



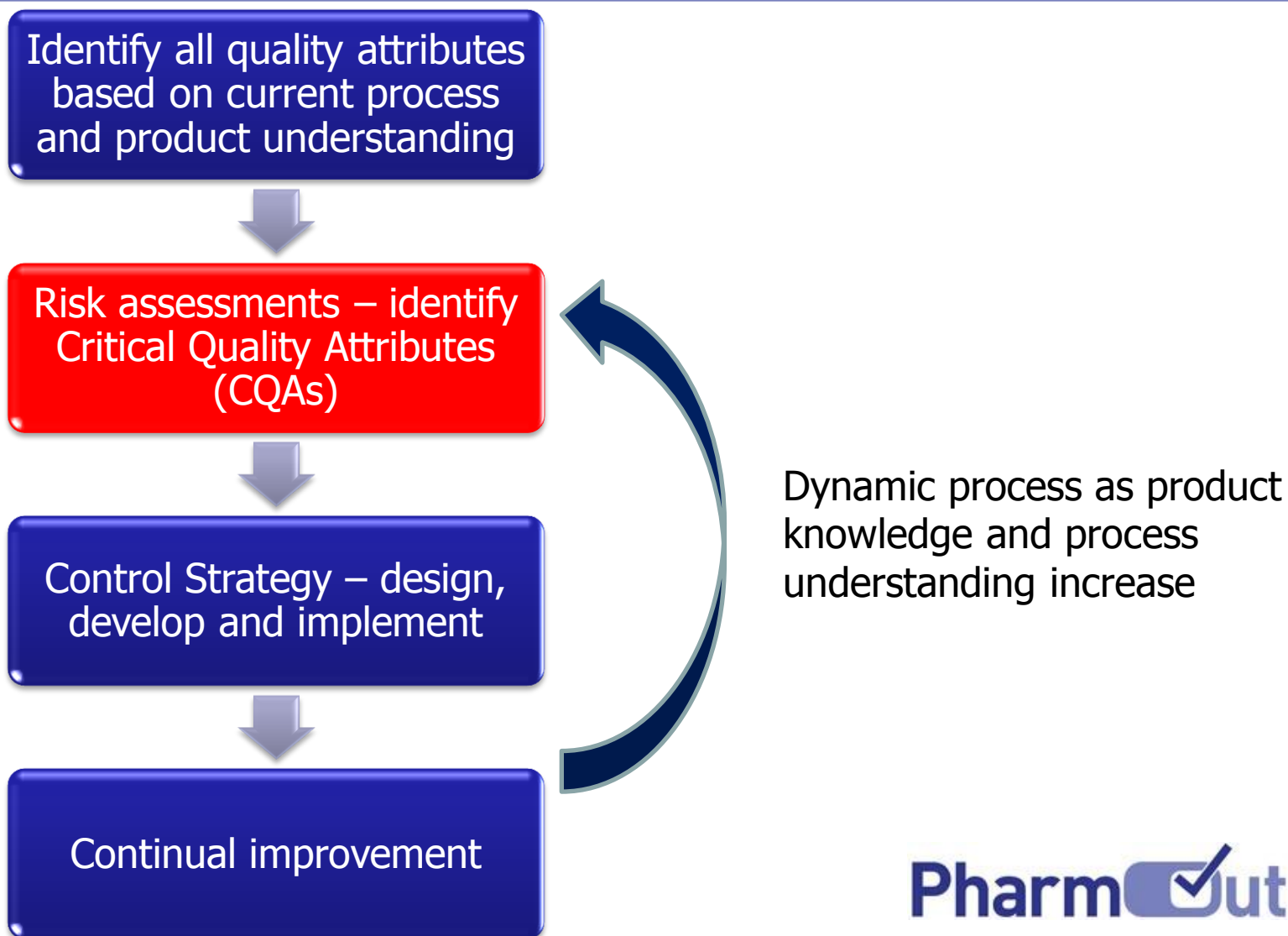
National Validation Forum



Control Strategy

John Montalto

Linking ICH Q8, Q9 and Q10 to develop a control strategy



Control Strategy – what's important?



Risk assessment – identify Critical Quality Attributes (CQAs)

	Appearance	Performance	Comfort	Stopping	Heating/ Cooling	Transmission
Severity (impact on quality)	L	H	L	H	L	L
Probability (risk likelihood)	L	M	M	M	L	M
Detectability	H	M	H	M	H	H
Total	L	H	L	H	L	L

Risk assessment – identify CQAs

	Appearance	Performance	Comfort	Stopping	Heating/ Cooling	Transmission
Colour						
Brake assembly						
Acceleration						
Suspension						
Seat covering						
Tyres						
Fuel type						

Developing Control Strategy

Stopping

Brake assembly

Stopping

Vehicle gradually stops by application of a foot peddle at 10m/s/s

Control Strategy

Qualification of manufacturing equipment
Assembly Process Validation

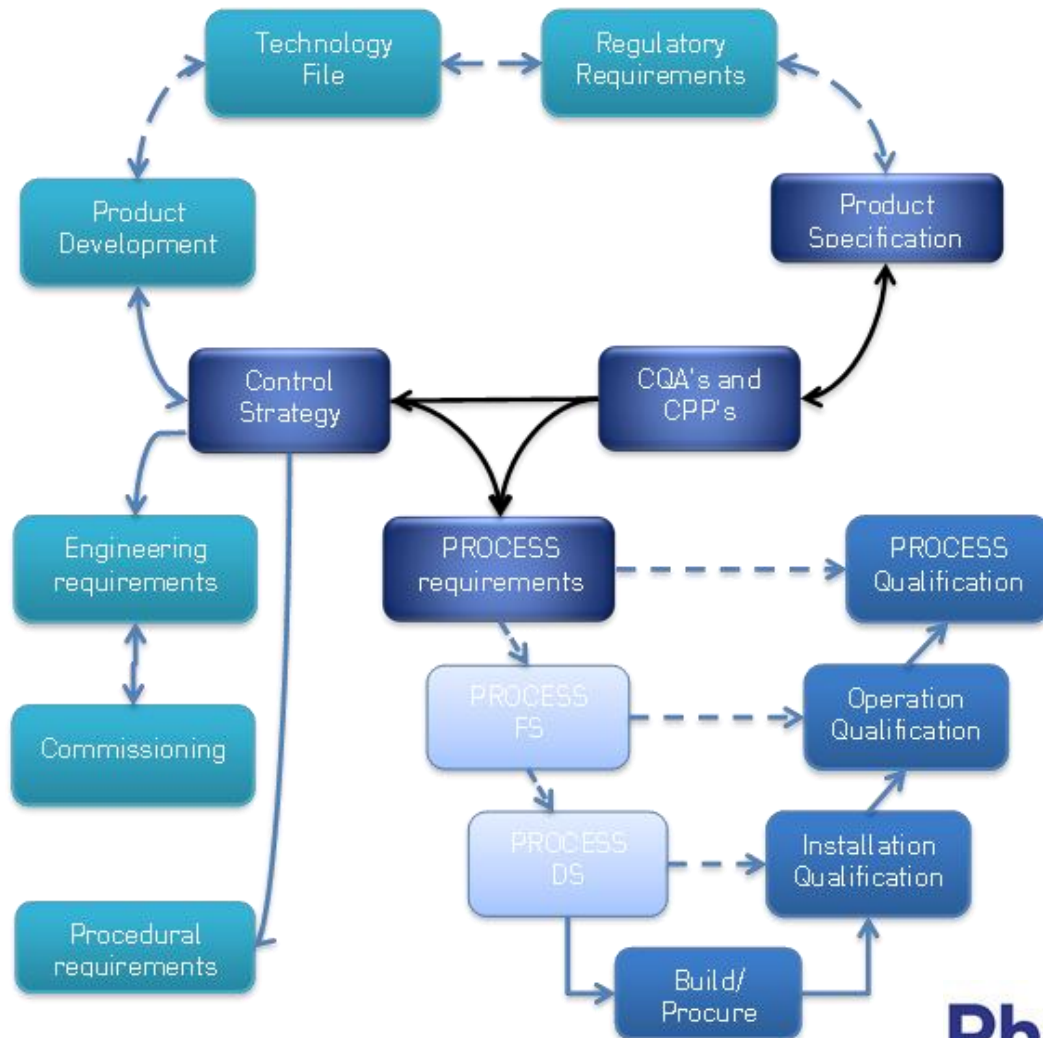
Control Strategy

Raw materials, lubricants and oils

Feedback systems

Maintenance Life Plans - Brake pressure switch calibration, inspection regime, anchor bolts, return springs, adjustor screws

Validation context



What is Control Strategy?

"It is everything that we do already to control the process to produce acceptable quality product"

- A great starting point for **validation**

An ongoing process

"While design space is optional, Control Strategy is never optional"

Jacques Morenas, PIC/S Chair, April 2011

An ongoing process

"Management review should provide assurance that process performance and product quality are managed over the lifecycle."

ICH Q10 The Pharmaceutical Quality System

CQA and CPP

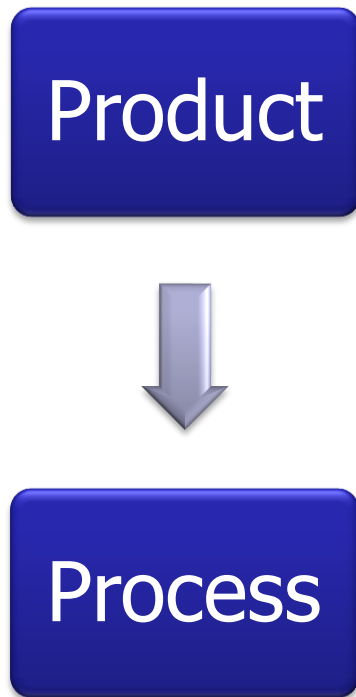
Critical Quality Attribute

- A CQA is a physical, chemical, biological, or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality
- Drug substance, excipients, intermediates

Critical Process Parameter

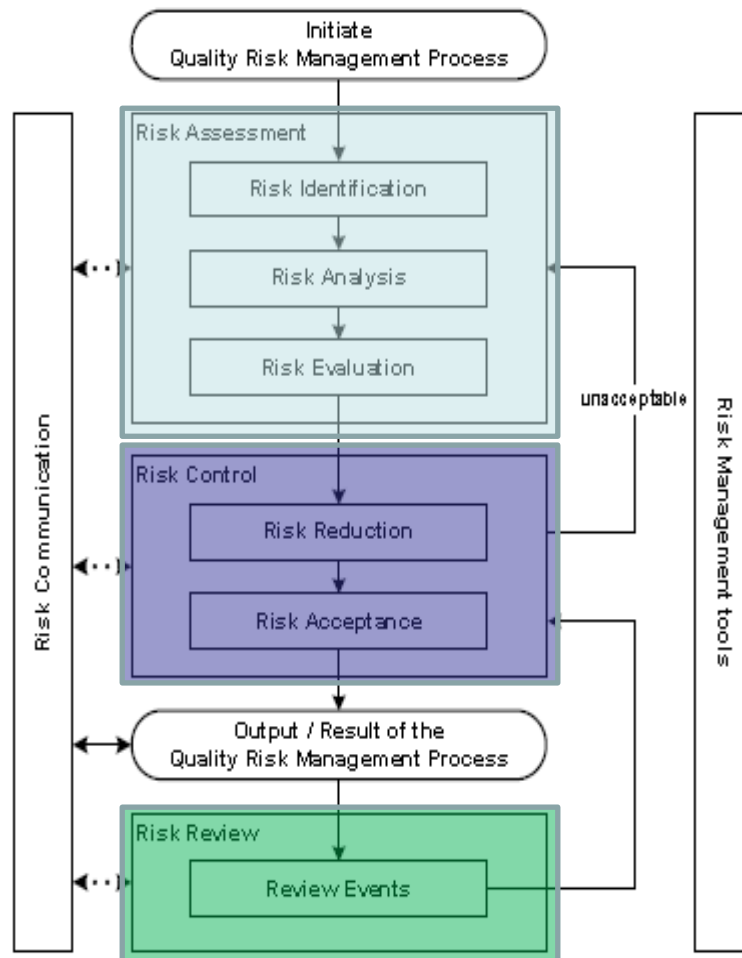
- A process parameter whose variability has an impact on a critical quality attribute and therefore should be monitored or controlled to ensure the process produces the desired quality

Knowledge



- Product understanding is required to design the process
- CQAs define the process

Quality Risk Management



Product knowledge drives Process development

Develop Control Strategy

Continual improvement

An ongoing process

"It is a requirement of GMP that manufacturers identify what validation work is needed to prove control of the critical aspects of their particular operations."

Annex 15, PIC/S Guide to Good Manufacturing Practice for Medicinal Products Annexes, January, 2009

Control Strategy

- Planned set of controls
- Derived from current product and process understanding
 - Assurance of process performance and product quality

Control Strategy is not...

Control Strategy

Is NOT a new concept

Your products and processes already have control strategies

Control Strategy

Is NOT just a list of specifications for QC testing requirements

Control Strategy

Is NOT optional

Implement Control Strategy

- Every process and product has an associated control strategy:
 - Overall strategy for a product
 - Discrete control strategy for an operation

Various approaches

Control strategy approaches

- In-process testing
- Real time release testing
- End-product testing

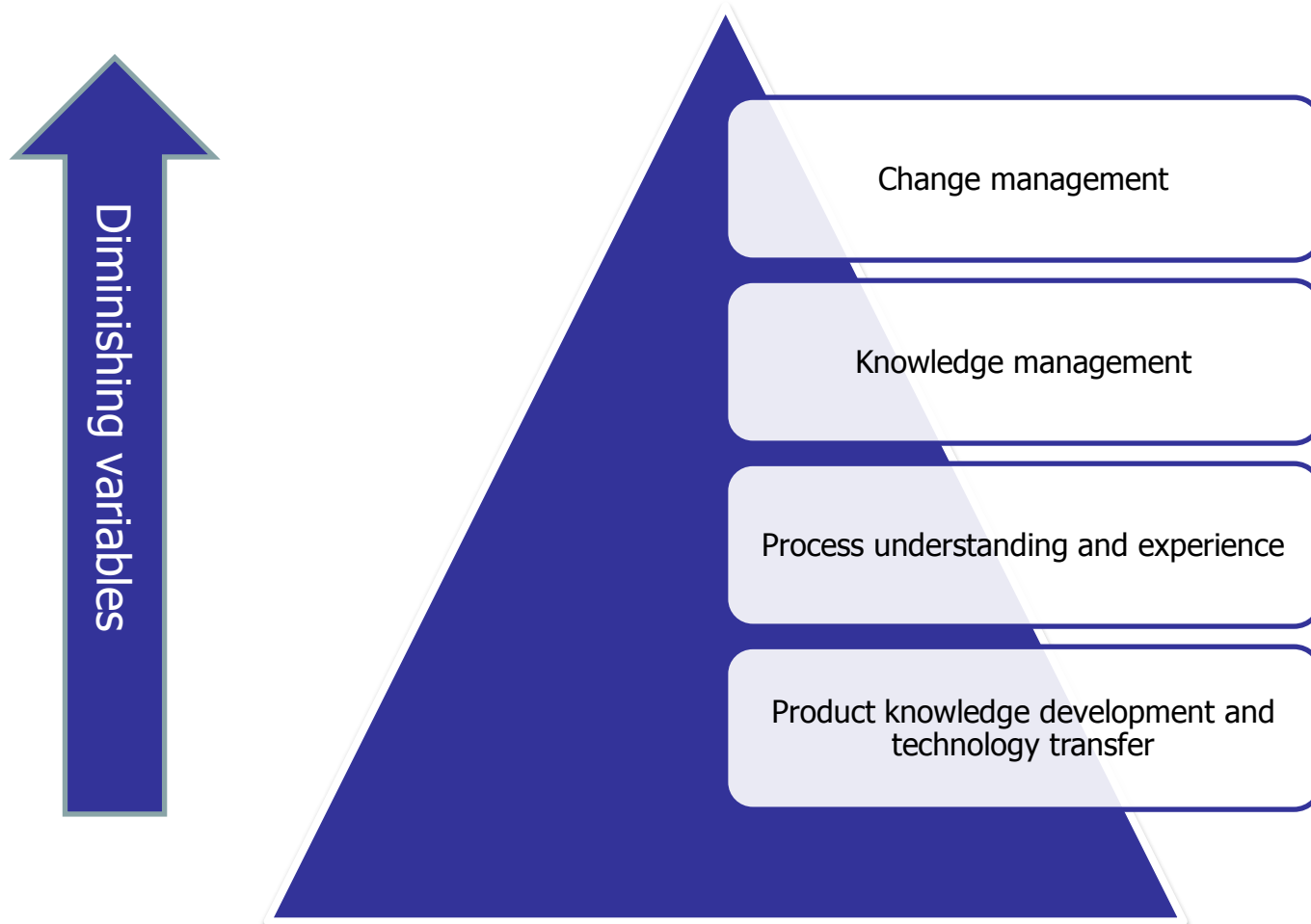
Localised Control strategy approaches

- Controls on raw and starting material attributes, intermediates and reagents
- Sequence of purification steps
- Order of addition of reagents
- Training and personnel matters
- Gowning and clean room behaviours

Batch release

- Control Strategy and batch release decisions are separate
- Control Strategy is not the only consideration when batch release decisions are determined

Establish, document, implement, maintain



Traditional approach

- Emphasis on end-product testing
- Operating ranges set on observed process data
 - Generally narrow target range
 - Process capability (or lack of capability)

In process approach

- In process determination that a CQA is within an appropriate range or limit
- A high degree of Assurance
 - Documented evidence
- In the not so distant future
 - Process Analytical Technologies (PAT)
 - Real Time Release Testing (RTRT)

What's your perspective?

Industry	Regulators
Analytical testing sensitivity	Has risk been adequately identified and controlled?
Equipment limitations	Quality Management System adequacy to support the Control Strategy
Cost	Locally, compliance with Annex 15

Summary

- Product Quality and Process Performance Monitoring:
 - Ensure a state of control is maintained (control inter and intra batch variability)
 - Plan and execute a system for monitoring CQAs and CPPs

Summary

- 1 Use QRM to establish Control Strategy
- 2 Control Strategy facilitates timely feedback/feed forward and appropriate CAPA
- 3 Provide tools for measurement and analysis of parameters and attributes within Control Strategy
- 4 Identify sources of variation affecting process performance and product quality – focus continuous improvement here
- 5 Use internal and external feedback
- 6 Provide and manage knowledge to enhance process understanding



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Any answers?

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