How the Bioanalyst Plays a Key Role in Interdisciplinary Project Teams in the Development of Biotherapeutics – a Reflection of the EBF

Daniela Stoellner
on behalf of the EBF TT-20

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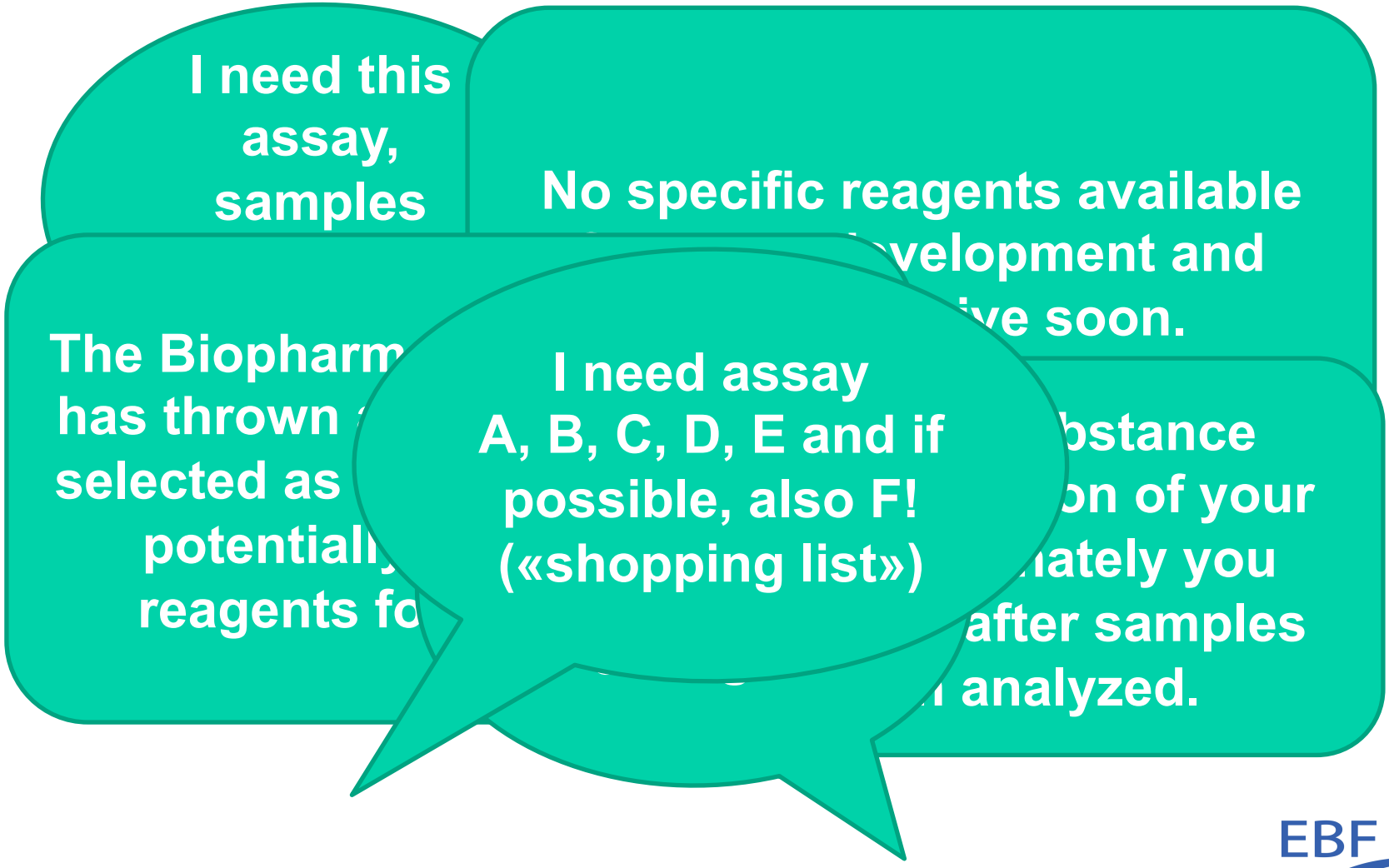
Imagine the Following Situations:



Consequence of...

...Bioanalyst NOT BEING INFORMED

...Key role of bioanalyst within project teams developing biotherapeutics not well understood

EBF TT-20 „Challenges of Free and Total Macromolecule Quantifications“

- Importance of scientific exchange between bioanalyst and data end users on a regular basis to better understand challenges faced by both sides

- Increase awareness and understanding of the BA needs from the different project team functions

Perspective
Special Focus Issue: Bioanalytical laboratory management

Bioanalysis

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How the bioanalytical scientist plays a key role in interdisciplinary project teams in the development of biotherapeutics: a reflection of the European Bioanalysis Forum

The bioanalytical scientist plays a key role in the project team for the drug development of biotherapeutics from the discovery to the marketing phase. Information from the project team members is required for assay development and sample analysis during the discovery, preclinical and clinical phases of the project and input is needed from the bioanalytical scientist to help data interpretation. The European Bioanalysis Forum target team 20 discussed many of the gaps in information and communication between the bioanalytical scientist and project team members as a base for providing a perspective on the bioanalytical scientist's role and interactions within the project team.

Keywords: assay development • bioanalysis • bioanalytical process • biotherapeutics • clinical • drug development • large molecules • preclinical • project team • sample analysis

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The key role of the **bioanalytical (BA) scientist** within project teams developing **biotherapeutics**, is still not well understood in most pharmaceutical companies. Thus, the goal of this article is to enhance the understanding of BA needs from the different project team functions and to highlight the advantage of scientific exchange between the different parties on a regular schedule. The ideas presented here come from an European Bioanalysis Forum (EBF) topic team assigned to elucidate the challenges of total and free macromolecule quantification. This topic team started its activities in 2011 following up on the publication of the White paper by *Lee et al.* [1] and held a break-out session at the EBF Open Symposium in Barcelona in November 2011, where all speakers agreed on the importance of interdisciplinary communication between BA scientists and data end users to better understand the challenges faced by both sides [2].

Project team

Bioanalysis of therapeutic proteins requires input from a number of project team functions in order to assure a fit-for-purpose assay and to carry out sample analysis to support preclinical and clinical work in a timely manner. If we take a look at the timing and how everyone works together from the BA assay development perspective, the key partners for the BA scientist are the **pharmacokineticist, disease area project leader** and the **biopharmaceutical scientist (Figure 1)**. These members require regular contact as they are directly dependent on each other. Frequent subteam meetings need to be held to ensure a continuous flow of information on the project. Finally, the more distant members to the BA scientist, such as the safety expert/toxicology leader, translational medicine representative and the clinical pharmacologist, can have an impact on BA activities before the start of the toxicokinetic studies and the first clinical study.

BA strategy

One of the first steps is to set-up a **bioanalytical strategy** to define the type and number of assays required to establish the pharmacokinetic–pharmacodynamic (PK–PD) relationship from early preclinical

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Overview

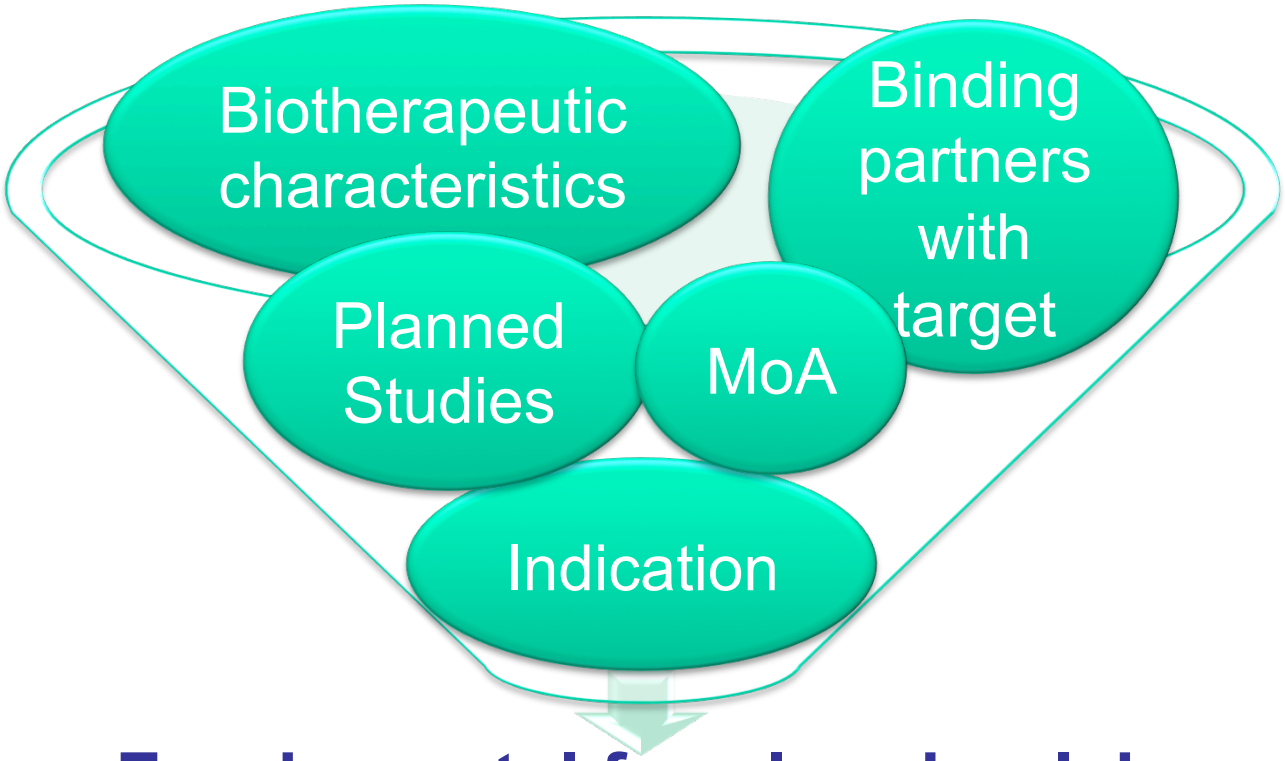
Bioanalytical Strategy

Interaction with Stakeholders

Assay Development and Sample Analysis to Generate Meaningful Data

Bioanalytical (BA) Strategy

- Defines the key methods required to understand drug disposition from early preclinical through to clinical phases (PK, PD, IG)



Fundamental for planning lab activities and to assign resources

Stakeholders – Key Partners

Pharmacokineticist

Biopharmaceutical Scientist

Disease Area Project lead

Safety expert / Toxicologist

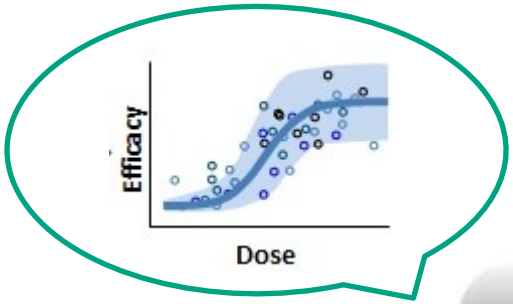
Translation medicine

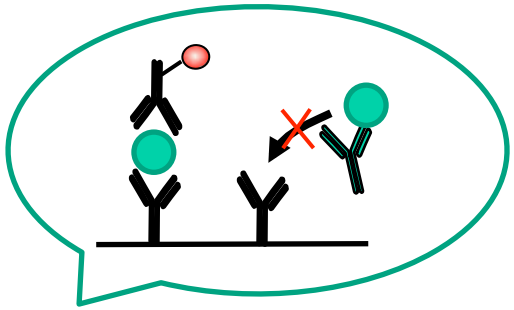
Data management
QA, documentation

EBF

Interaction with Pharmacokineticist

- Pharmacokineticist plans studies to better understand biotherapeutic drug disposition and PK-PD relationship
- Bioanalyst designs and suggests assay format alternatives





Interaction with Pharmacokineticist

- Important factors:
  - Analyte form: free vs. complexed vs. total
  - Assay format
  - Sensitivity (driven by dosing)
  - Assay technology
  - Species, matrix, route of administration
  - Analyte binding partners, interfering proteins

Interaction with Disease Area Project Lead

- Mode of action of target and biotherapeutic
- Baseline levels of target
- Target turnover, expression
- Analyte form present in matrix (e.g. dimers, complex)
- Interfering substances in matrix
- Receptor shedding
- Binding partners
- Available assays?

Interaction with Biopharmaceutical Scientist

- BA needs to understand the nature of the biotherapeutic to develop an adequate LBA!
- Information on physicochemical and biological characteristics of the biotherapeutic
  - Construct/structure
  - Binding affinity for target
  - Purity, aggregation
  - Formulation
  - Concentration
- Choice of assay reagents is key to performance of assay
  - Support in assay reagent production
  - Availability of reagents?

Sample Analysis

- Rapidly measure variety of Bx candidates
- Test functionality of assay with real samples

- GLP regulated
- Validation
- QA
- Documentation
- Outsourced?

- GCP regulated
- QA
- Documentation
- Data management
- Clinical team
- Clinical sites
- Central labs
- Outsourced?

Data Interpretation

- Seeing the big picture
- Impact on data:
  - ADA/target protein can affect PK profile
  - Biotherapeutic/target can affect ADA measurements
  - Biotherapeutic can affect target measurements
- Crucial to get input from bioanalyst who understands assay performance

Inform and be informed!

Regular crossfunctional and **iterative communication** of all involved parties is required for successful support of project milestones

Future Perspective

- New biotherapeutic formats
  - Higher demands for analyte form analysis
  - Increasing number of assays per projects
- New technologies
- Strong trend towards point-of-care testing
- Acceleration of drug development
- Beneficial to the community in setting expectations for BA scientist and partner line roles

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