CoU implementation at Roche

Pratiksha Gulati

Bioanalysis and Biomarkers (BioAM) Chapter

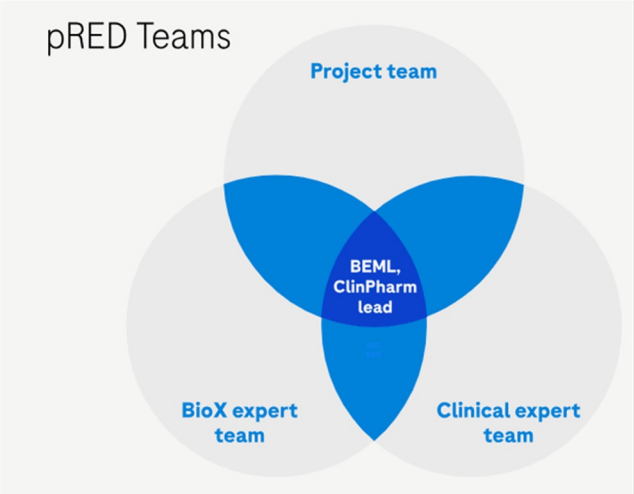
Roche Pharma Research and Early Development (pRED)

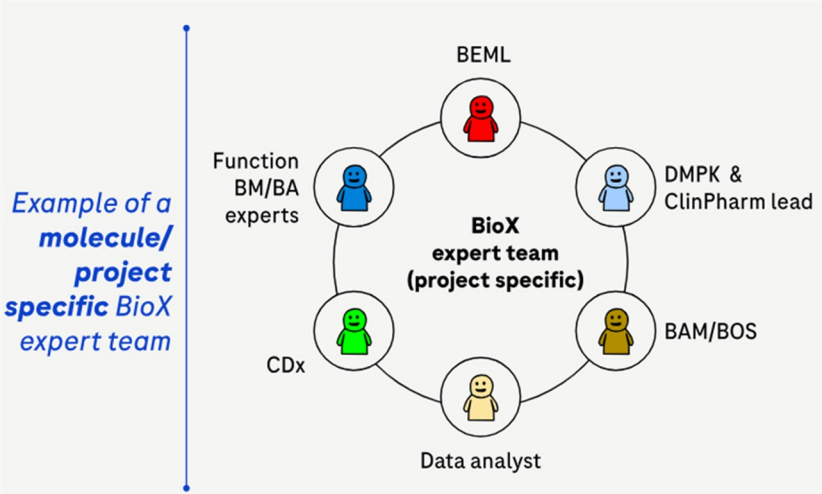
Roche Innovation Center Basel

One BioX (Biosamples, Biomarkers and Bioanalytics)

- BioX expert team operates at a Project level including all relevant stakeholders and integrating feedback from Biomarker, DMPK, Clinical Science and Clinical Pharmacology strategies

- BioX Expert Teams develop and discuss biomarker strategies; while integrating other topics like PK/PD modeling, immunogenicity, PoM, patient enrichment and disease understanding.





Biomarker Request Form to understand the CoU

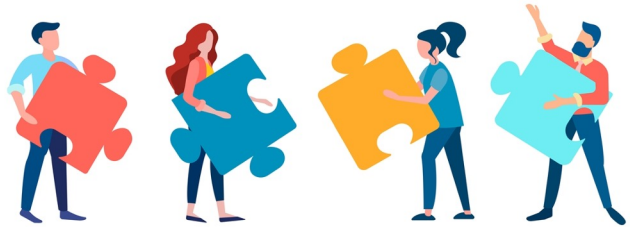
Biomarker Request Form (BRF)

Document Location	*Project Folder*
Electronic version *	*<Add link to relevant folder>*
Document guidance	• *This document serves as entry point for all biomarker requests* • *The document is to be filled out and signed by the requester (BEML, TBL, etc) in consultation with the supporting PS scientists* • *Completion of this document is a prerequisite to initiate any biomarker activities* • *Any changes to the initial biomarker request should be captured in this document, agreed upon, versioned and appended*

Name	Department	Signature and date
BioAM Scientist(s) (responsible for the activity)		
BEML / TBL / BEMS / ClinPharm (activity requestor)		
Biosample Operations Specialist		
BAM (if applicable, delete line if not)		

Document History	Version	Reason for Change	Date
	Version 1.0	Initial Request	

*: mandatory



FBE ***(Functional Biomarker Expert)***

BEML ***(Biomarker Experimental Medicine Leader)***

BAM ***(Bioanalytical Manager)***

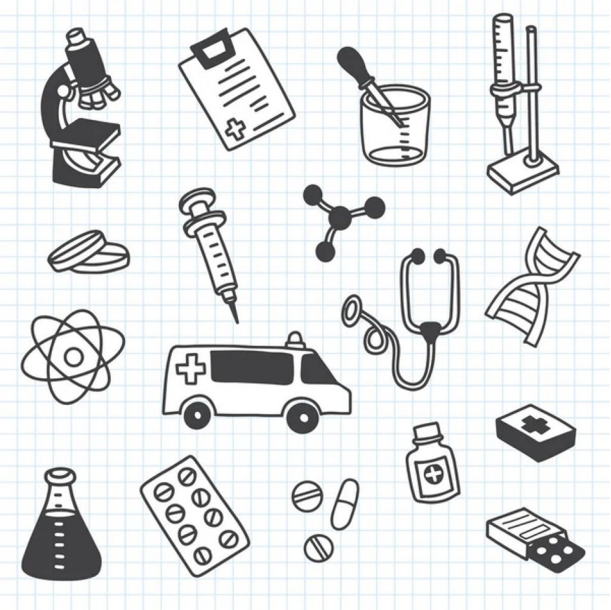
BOS ***(Biosample Operation Specialist)***

- Setup per study/Project
- Consolidated information on all Biomarker assessments
- Entry point for all biomarker requests
- Evolving document that is versioned
- All relevant functions are involved

Biomarker Request Questionnaire

Scientific Information and Rationale

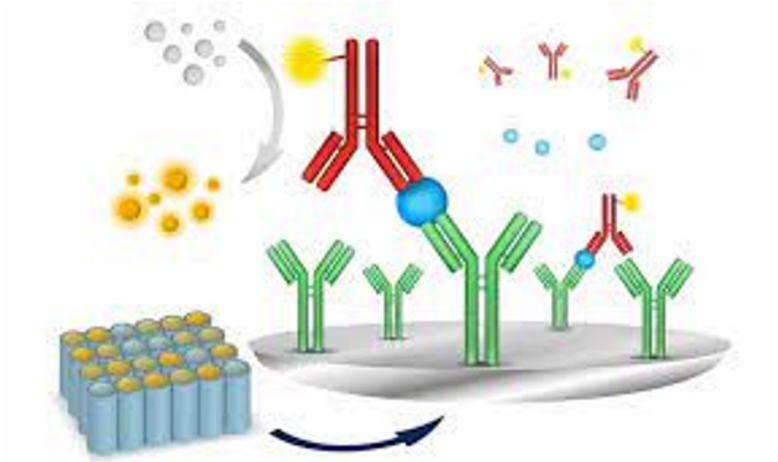
- Scientific Background – biological questions, disease indication
- Rationale to measure the biomarkers
- Are different proteoforms described for any of the biomarkers? If yes, which proteoform is of interest? Do PTMs, splice variants or disease specific SNPs play a role?
- Are there any known binding partners? Is the aim to measure bound or unbound protein complexes?
- What is the expected range of biomarker concentrations in the relevant sample type and study populations?
- What is the expected level of change? Are the levels expected to increase or decrease? Please specify respectively for total vs free (target engagement) analyte levels
- Are change in levels expected due to therapeutic intervention or general biology (eg, disease progression, protein shedding from cell surface)



Biomarker Request Questionnaire

Technical Aspects

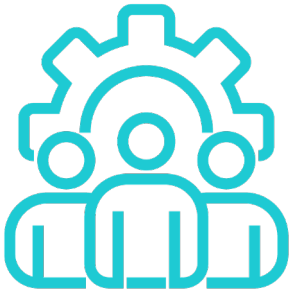
- Sample type and matrix/tube of choice (eg, anticoagulants). Consider artificial release during sample processing (eg, platelet activation, temperature instability, aggregation, tricky stability such as complement proteins)
- Technologies in consideration
- Is there an existing prototype assay or internal/external evidence from specific technology?
- Any known or expected drug interference?
- Are there any pre-meds or co-meds that could interfere with the measurements?
- What is the minimal change the assay needs to demonstrate?
- Is a custom assay generation needed? Are reagents available?



Biomarker Request Questionnaire

Operational and Protocol related

- Is there access to relevant diseased samples for development/validation work?
- Does the ICF wording allow samples to be used for method development (eg, in-study clinical verification/validation extension)?
- Estimated total sample volume available
- How will the data be utilized? (For eg, fold changes in levels, relative/absolute concentration reporting)
- What does this entail in terms of decision making? (For eg, internal decision making, dose selection, patient safety monitoring, subject inclusion/exclusion, label claim, hypothesis testing, efficacy readouts, others)
- Is there potential for the data to support a regulatory claim or for submission to HA?
- How are the biomarkers placed in terms of clinical endpoints?
- What is the expected analysis frequency (eg, batch analysis, cohort driven analysis, end of the study analysis, etc)



Capturing the CoU

Table-1

Definition and agreement on the Context of Use

To be filled by BEML and BioAM scientist. This table captures a summary of biomarkers needed and their intended CoU in the study. For cellular biomarkers, please only list critical populations of interest.
Define CoU per biomarker in a clear and concise way

(for eg, The purpose of the assay is to measure [free/unbound] biomarker [A] in [matrix_X] on [platform_X] to evaluate levels in [population_Y] to enable a change of [Y%] from baseline to allow decision [Z])

Biomarker	Type	Intended Context of Use
	Cellular	
	soluble	
	soluble	
	Cellular	
	Cellular	

- Intended CoU captured in the Biomarker Request Form (tabular format) - what is needed
- Signed and agreed with stakeholders (BioA Scientist, BPL, BEML, FBE)
- Final technical CoU statement (what the method can deliver) to be captured in the validation report

Technical CoU statement:

The purpose of the assay is to measure [free/unbound] biomarker [A] in [matrix_X] on [platform_X] to evaluate levels in [population_Y] to enable a change of [Y%] from baseline to allow decision [Z]

Doing now what patients need next