14th EBF Open Symposium

Science – Our Universal Language

Biomarker Strategy Team 2021

Organisational design driving or preventing CoU:

Challenge or Opportunity

A Pharma/Sponsor perspective

<< Kyra Cowan, on behalf of the EBF >>

24-26 November 2021, Barcelona

Biomarker Assay CoU: The Game-Changer for Many

- **Understand what it is**
- **Understand why it is critical**
- **Understand how to implement it, considering the many challenges**
  - Scientific
  - Analytical
  - Strategic: communication, stakeholder management, operational

What is Context-of-Use for BM Assays?

- **Detailed definition of the purpose of the assay for each analyte**
  - Understood and agreed upon by all stakeholders
  - Documented in method summaries, validation plans, validation reports

- What does it look like?:
  - **2-4 sentences defining biomarker to support assay needs.**
- Key thoughts: To understand the biology, pharmacological effect; to understand what the data will be used for, eg. scientific or safety decisions taken, to then consider what is possible from a BA perspective; to understand biological, analytical variability…
- Ultimately: **To ensure the appropriate interpretation of data to serve patients.**

- What does it not look like?:
  - „To quantify the analyte“

Why is Documenting Context-of-Use for BM Assays Important?

- **The purpose of the assay may change from one study to the next**
  - The types of decisions being made based on the results may vary and should be communicated each time.
  - Without an agreed CoU there is a risk of implementing the wrong assay, with inappropriate characterizations and therefore validation.
  - Leads to incorrect data and decisions, negatively impacting patients.

- **Institutional knowledge may change:** new team members, people may leave.

Bottom Line: Bioanalytical scientist takes ownership and accountability to communicate with their stakeholders and provide adequate education.

EBF Recommendations on BM Assay Characterisation

- **CoU must first be defined and agreed upon by all stakeholders:**
  - **EBF recommends** this to fully understand what question(s) the biomarker data will address.

- **The identified questions would then address:**
  - **Type of assay** required (e.g. free or total, in-house assay, commercial kit, single analyte, multiplex, research use, diagnostic)
  - **Format** of the assay and critical reagents
  - **Technology** choice, with pros and cons
  - Access to appropriate **biomarker samples**

Recognizing the urgency of this game-changer

Cross-Industry Implementation of CoU for patients

- **Omission of CoU for Biomarker Assays is Risky**
  - Wrong CoU: inappropriate acceptance criteria, poor use of resources and time, wrong decisions, failed drug development.
  - CoU must be constantly re-evaluated: changes in purpose dictates assay characterization and much later validation.
  - Decisions need to be driven by the science, not a validation framework.
- **CoU is platform and technology agnostic**
  - Diversity and complexity of biomarker assays is wide
  - Framework or set of categories may stifle the crucial conversations that are needed for defining the assay purpose.
  - Acceptance criteria should not be pre-defined.

Quotes from Stakeholders, Community:

- I believe that we understand and apply this principle to our development and degree of validation efforts, but I don't think the rest of the world is aligned to this.
- Often I feel that people cite CoU without understanding what boundaries are defined.
- There is a misunderstanding from high stakeholders on CoU.
- I guess I know what it is but not sure I fully understand what it involves

2021 Objectives	Biomarker Strategy Subteam
Project Title:	Biomarker CoU: Implications for the assay
Team Leader:	Kyra Cowan, Merck KGaA
Team *(from organizing committee)*	Jo Goodman, AstraZeneca; Michaela Golob, Nuvisan; Anna Lauren, Novo Nordisk; Philip Timmerman, EBF
Team	Laetitia Sorde, Sobi; Peter Groenen, Idorsia; Ulrich Kunz, Boehringer-Ingelheim; James Lawrence, F-Star; Lien Dejager, UCB; Alessandra Vitaliti, Novartis; Laurent Vermet, Sanofi; Lene Andersen, Orphazyme; Marianne Fjording, Bioagilytix; Mario Richter, Abbvie; Matti Kimberg, Synexa; Mike Wright, GSK; Nicole Justies, Roche; Philip De Decker, argenx; Radboud van Trigt, PRAHS; Renaud Jasnowski, Active-Biomarkers;
Goals *(for this year)*	**First: battle for industry-wide implementation of CoU**

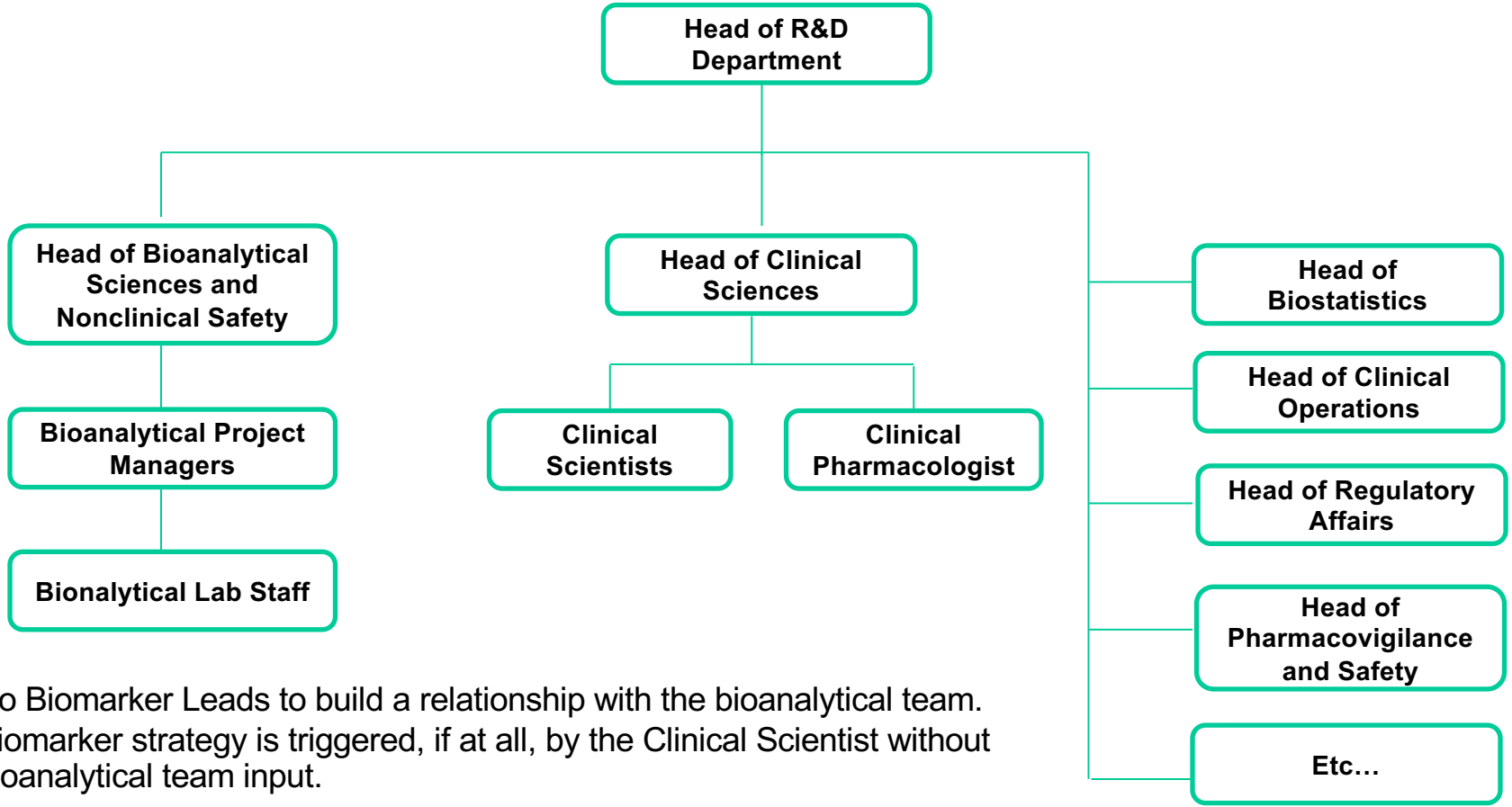
Biomarker Strategy Team 2021

- Building from BM FW April 27-28 on CoU
  - We need to keep the momentum going
  - Still have issues with understanding/alignment within BA space
  - **To our EBF Community:**
    - You are the multipliers, the sponsors, the champions of the message for CoU throughout industry, to drive the topic internally and externally
    - We need to avoid inappropriate guidance from HAs, inappropriate implementation of BMV guidance on BM assays in general
    - How do we change the way of thinking? – this is not repackaging of the Jean Lee or subsequent FFP papers – rather diving deeper into the strategy and the science that supports CoU implementation.
  - Clarity and alignment across industry
- **First team meeting: What works, doesn't work, in organisational structures**
  - **Volunteers** to describe their organisations
  - **Agreed:** BA scientist is in the driver's seat, and it's critical that BA scientists are considered integral on the core team, for example.
  - **Agreed:** CoU should be discussed early, and confidence needs to be built in what we have to offer, so that the importance of CoU is convincing.

Case Study 1: Challenges to CoU

- **Bioanalytical Team separate**, physically and organisationally, from rest of organisation

- Bioanalytical Team currently involved in :
  - PK/PD/Biomarkers are run internally and in the same unit, ADA/Nab outsourced, for some studies.
  - For clincial studies on newly acquired constructs, bioanalytical analyses are fully outsourced.



- No Biomarker Leads to build a relationship with the bioanalytical team.
- Biomarker strategy is triggered, if at all, by the Clinical Scientist without bioanalytical team input.

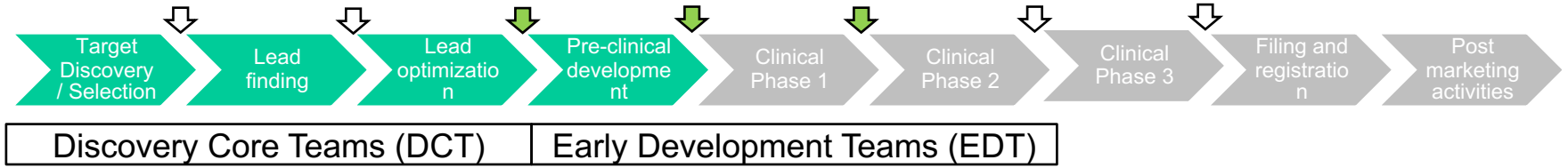
Challenges around Biomarkers in Case Study 1:

- No organisational design specific to biomarkers
- Bioanalytical team not involved in clinical protocol writing.
- Biomarker strategy is not clearly defined and is not a priority for studies.
- In general there is no CoU defined in the clinical protocol.
- Biomarker «lists» are triggered by KOL (e.g. PI) without strong rationale for each biomarker.
- Clinical Team does not share biomarker results with the bioanalytical team unless especially requested for.

- *In progress: biomarker strategy is under re-organization with more power given to the bioanalytical department, and more interaction with the clinical team.*

Case Study 2: Integrated Biomarker Approach

- **Translational Biomarker Representatives are part** of the Early Development Teams and Life Cycle Teams.
- BM assay activities (preclinical and clinical) are only within Translational BM group, separate from PK/ADA bioanalytical team, research groups, clin pharm, nonclinical safety, etc.
- Bench to bedside and back.



Case Study 2: Assigned Biomarker Expert Roles Works

Biomarker experts have multiple roles as they also run labs or conduct experiments

- At lead optimization, BM lead/expert initiates the BM strategy, defined and refined with team.
  - Appointed to a core team, acts as advisor for indications and biomarkers.
  - Initiates question-based approach (i.e. CoU documentation) in living, online, time-stamped document.
  - Responsible for execution of:
    - BM strategy
    - Operational (outsourcing)
    - Analytical (assays)
    - Data interpretation
    - Documentation, including “COU”

Summary on Common Ground

- **What works:**
  - Clear and documented BM strategy and integrated BM approach.
    - Ensure that the biology is discussed and understood.
  - Clearly defined, centralised BM group that covers BM assay, operational, and BM strategy expertise and corresponding responsibilities.
    - Overarching view on CoU, all BM activities (assays, samples, data analysis, CoU).
    - High functioning matrix work environment with clear R&Rs and close collaborations.
    - Ideally, operational separation of decision-making BM assays from PK/ADA BA team.
      - Depending on CoU, separate processes for PK v BM
  - If not one BM group:
    - Close collaboration between BA and BM leads, if separate functions.
      - Co-location of these groups preferred.
    - Close collaboration with all stakeholders, including outsourcing, to implement BM strategy.
  - Implementation and documentation of Purpose (CoU) for each BM data
    - In method summaries, in validation plans, in SAPs, in assay specification document or online „living document“, etc., for each purpose for each BM
  - Inclusion in clinical protocol review

Summary on Common Ground

- **What doesn‘t work:**

  - Lack of Biomarker assay expertise, or relying on PK assay experts.
  - Siloed operational teams, or complex team organisation, and/or gap in communication btw Sponsor/CRO, so that BA input and involvement is lost.
  - Fractioned responsibilities across functions without single BM lead with overarching investment in all BM deliverables.
  - Applying the wrong regulations and check boxes (eg. PK SOP, QA vs independent QC, etc.).
  - Lack of a possibility to have scientific rationale, discussion, and therefore being beholden to BMV.

Simple Structure, starting at Lead Optimisation

Discovery Team

DMPK

Research

Nonclinical safety

Bioanalytical PK/ADA

Translational BM Lead

BM Integrator

BM Techno

Biomarker selection, strategy

Analytical, Operations

Data Interpretation

CoU statement per analyte, Documentation

Development Team

Medical

Drug Safety

Pharmacometrics

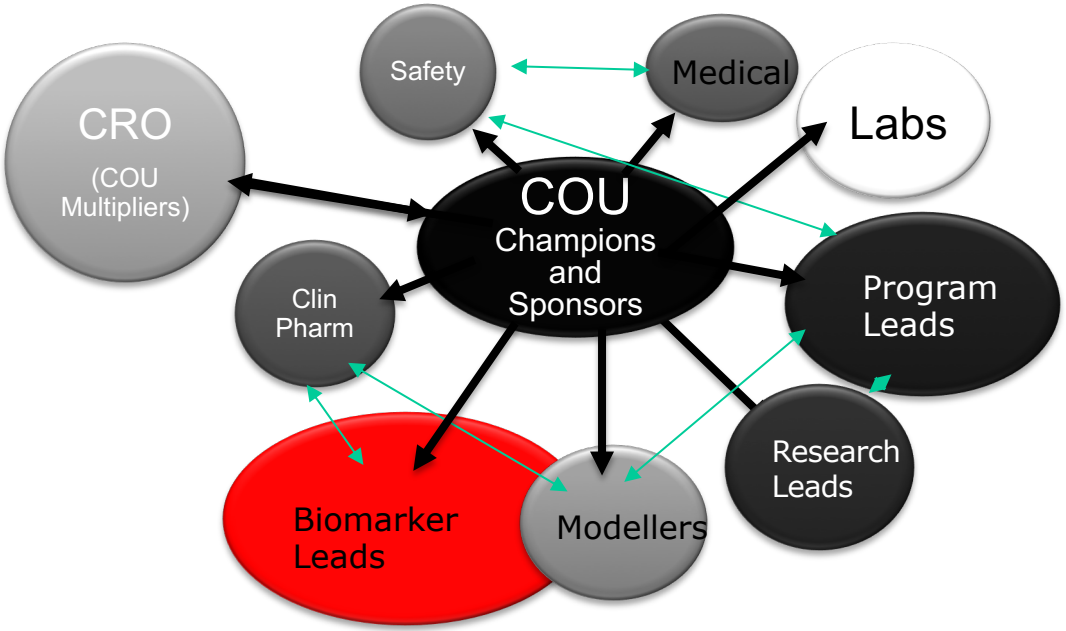
Clinical Pharmacology

Touchpoint Meetings*

*Touchpoint meetings with BM Lead would need to involve all relevant functions

Changing the mindset with defined responsibilities and documented communications

Truly matrix approach to communication for simplified org:



Stakeholder Management is key:

- How can we ensure COU is implemented and communicated?
- What is missing in the communication?
- How can we best educate/train?
- How can we make sure we are relaying the right message?
- How do we relay a sense of urgency for COU?
- How do we ensure consistent buy-in?

How to make CoU implementation successful?

1 **Create awareness**
- Create a feeling for urgency for CoU.
- Develop an understanding of the situation, risks, impact and activities in implementing CoU (train and explain).

2 **Win supporters**
- Get top management commitment.
- Build a team that supports the message.

3 **Develop a vision**
- Make it clear and understandable what's being implemented and why.
- Explain the outcome of using CoU.

4 **Communicate the vision**
- Provide timely and honest information.
- Get buy-in for CoU.

5 **Empower Action**
- Win-Win-Strategy: make your stakeholders to your partners.
- Involve your stakeholders e.g. the employees in decisions.

6 **Create short-term wins**
- Get change blockers or neutral people on your side by showing successes of the project.
- Communicate about your wins.

7 **Leverage wins to drive change**
- Use the energy from the quick wins to drive your change initiative forward.

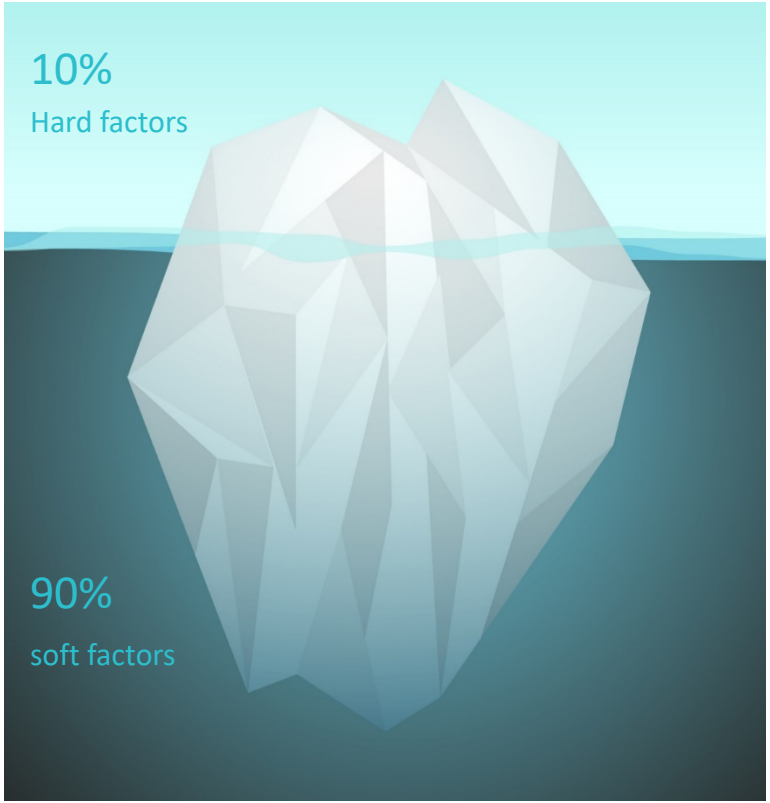
8 **Embed in culture**
- Stabilize the situation again and develop attitudes and behaviors which embed the changes in the culture and daily work.
- Make long-term objectives measurable.

The iceberg model

What are key factors that will make implementing COU successful?

- Training programs
- Costs
- Timeline
- Organisational structure
- Available technologies
- Regulatory domain knowledge

- **Involving the employees/stakeholders**
- **Honest and timely communication**
- **Normal routines, habits**
- **Top management commitment**
- **Motivating organizational culture**
- **Change promoters (those willing and understanding CoU)**
- **Corporate culture of continuous change**

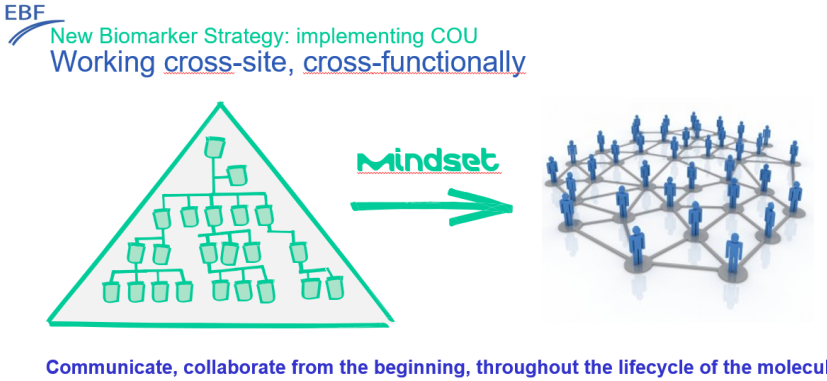


Conclusion

The base of change management lies below the surface of the iceberg.

Involving the stakeholders in an honest and timely communication is key to successful and regular implementation of CoU principles for all biomarkers

Acknowledgements



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Mario Richter, Abbvie
Radboud van Trigt, PRAHS
Laurent Vermet, Sanofi
Alessandra Vitaliti, Novartis
Mike Wright, GSK

Biomarker Workshop: An Introduction...

16:20-18:10: Session 5: Workshop – Biomarkers – Organisational design driving CoU

16:20- 16:40: Kyra Cowan, on behalf of the EBF
Organisational design driving CoU – feedback from pre-meeting survey

16:40-18:00: Workshop discussion, incl. organisational design Case studies.
Company perspectives from:
16:40 – 16:50 Laetitia Sordé, Sobi
16:50 – 17:00 Ulrich Kunz, Boehringer Ingelheim
17:00 – 18:00 Panel discussion

18:00-18:10: Wrap up

Contact Information

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