From vulnerability to resilience:

Industry strategies for dealing with critical materials in analytical procedures

Virtual Europe Discussion Group, 13 November 2025

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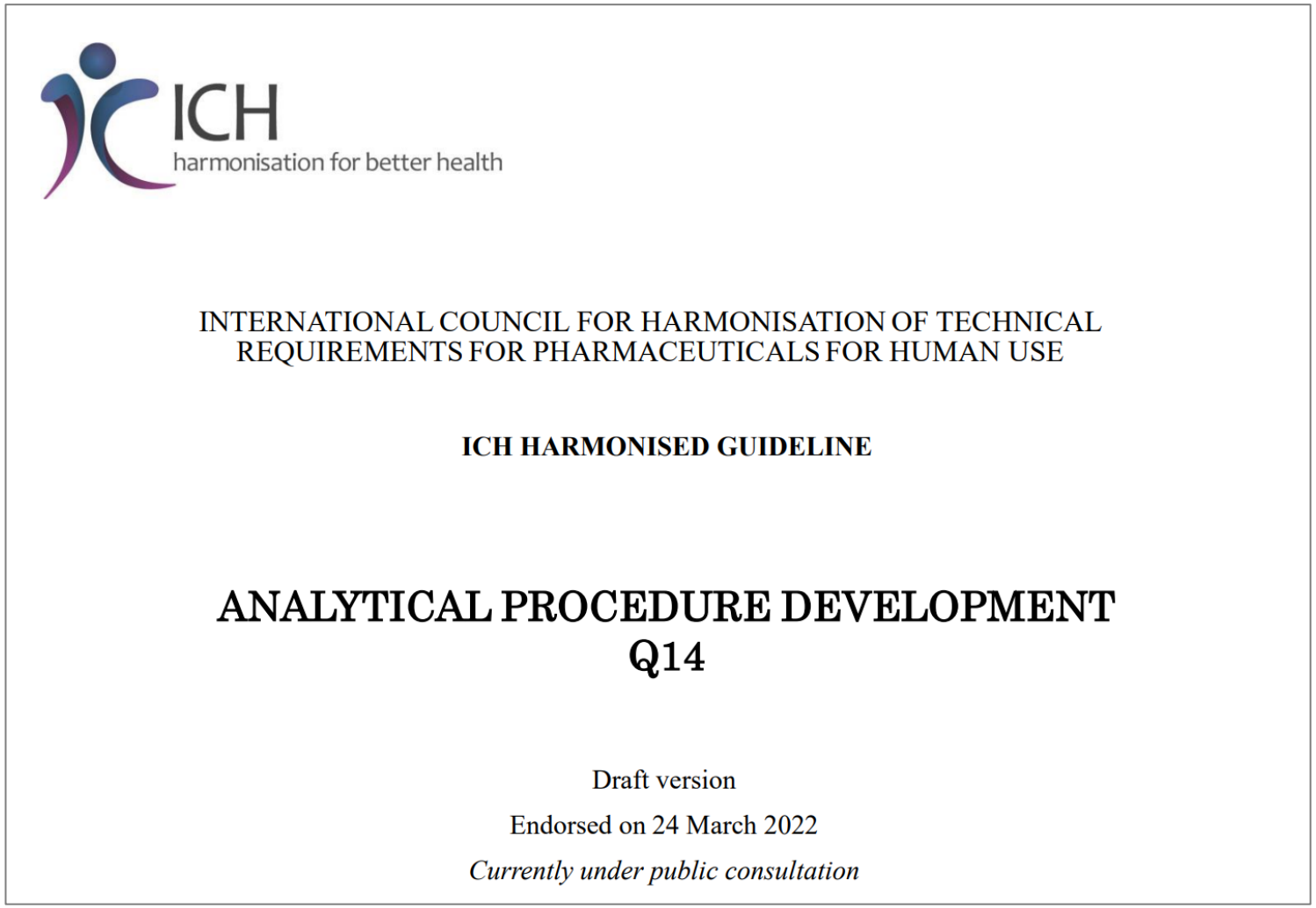
INNOVATING PHARMACEUTICAL ANALYSIS

Method development according ICH Q14



ICH
harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

ANALYTICAL PROCEDURE DEVELOPMENT
Q14

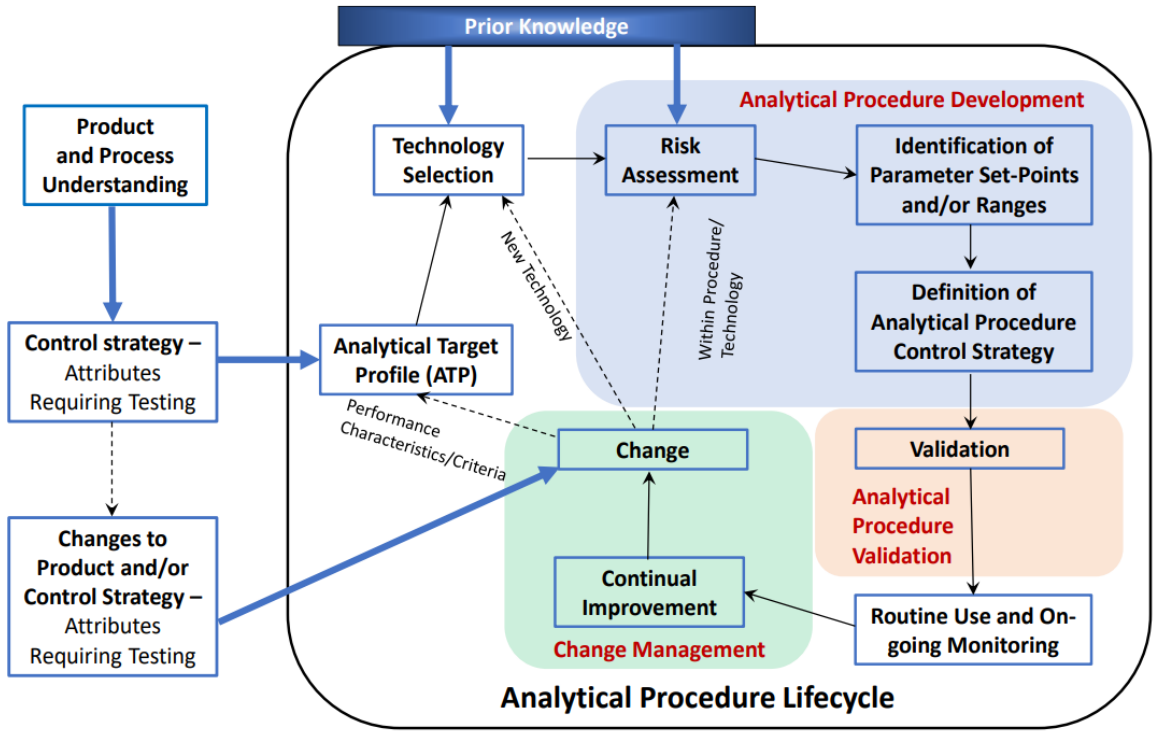
Draft version

Endorsed on 24 March 2022

Currently under public consultation

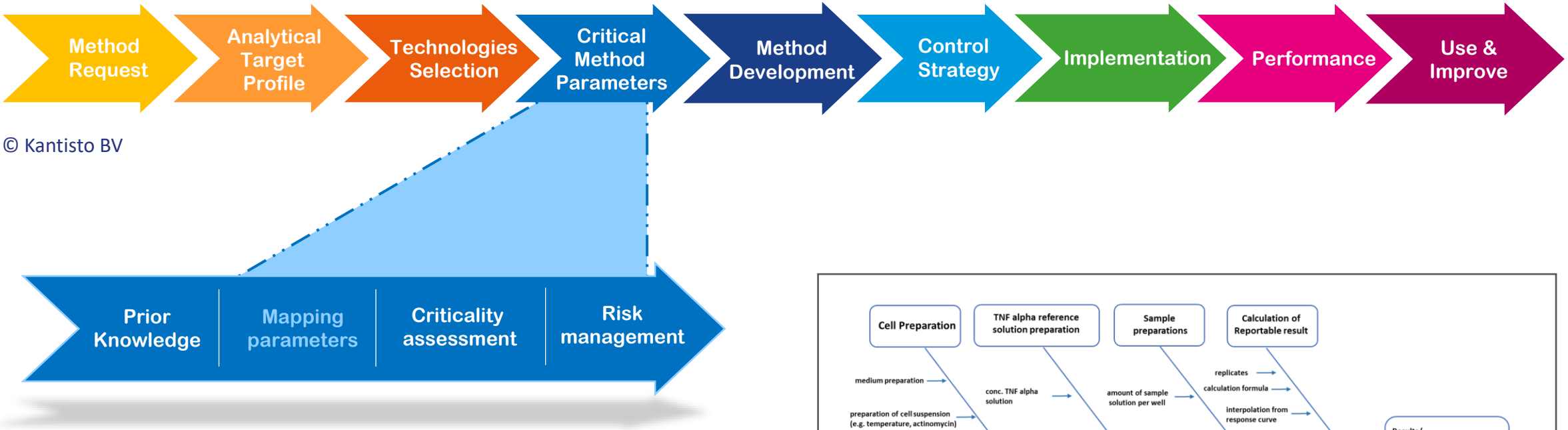
Method development according ICH Q14

Figure 1: The Analytical Procedure Lifecycle



https://database.ich.org/sites/default/files/ICH_Q14_Document_Step2_Guideline_2022_0324.pdf

From method parameter to analytical control strategy



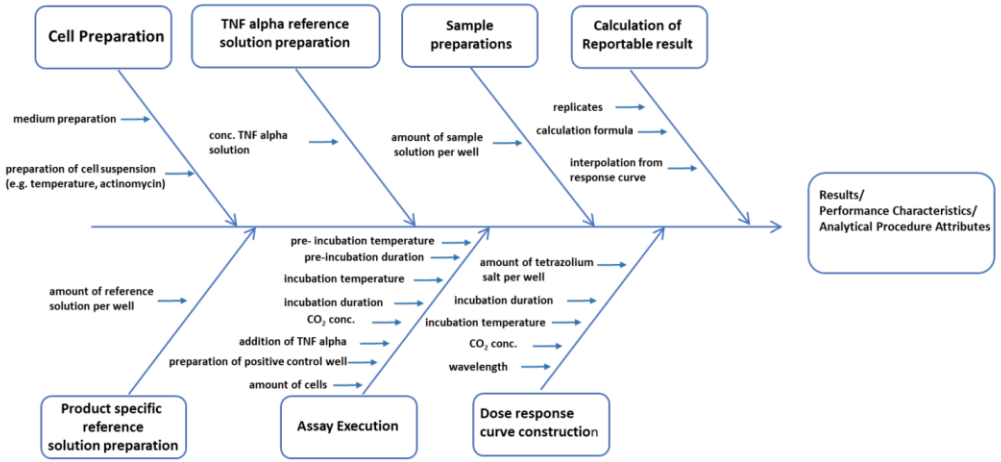
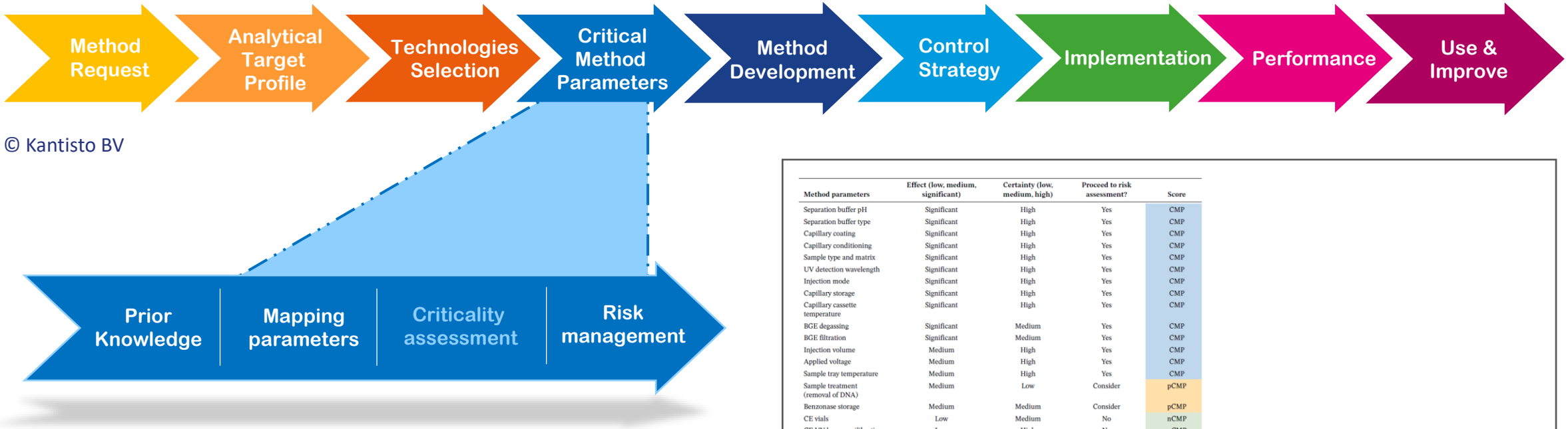


Figure 2 in Annex A of ICH Q14

From method parameter to analytical control strategy



Method parameters	Effect (low, medium, significant)	Certainty (low, medium, high)	Proceed to risk assessment?	Score
Separation buffer pH	Significant	High	Yes	CMP
Separation buffer type	Significant	High	Yes	CMP
Capillary coating	Significant	High	Yes	CMP
Capillary conditioning	Significant	High	Yes	CMP
Sample type and matrix	Significant	High	Yes	CMP
UV detection wavelength	Significant	High	Yes	CMP
Injection mode	Significant	High	Yes	CMP
Capillary storage	Significant	High	Yes	CMP
Capillary cassette temperature	Significant	High	Yes	CMP
BGE degassing	Significant	Medium	Yes	CMP
BGE filtration	Significant	Medium	Yes	CMP
Injection volume	Medium	High	Yes	CMP
Applied voltage	Medium	High	Yes	CMP
Sample tray temperature	Medium	High	Yes	CMP
Sample treatment (removal of DNA)	Medium	Low	Consider	pCMP
Benzonase storage	Medium	Medium	Consider	pCMP
CE vials	Low	Medium	No	nCMP
CE UV lamp equilibration time	Low	High	No	nCMP
Pipette step for sample transfer	Low	High	No	nCMP
Capillary length	Low	High	No	nCMP
Capillary diameter	Low	High	No	nCMP
Capillary detection window diameter	Low	High	No	nCMP
Sample buffer concentration	Low	High	No	nCMP
Benzonase type	Low	High	No	nCMP

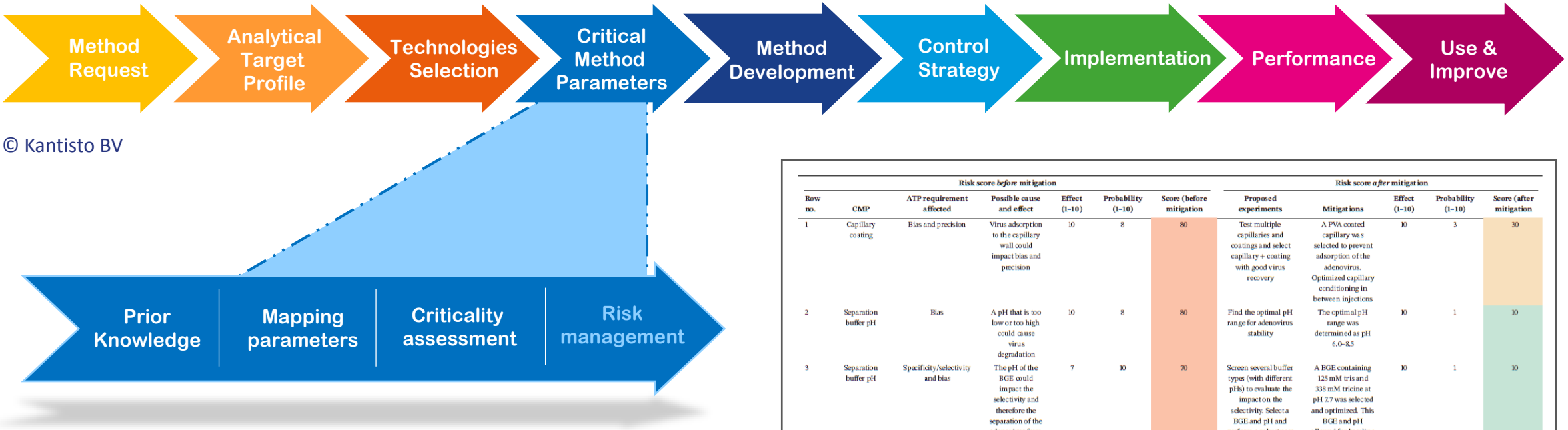
		Certainty		
		Low	Medium	High
Effect	Low	pCMP	nCMP	nCMP
	Medium	pCMP	pCMP	CMP
	Significant	CMP	CMP	CMP

CMP = critical method parameter
pCMP = potential critical method parameter
nCMP = non-critical method parameter

Table 3 and 4 from reference:

https://doi.org/10.1002/elps.8110

From method parameter to analytical control strategy



				Risk score *before* mitigation					Risk score *after* mitigation		
Row no.	CMP	ATP requirement affected	Possible cause and effect	Effect (1–10)	Probability (1–10)	Score (before mitigation	Proposed experiments	Mitigations	Effect (1–10)	Probability (1–10)	Score (after mitigation
1	Capillary coating	Bias and precision	Virus adsorption to the capillary wall could impact bias and precision	10	8	80	Test multiple capillaries and coatings and select capillary + coating with good virus recovery	A PVA coated capillary was selected to prevent adsorption of the adenovirus. Optimized capillary conditioning in between injections	10	3	30
2	Separation buffer pH	Bias	A pH that is too low or too high could cause virus degradation	10	8	80	Find the optimal pH range for adenovirus stability	The optimal pH range was determined as pH 6.0–8.5	10	1	10
3	Separation buffer pH	Specificity/selectivity and bias	The pH of the BGE could impact the selectivity and therefore the separation of the adenovirus from its matrix components or other Ad types	7	10	70	Screen several buffer types (with different pHs) to evaluate the impact on the selectivity. Select a BGE and pH and perform a robustness experiment	A BGE containing 125 mM tris and 338 mM tricine at pH 7.7 was selected and optimized. This BGE and pH allowed for baseline separation of all peaks and could be reproducibility prepared (robust)	10	1	10
4	BGE composition	Bias and precision	Inadequate BGE composition could cause the matrix components or adenovirus to adsorb, precipitate, or aggregate and cause an inaccurate and imprecise results	10	8	80	Screening of BGE and capillaries screening to reduce adsorption optimize conditions	Use tris/tricine buffer Add PS-20 to BGE. Set BGE to 125 mM tris and 338 mM tricine and 0.2% w/v PS-20. Introduce an adenovirus control sample to monitor accuracy and precision	10	1	10

Table 5 from reference: https://doi.org/10.1002/elps.8110

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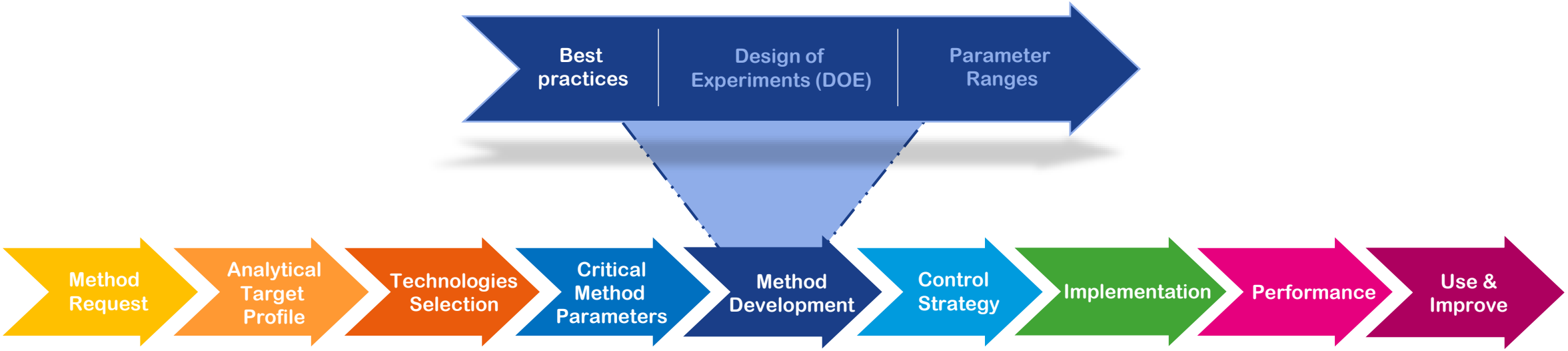

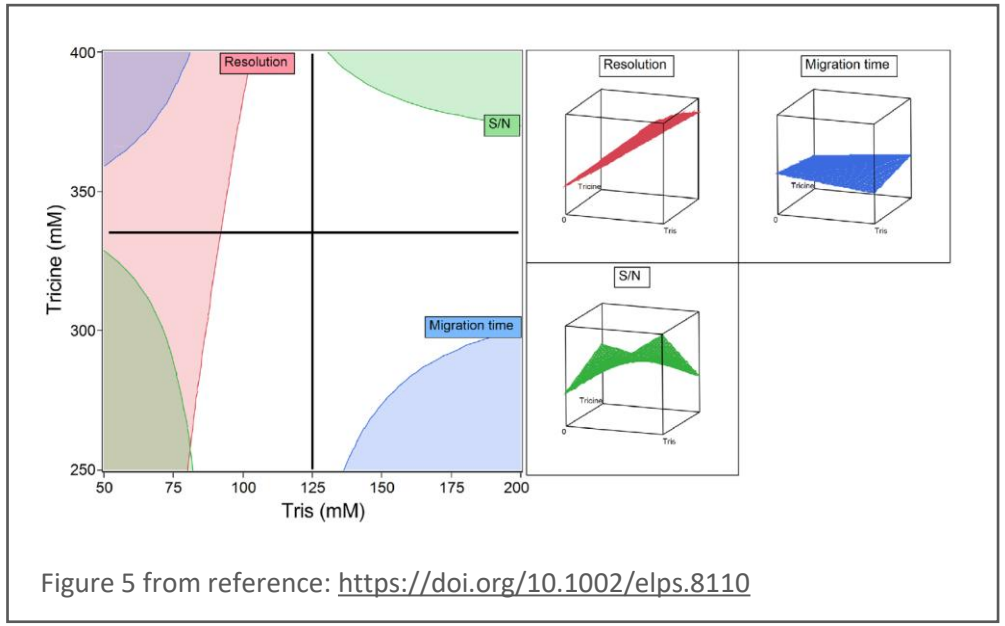

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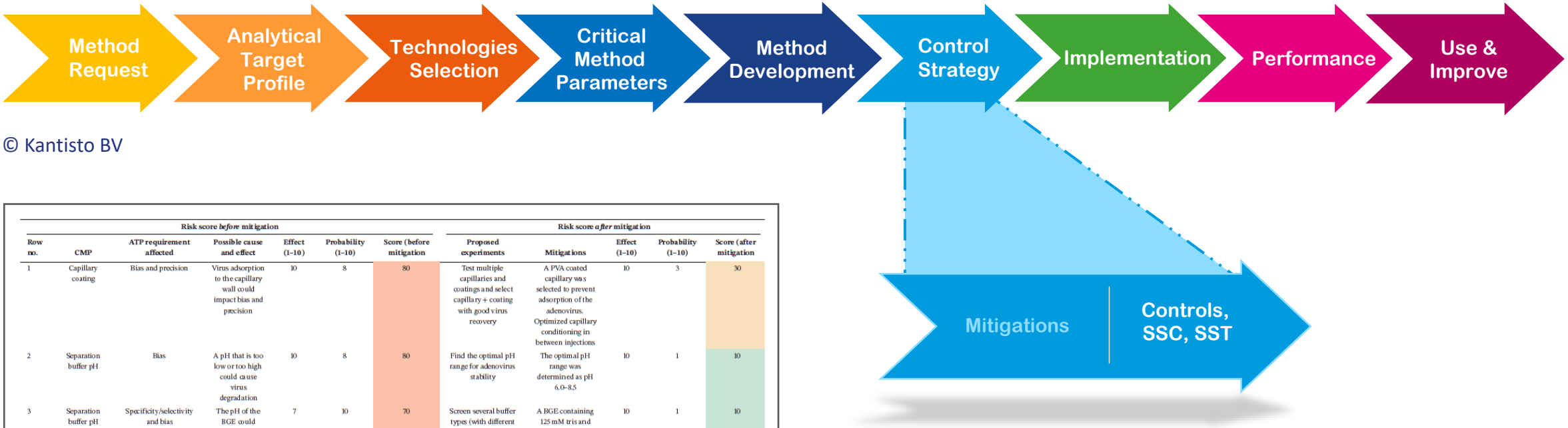

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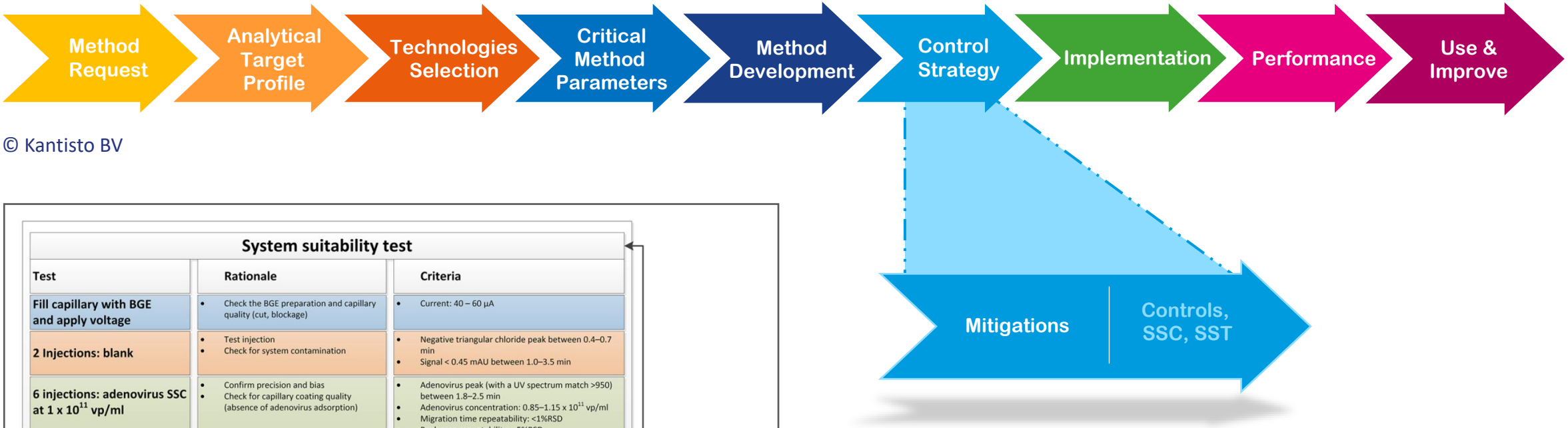


System suitability test

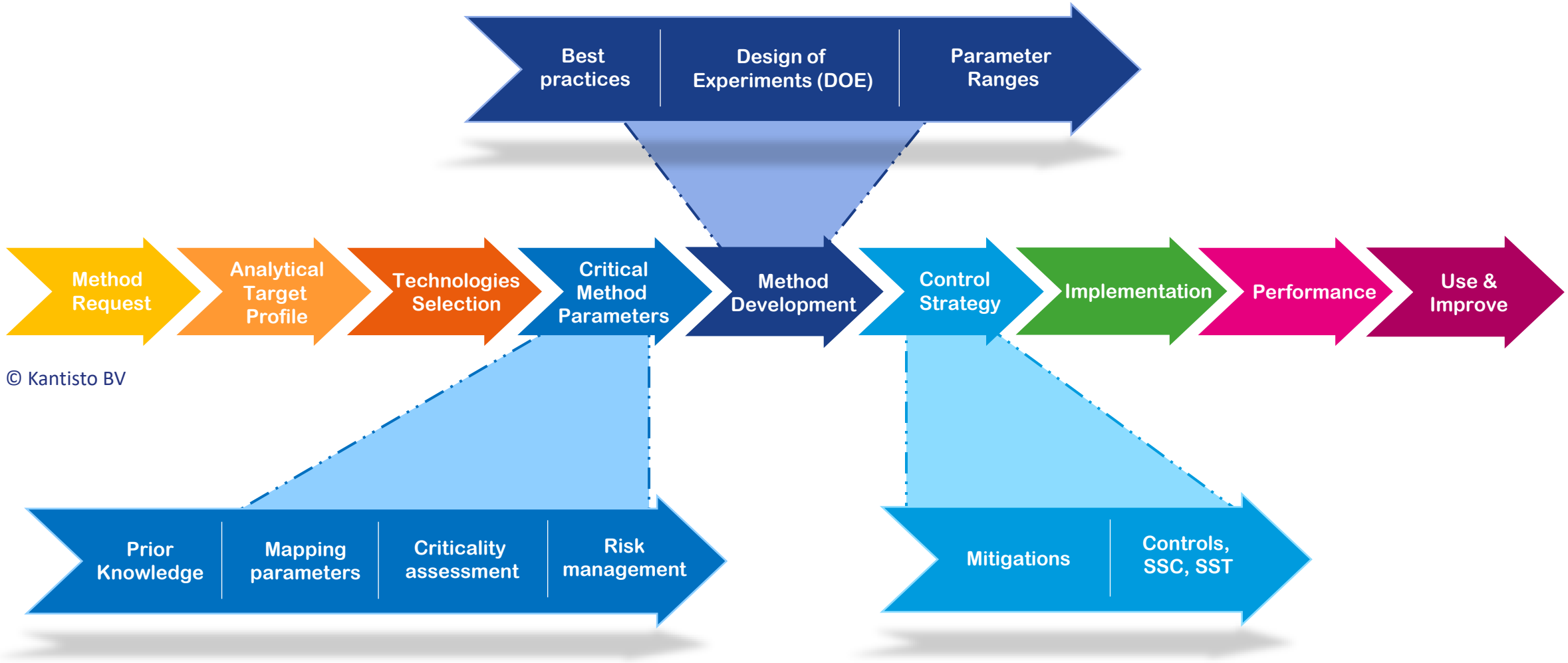
Test	Rationale	Criteria
Fill capillary with BGE and apply voltage	• Check the BGE preparation and capillary quality (cut, blockage)	• Current: 40 – 60 µA
2 Injections: blank	• Test injection • Check for system contamination	• Negative triangular chloride peak between 0.4–0.7 min • Signal < 0.45 mAU between 1.0–3.5 min
6 injections: adenovirus SSC at 1 x 10^{11} vp/ml	• Confirm precision and bias • Check for capillary coating quality (absence of adenovirus adsorption)	• Adenovirus peak (with a UV spectrum match >950) between 1.8–2.5 min • Adenovirus concentration: 0.85–1.15 x 10^{11} vp/ml • Migration time repeatability: <1%RSD • Peak area repeatability: <5%RSD
1 injection: blank	• Check for carry-over	• Negative triangular chloride peak between 0.4–0.7 min • Signal < 0.45 mAU between 1.0 and 3.5 min
1 injection: Calibrant at 7.3 x 10^{11} vp/ml	• Used to determine the concentration of the SSC and samples (if the SST passed)	• Adenovirus peak (with a UV spectrum match >950) between 1.8–2.5 min

System suitability test – passed → Sample analysis → Calibrant (as assay control) analyzed after every 5 samples

System suitability test – failed → Troubleshooting

Figure 6 from reference: https://doi.org/10.1002/elps.8110

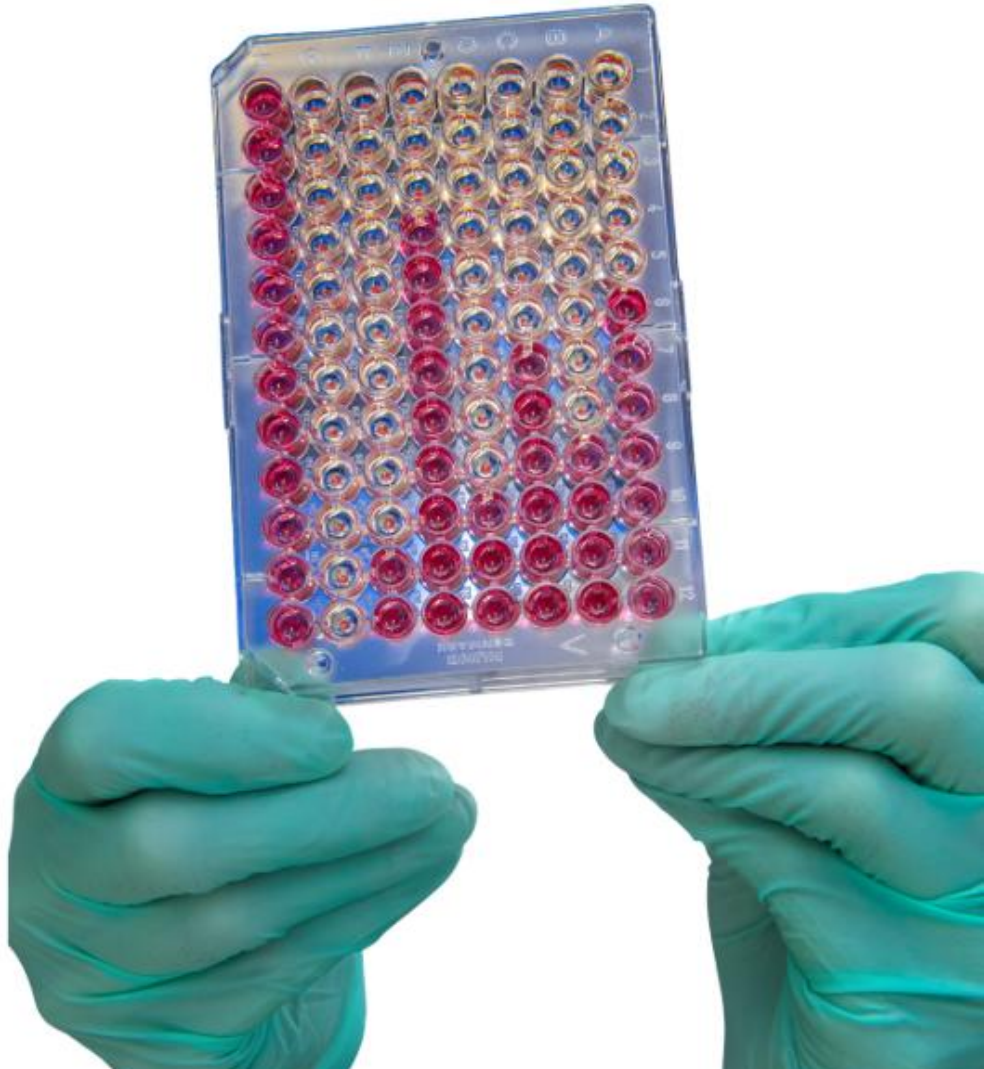
From method parameter to analytical control strategy



But what if you use ready-to-use kits and materials?

Examples

- qPCR Master Mixes
- ELISA kits
- CGE kits
- cIEF kits
- HPLC - Pre-mixed mobile phases
- Endotoxin detection kits
- Residual DNA test kits
- DNA/RNA extraction kits
- Bioassay kits for potency or cytotoxicity
- CHO cell line-based potency assays
- Reference standards, calibrants, reagents etc.



But what if you use ready-to-use kits and materials?

- What is the exact composition and reagent quality?
- What are the suitable parameters ranges?
- How is the robustness of the kit or material?
- What if the kit, reagent, or column chemistry is modified or discontinued?
- How are lot-to-lot variations managed?

Convenience comes with risk – without understanding, there is no control

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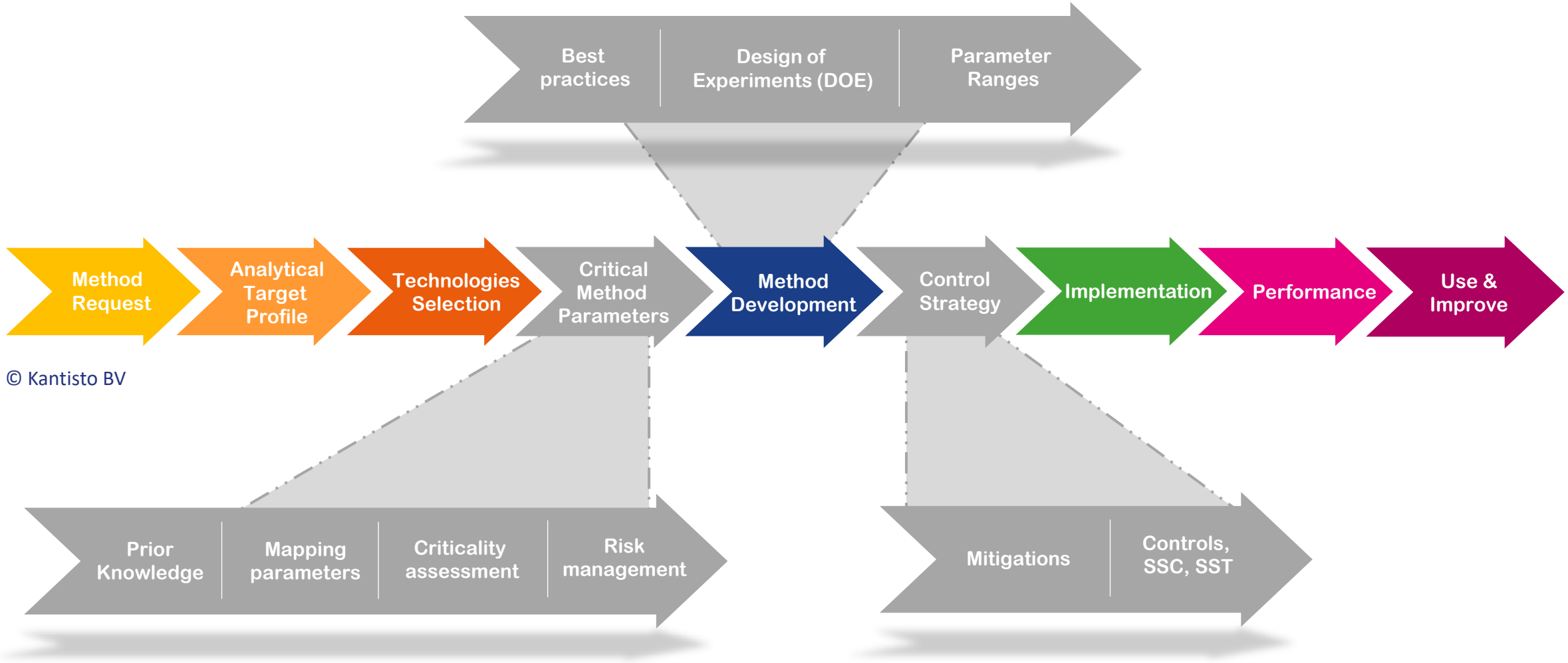


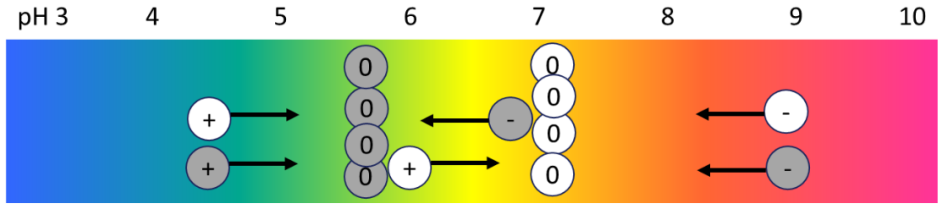
Convenience comes with risk – without understanding, there is no control

Summary Solutions for Pharmalyte™ Shortage
-- The short version --

Cari Sänger-van de Griend and Hermann Wätzig

What is Pharmalyte™?

Pharmalyte™ is a commercial brand of carrier ampholytes used in capillary isoelectric focusing (cIEF), a technique for separating proteins based on their isoelectric point (pI).



Dealing with the Pharmalyte™ Shortage: Three Scientific Solutions

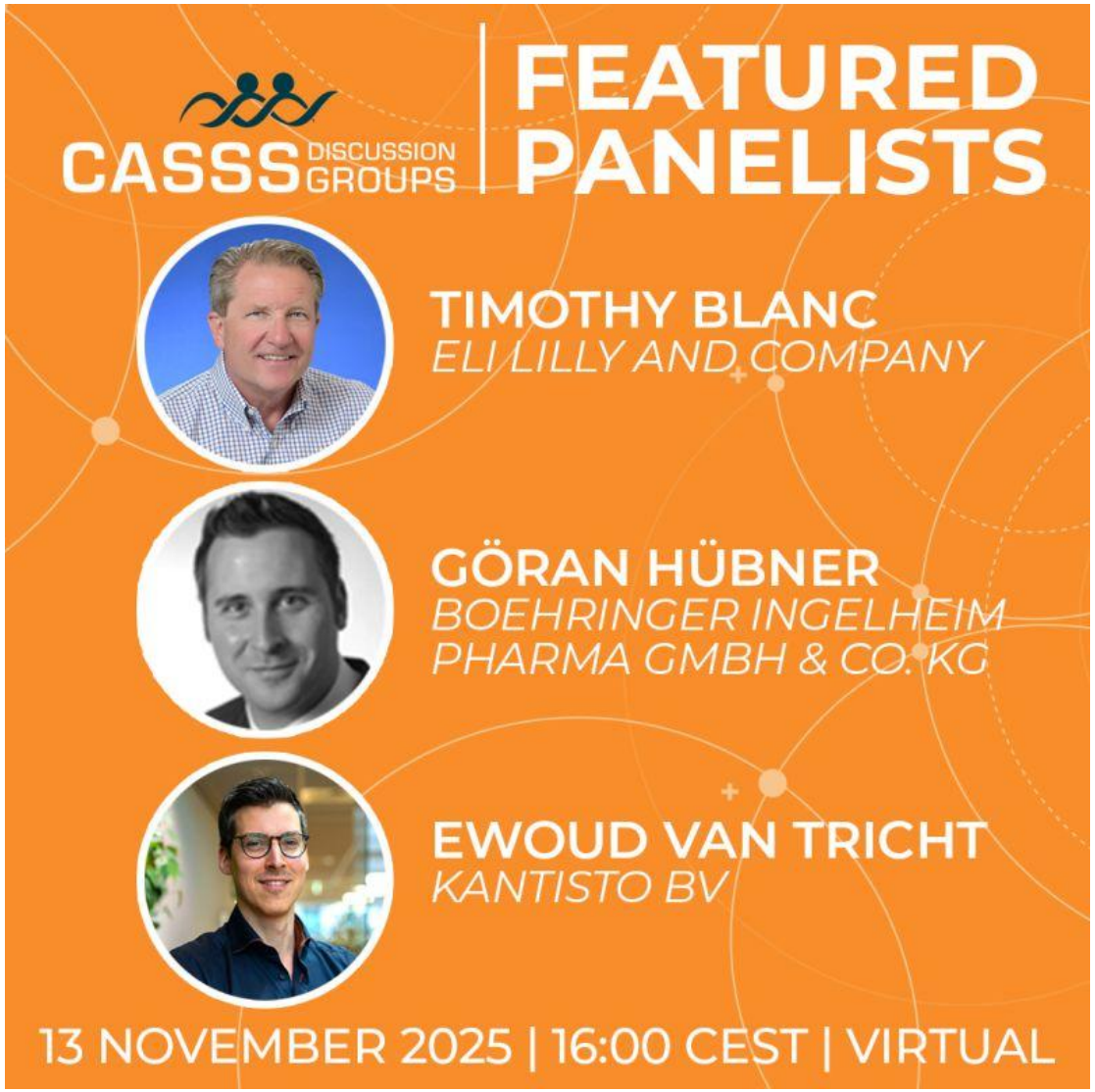
(1) Dedicated use of available stock

(2) Alternative ampholytes

(3) Alternative procedures

https://www.linkedin.com/pulse/summary-solutions-pharmalytetm-shortage-short-version-kantisto-of0pc

From vulnerability to resilience: Industry strategies for dealing with critical materials in analytical procedures



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