A biomarker assay validation approach tailored to the context of use and bioanalytical platform

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On behalf of UCB Biomarker Assay Validation Work Group

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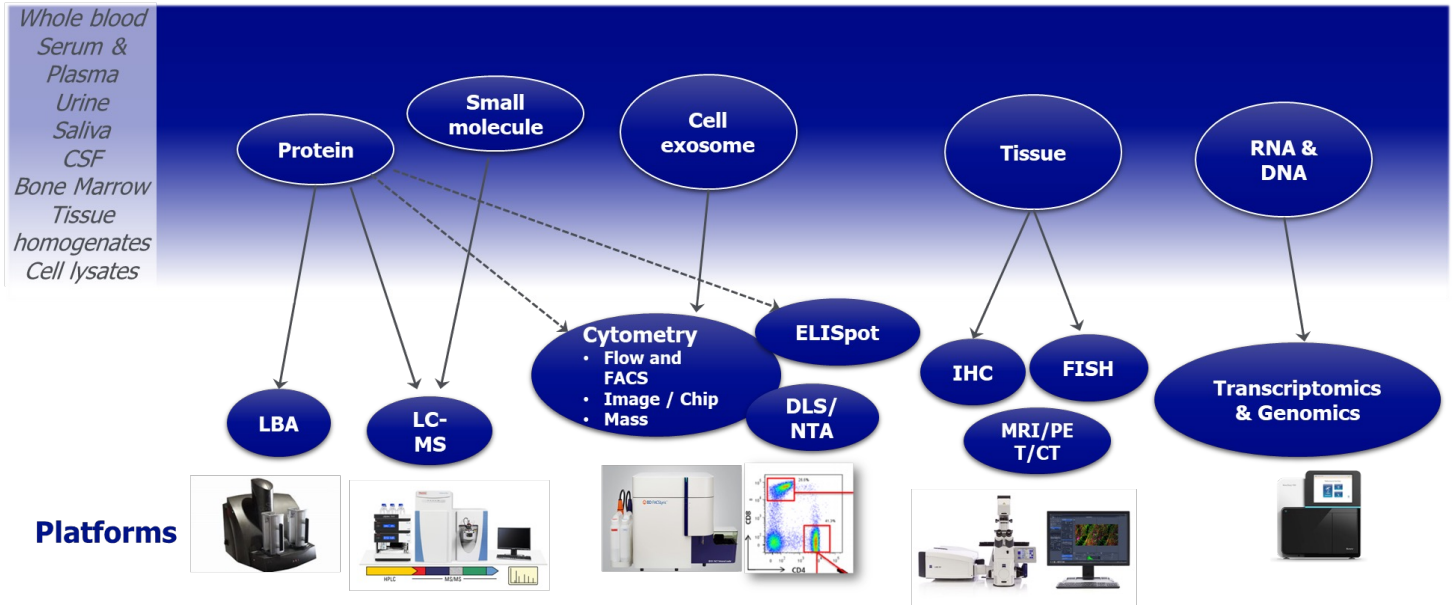
Inspired by **patients.**
Driven by **science.**

Biomarker assay complexity



- Levels of the molecule
- Expected magnitude of change
- Molecular heterogeneity
- Reagent selection and availability
- Biomarker localisation
- Individual study specifics
- Drug tolerance

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Additional complexity from:

- Regulatory expectations for biomarker assays unclear.
- Limited alignment between different organisations.
- Different contexts of use.
- Large bioanalytical team utilising multiple analytical technology platforms.
- Expectations from different groups within the organisation.

- To address these challenges we needed a consistent approach to maintain flexibility.
- Working group set up within Translational Biomarkers & Bioanalysis to develop and implement our approach to biomarker assay validation.

Current landscape

Lee et al, 2006
- Seminal paper on fit-for-purpose validation of biomarker assays.

EBF 2012
- Importance of integrating all scientific aspects
- Decision tree to classify biomarkers

Crystal City VI Workshop
- A framework would be useful to improve quality but relevance of FDA BMV guidance limited to PK assays
- Arnold et al. 2016 AAPS J; Lowes & Ackermann 2016 Bioanalysis

FDA BMV 2018 update
- Biomarker assays included, with reference to FFP validations, but still limited relevance to multiple contexts of use of biomarker assays.

Critical Path Institute, 2019
- Points to Consider document: scientific insight on how to address common bioanalytical obstacles when qualifying biomarkers as drug development tools.
- But also includes fit-for-purpose concept, based on context of use.

- Focus on analytical platforms used for PK.
- Many articles on biomarker analysis using flow cytometry, immunohistochemistry, ELISpot, PCR, Western blot.

Biomarker method validation overview

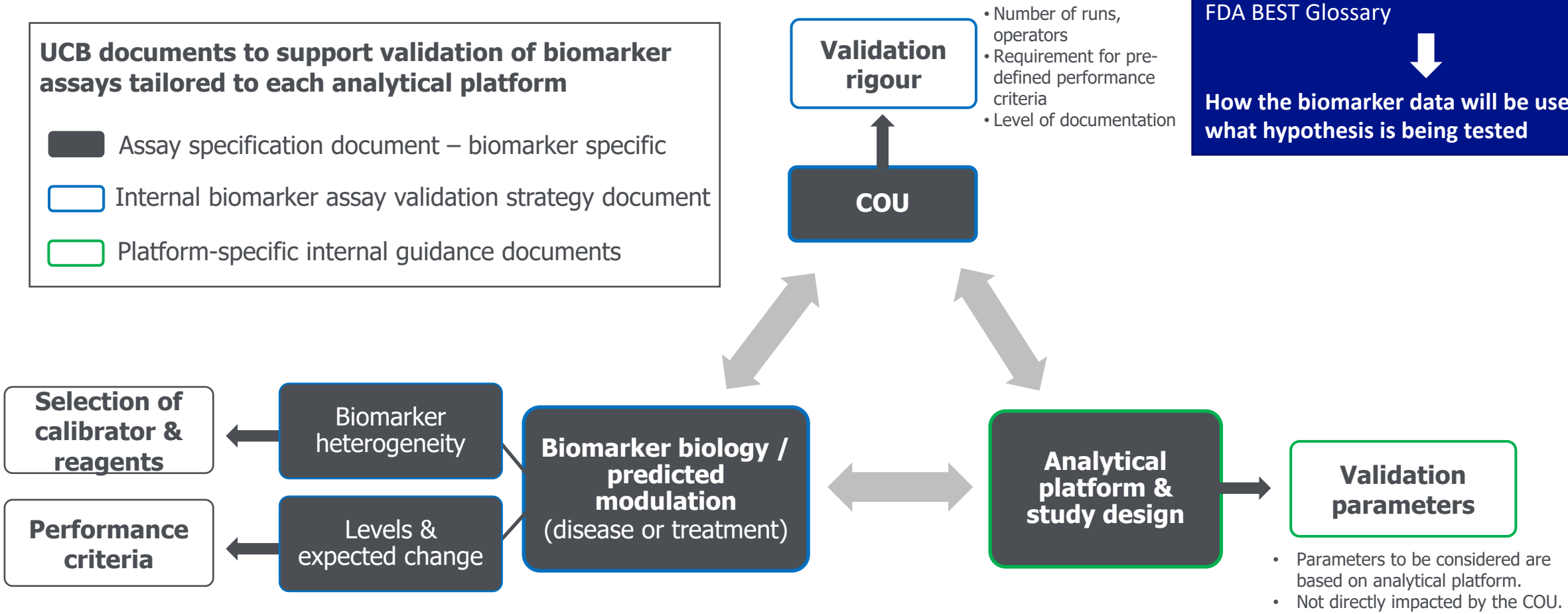
UCB internal guidance documents

Context of use:
"statement that fully and clearly describes the way the medical product development tool is to be used and the medical product development-related purpose of the use".
FDA BEST Glossary

How the biomarker data will be used and what hypothesis is being tested

UCB documents to support validation of biomarker assays tailored to each analytical platform

- Assay specification document – biomarker specific
- Internal biomarker assay validation strategy document
- Platform-specific internal guidance documents



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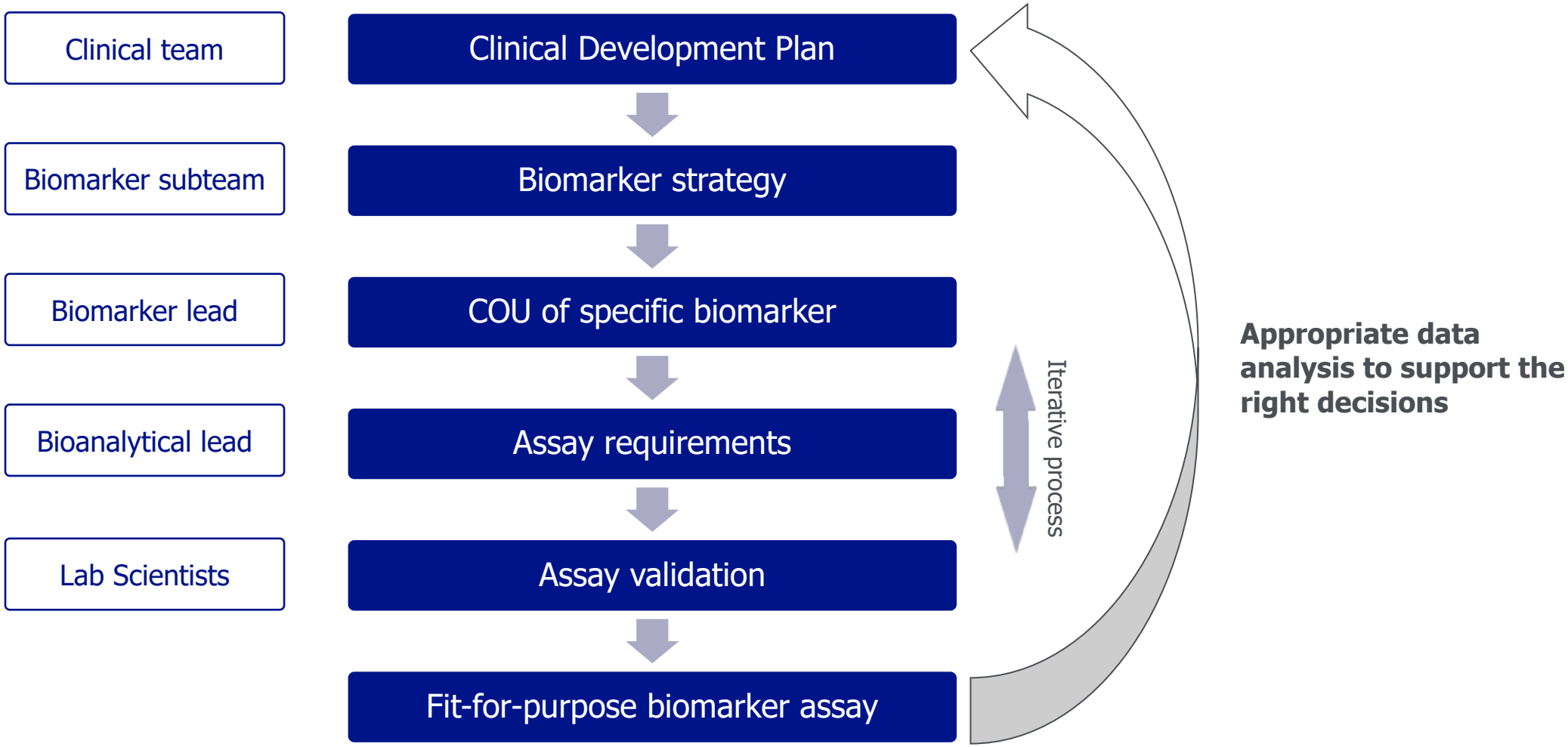
Fit-for-purpose biomarker assays

From clinical development strategy to FFP validation of BM assays



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Fit-for-purpose biomarker assays

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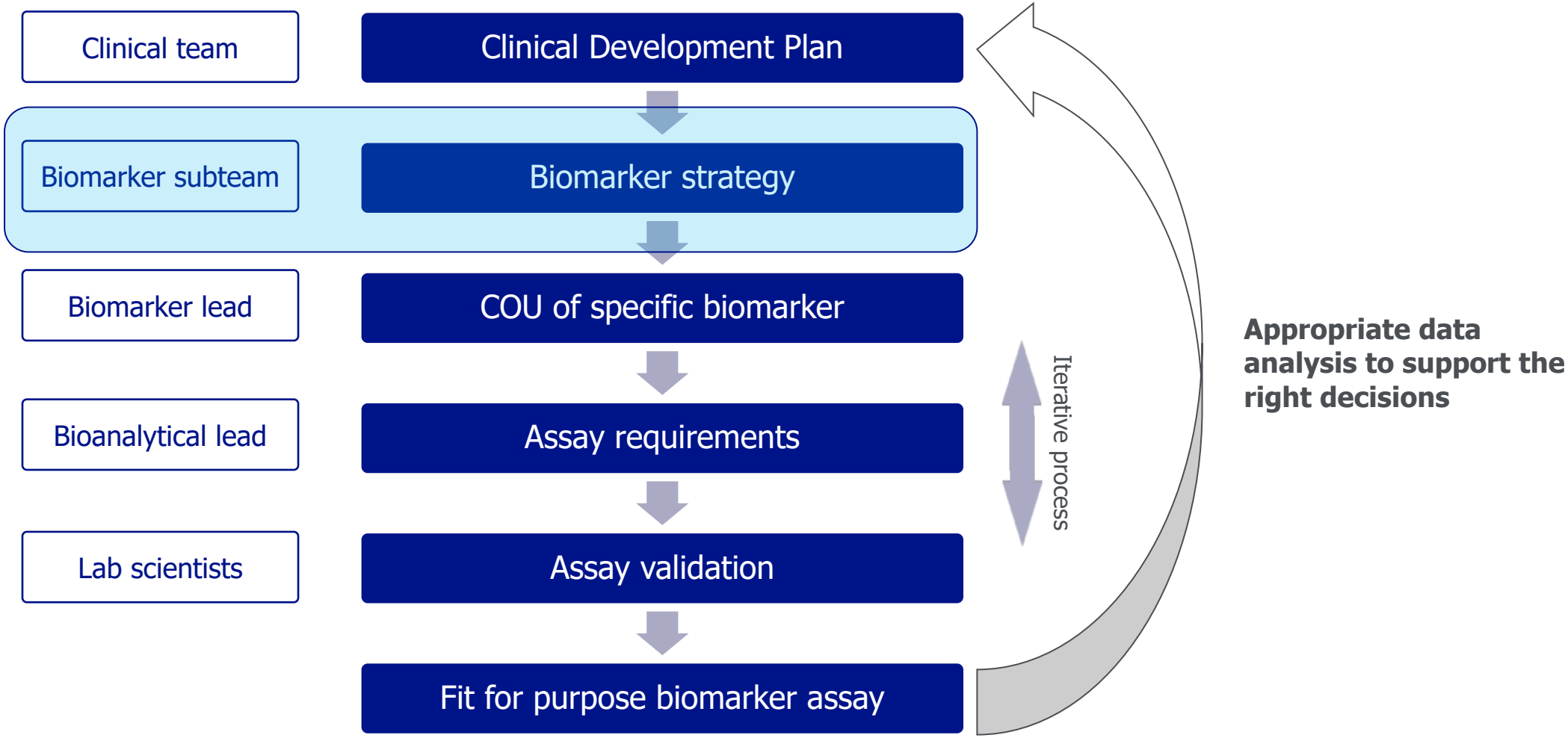

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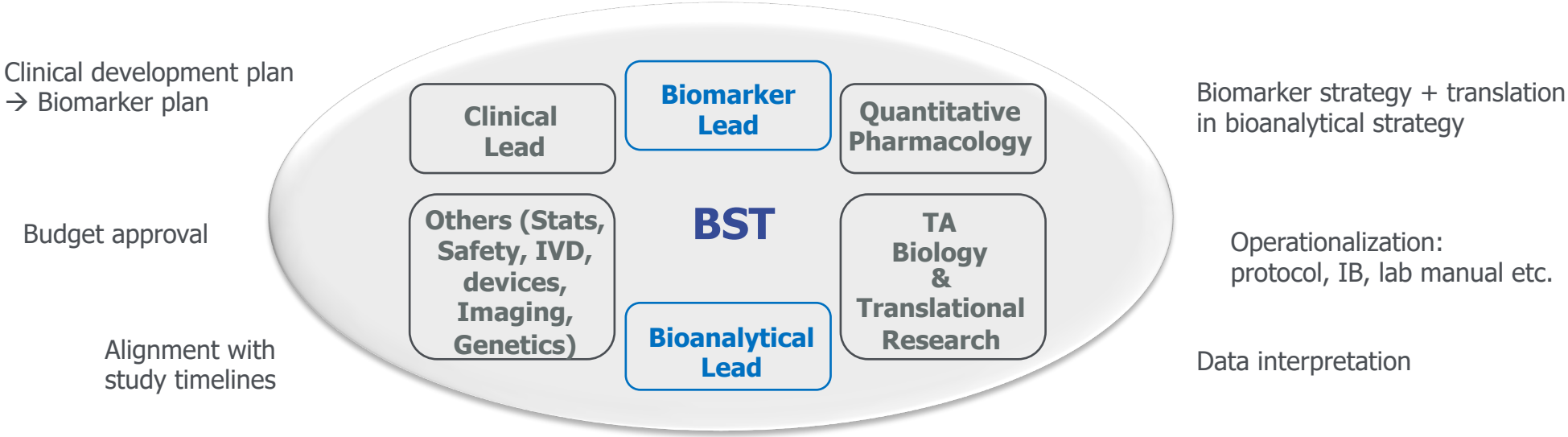
UCB Biomarker subteam

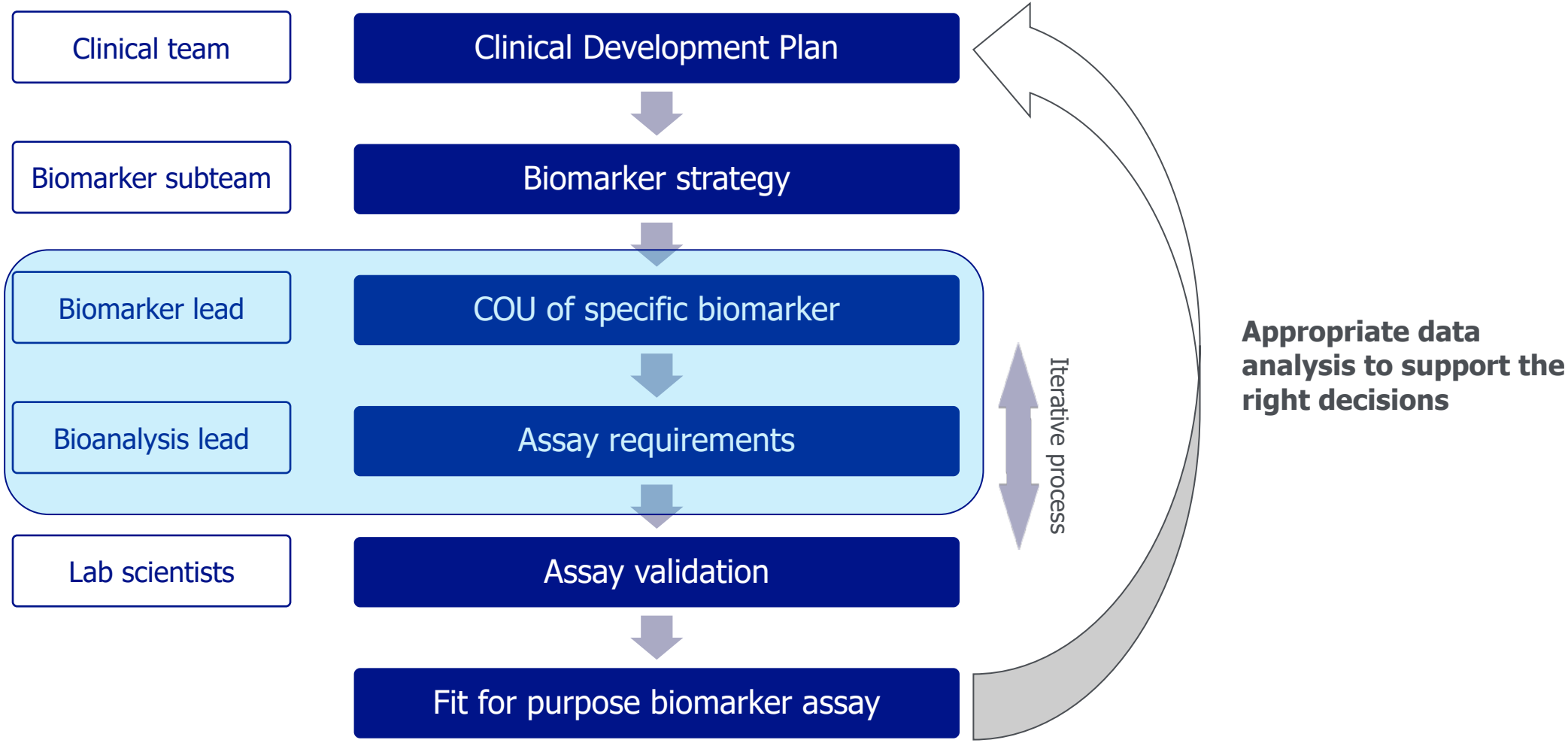
Cross-functional interactions driving the biomarker strategy and establishment of COU

- Biomarker subteams (BST) are responsible for:
  - the **development** and **implementation** of biomarker strategies to support clinical development
  - the **interpretation** of biomarker data in the context of overall clinical trial and project goals
- Within the BST, key accountable roles are held by the:
  - **Biomarker lead** – chairing the BST to agree and deliver a biomarker strategy and final data interpretation & reporting
  - **Bioanalytical lead** – translation of the biomarker strategy into a bioanalytical strategy and data delivery



Fit-for-purpose biomarker assays

From clinical development strategy to FFP validation of BM assays



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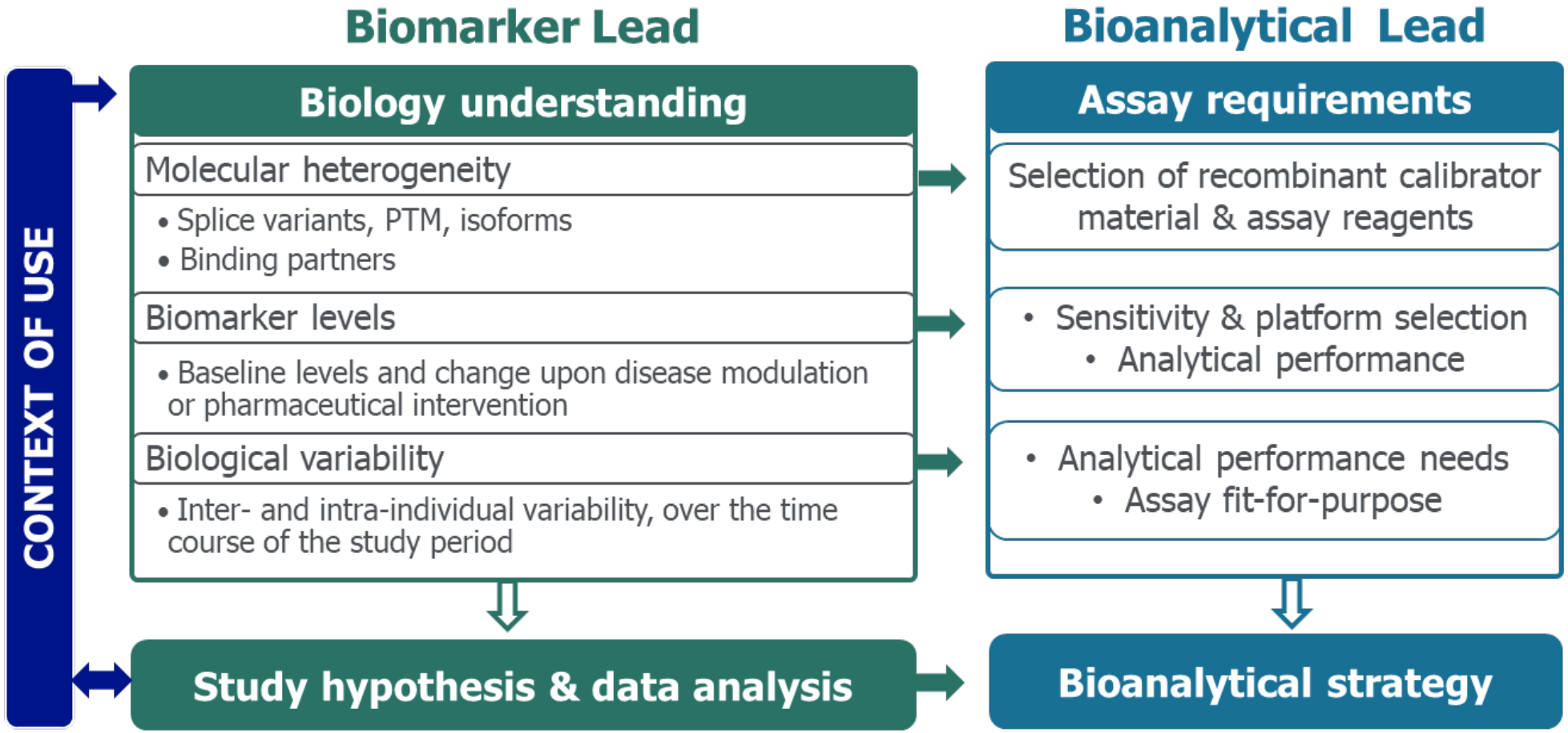
From COU to assay requirements

Assay specification document



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Fit-for-purpose biomarker assays

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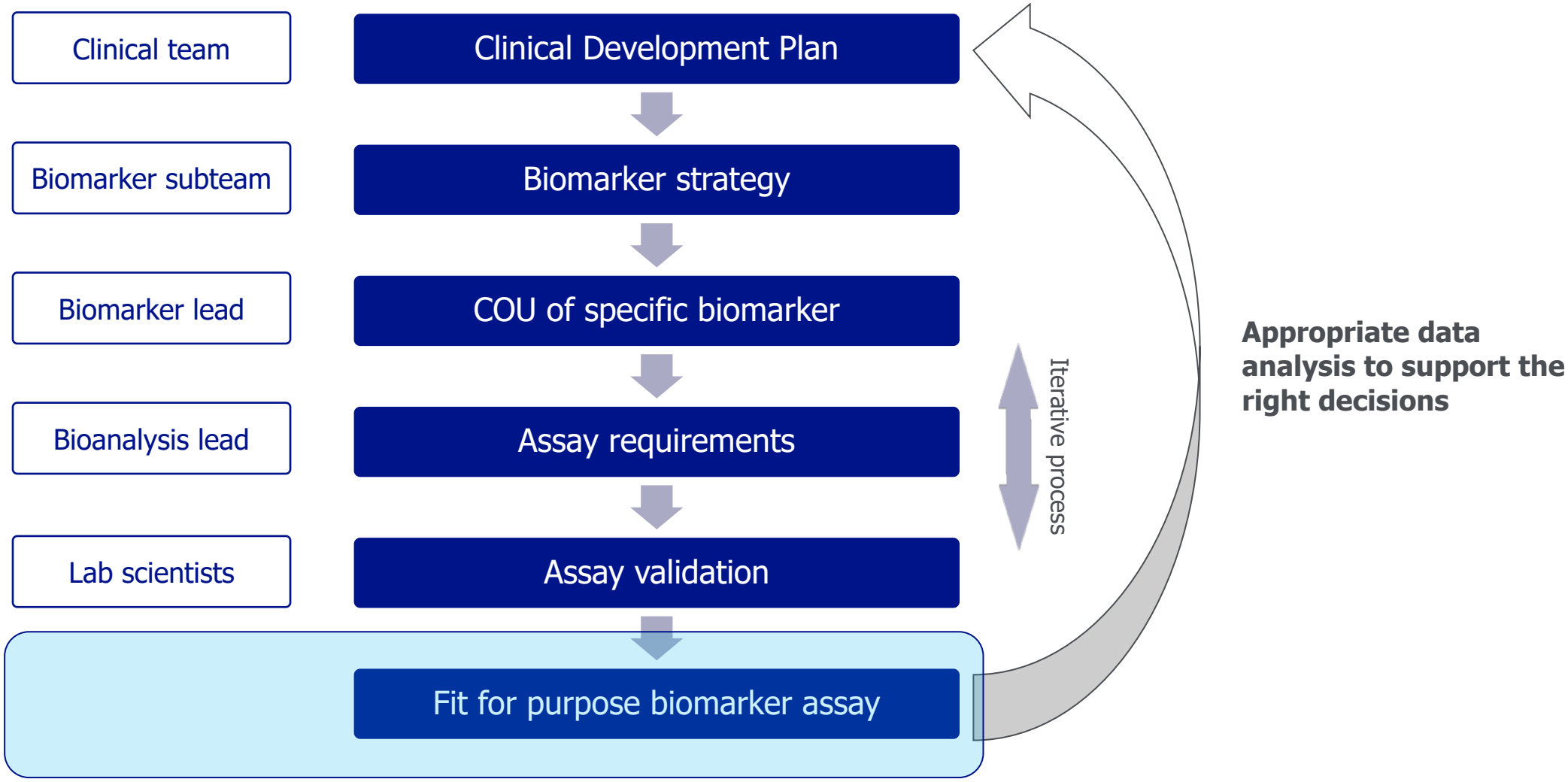

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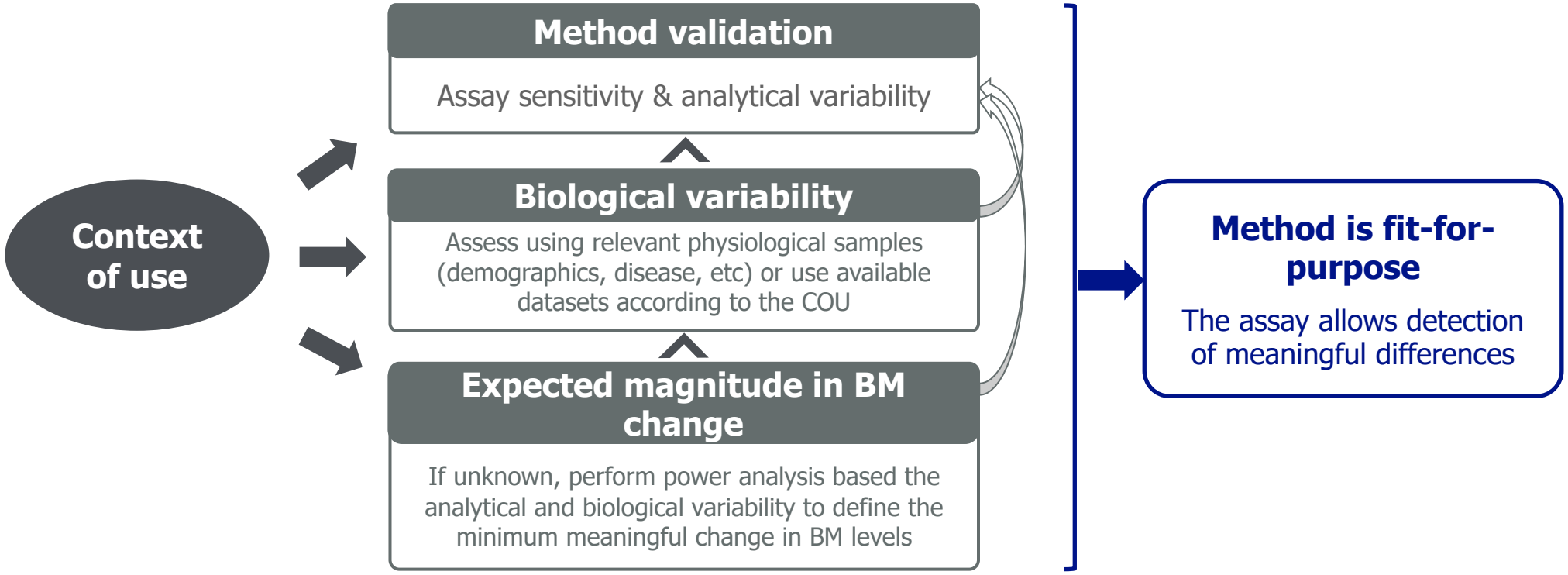
Define whether BM method is fit-for-purpose

Can the validated method support the pre-defined COU?



Parameters assessed are based on bioanalytical platform

Flow cytometry key parameters *to be considered*

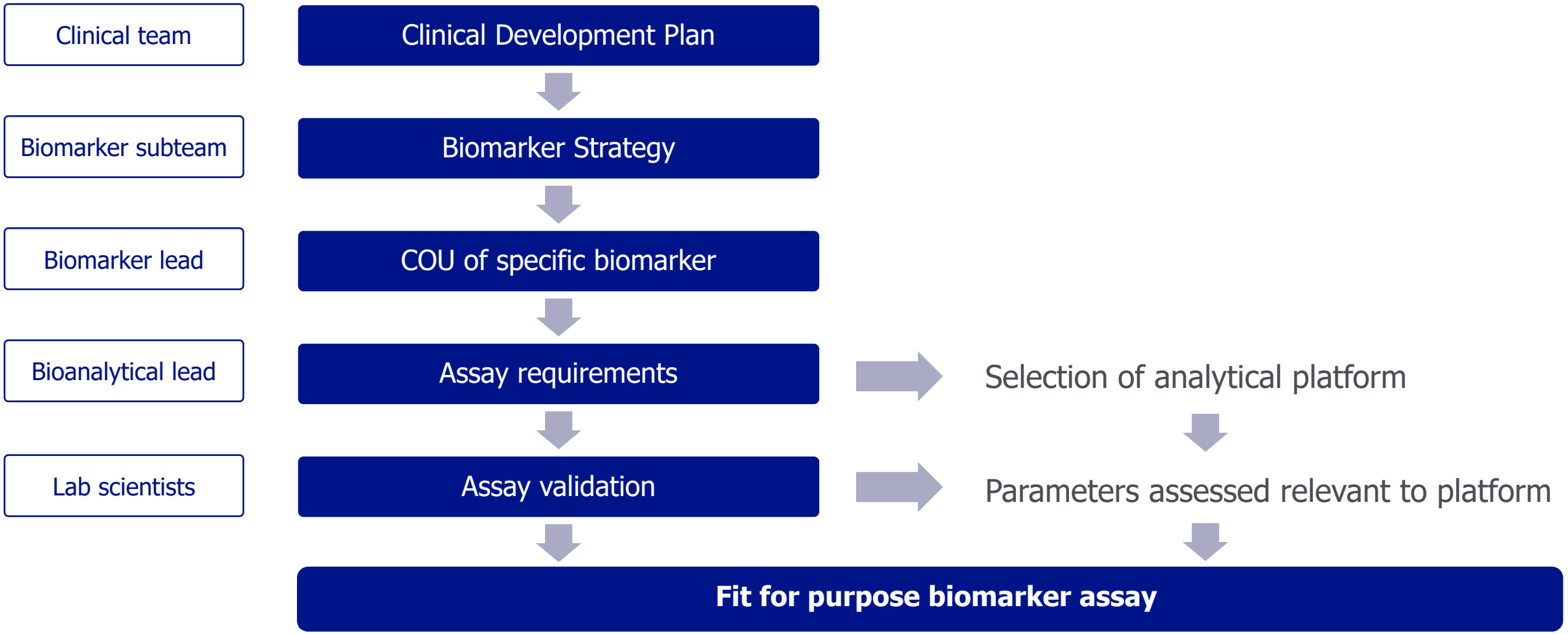
Platform	Read-out	Performance characteristics								
		Accuracy	Trueness (bias)	Precision	Assay range	Sensitivity	Reproducibility	Specificity	Parallelism	Stability
LC-MS	Definitive quantitative, relative quantitative									
LBA	Relative quantitative, quasi-quantitative									
Flow cytometry	Quasi-quantitative			Precision	Assay range	Sensitivity	Reproducibility	Specificity		Stability
IHC	Quasi-quantitative, qualitative									

Parameters assessed are based on bioanalytical platform

Immunohistochemistry key parameters *to be considered*

Platform	Read-out	Performance characteristics								
		Accuracy	Trueness (bias)	Precision	Assay range	Sensitivity	Reproducibility	Specificity	Parallelism	Stability
LC-MS	Definitive quantitative, relative quantitative				LLOQ-ULOQ					
LBA	Relative quantitative, quasi-quantitative				LLOQ-ULOQ / LOD					
Flow cytometry	Quasi-quantitative									
IHC	Quasi-quantitative, qualitative			Precision	Assay range	Sensitivity	Reproducibility	Specificity		Stability

Consistent approach regardless of bioanalytical platform



Summary

- The complexity of biomarker assays means that a flexible approach taking into account the context of use and biological factors is required.
- We have developed a consistent yet flexible framework to apply to biomarker assay validations on multiple bioanalytical platforms.
- A series of strategy and platform-specific technical documents enables a consistent approach to fit-for-purpose biomarker validation specific for the context of use.
- This supports the implementation of high quality assays to answer key questions to support the drug development pipeline.
- Alignment with CRO partners is in progress.

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Thank you

Any questions?