist of, but is not limited to, lot release, in-process, control of incoming materials, purchasing controls, etc."

Determining Essential Performance Requirements

FDA

Design inputs that "….focus on device clinical performance at the time of use"

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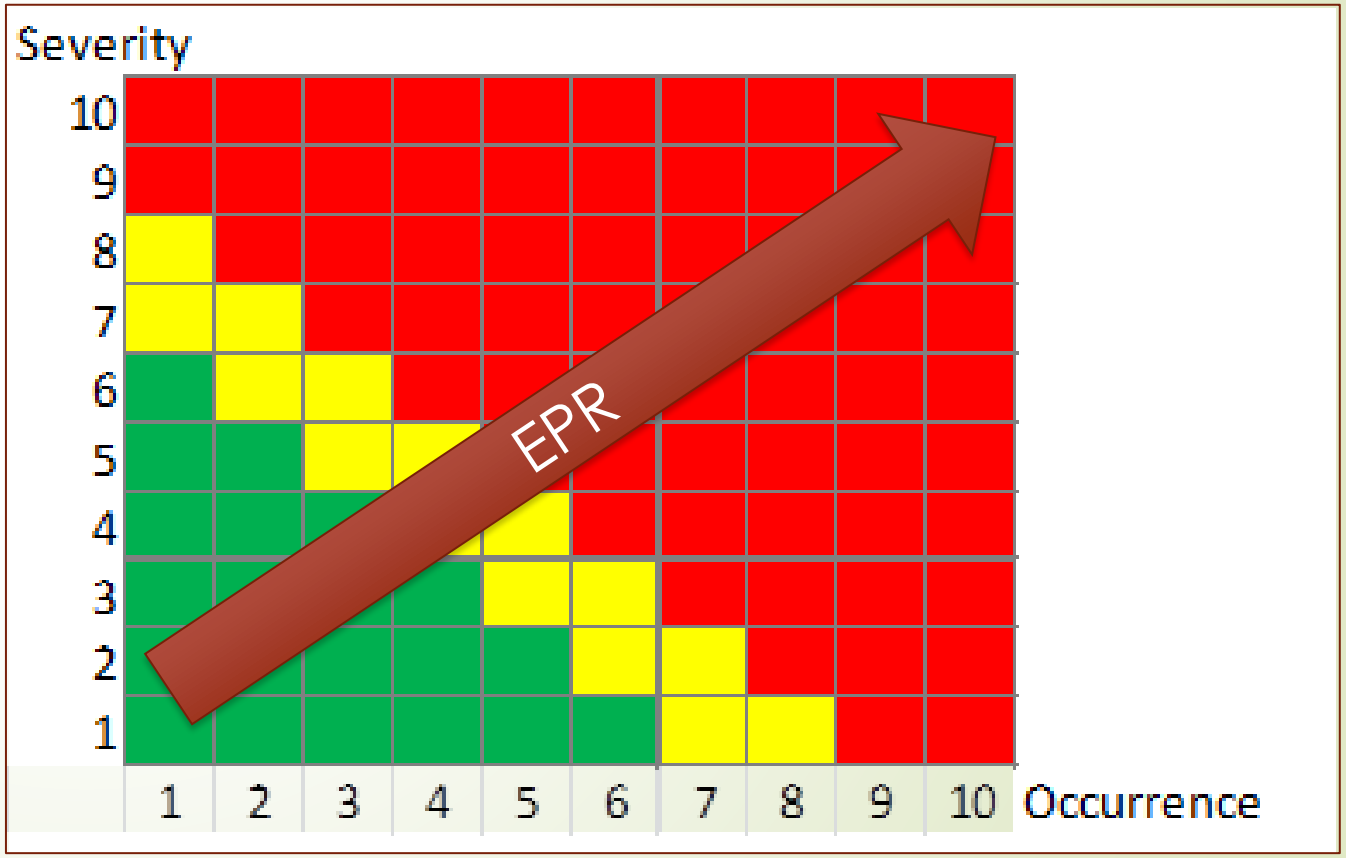
IEC 60601

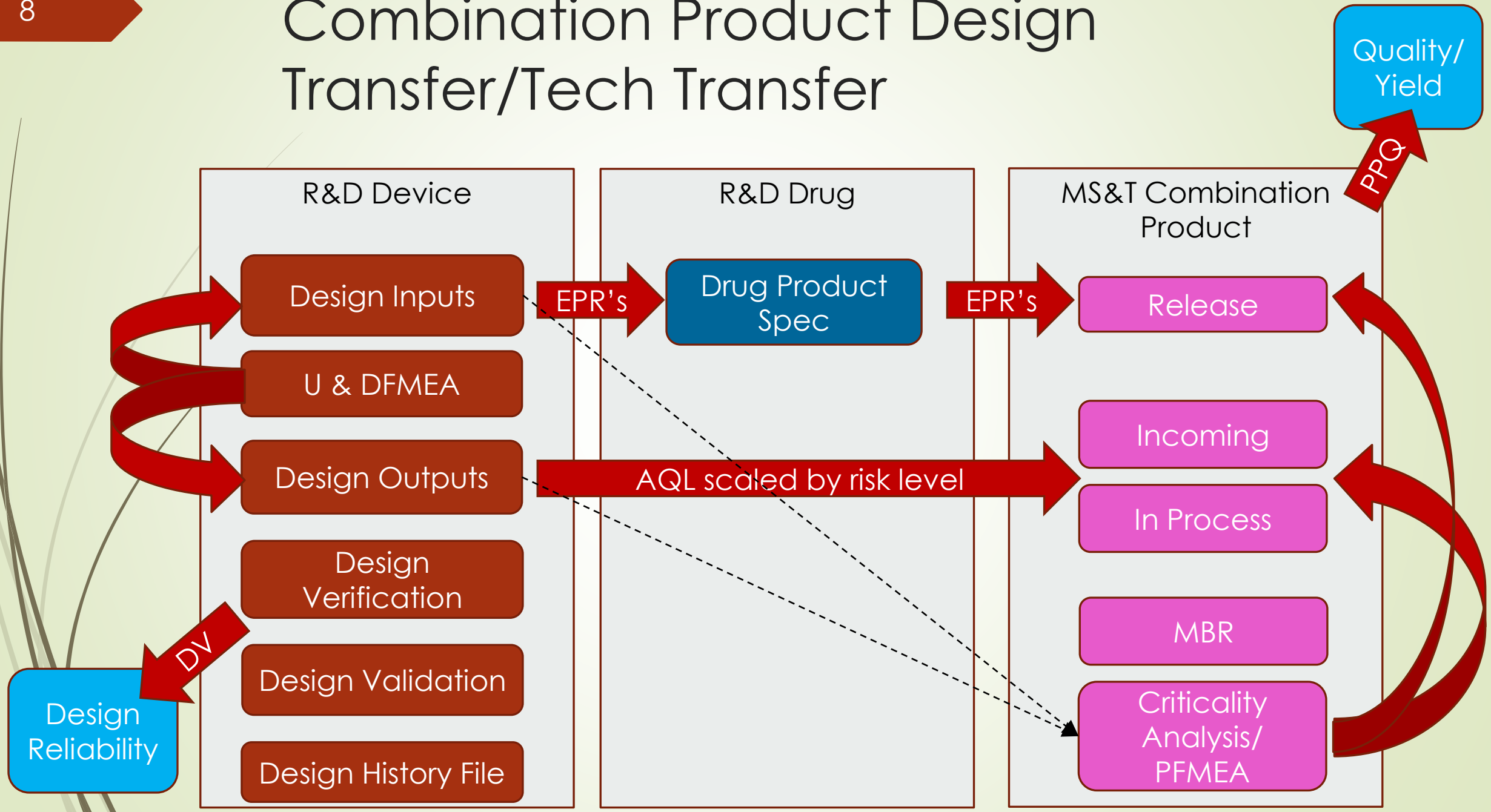


Quality Risk Management and ISO 14971

CQA	Thawing	Mixing	Dilution	Filtration	Filling and stoppering
CQA1	Low	Low	Low	Medium	High
CQA2	Low	Low	High	Low	Low
CQA3	Low	High	High	Medium	Medium
CQA4	Low	Low	Low	Low	Low
CQA5	Low	Low	Low	Low	High

Process Step	Failure Mode	Cause	Hazard	Harm	Severity	CQA/Design Input affected	Occurrence	Control	Detection	Risk Priority
Filling	Under fill	Incorrect fill setting	Underdose	Worsening of condition	3	Extractable Volume/Dose Accuracy	3	Fill weight IPC	1	Low

Combination Product Design Transfer/Tech Transfer



Conclusions

- Take advantage of the Part 4 streamlined approach
- Leverage the synergies between QbD and Design Controls to gain efficiencies
- Develop a process for determining Essential Performance Requirements and incorporate into your development process
- Ensure that you can show control strategies for Essential Performance Requirements