Outsourcing and Assay Transfer Strategies for Biologics Programs

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Introduction

Outsourcing is now fully integrated in many different industrial areas.

Within the Pharma companies, bioanalytical assay transfers are an integrated step of the life cycle of an analytical method.

The strategy and processes discussed here applied to:

- Large molecules bioanalytics
- PK, PD (target) and Immunogenicity bioanalytical methods
    - ➢ Complex methods, usually less robust than physico-chemical methods
    - ➢ Assays not commercially available (require the availability of the therapeutic molecule)

Agenda

- Appropriate Outsourcing Strategy
- CRO selection
- Bioanalytical Method Transfer
- Monitoring
- Do / Do Not
- Conclusion

How to set up the appropriate outsourcing strategy?

- Do not consider outsourcing as a case by case solution and ensure you have a strategy in place

- Key points to consider to get a realistic and efficient model:

  - The best outsourcing strategy does not exist
  - It must fit your needs
  - Your model must be clearly defined
  - Your model should be as easy as possible

How to define your needs?

The key critical criteria

Most critical milestones for a project within your organization?

✓ When to outsource

Gap Analysis (internal resource, expertise, skills, ...)

✓ What to outsource

Risk identification

✓ Where and when to define a plan B

Risk / Benefit assessment

✓ When and What to outsource

Estimation of the required flexibility

✓ What to outsource

Large CRO portfolio vs preferred vendors

✓ How to manage the collaborations/partnerships

✓ How to organize the monitoring

Accurate estimation of the related internal processes

✓ How to organize the monitoring

Evaluate the required monitoring

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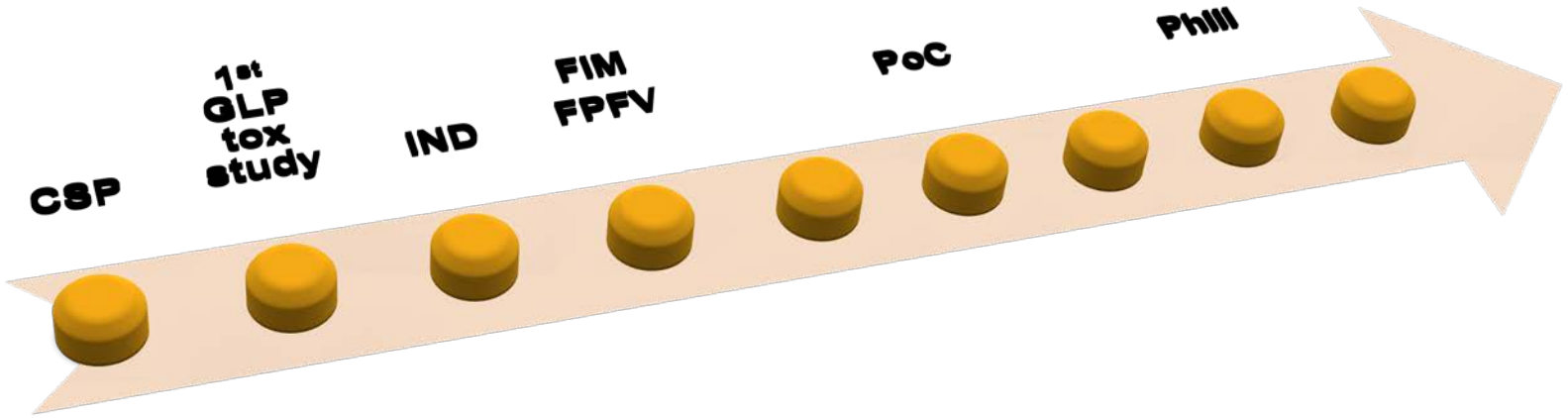

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CRO selection criteria

Well defined requirements

- Review of commonly available external resource and expertise. Check if this matches with the pre-defined needs.
- CRO selection process:

  Set up the minimum requirements (e.g. GLP certification, compatible software or database systems, critical size, ...)

  RFI can help (first time you outsource, looking for new technologies)

  Don’t accept compromise during the selection phase

  MEET with the CRO and VISIT their facility (involve QA), CLARIFY any unclear aspect

  Whenever possible “test” the new CRO with a pilot project before taking the final decision

- Specific requirements for exceptional cases (e.g. specific technologies (niche)) should be defined in advance and CRO identified
- New technologies as well as new compounds (novel constructs) require a periodic review of the CRO selection criteria (every 1-2 years)
- Anticipate future needs by at least 9-12 months

Method Transfer

Thorough sharing

- Standardized Assay Transfer process:
  - Define each step and when it should start (initiation of the contract, sharing project background and then detailed documentation, start of the first lab experiments, ...)
  - Number of tests to be done, number of analysts to be involved
  - Pre-defined acceptance criteria
  - Pre-defined documentation and information to be available from internal labs (level of details to be provided), by when
  - Kick-off meeting:
    - **provide** maximum of information (including the weaknesses of the method!)
    - **share** expectations
    - set up **common goals**
    - define and **assign clear roles**
    - Clarify all CRO questions
    - **Agree** on timelines, regular TCs (weekly)
  - Plan for sponsor analyst visit and “assay demo”

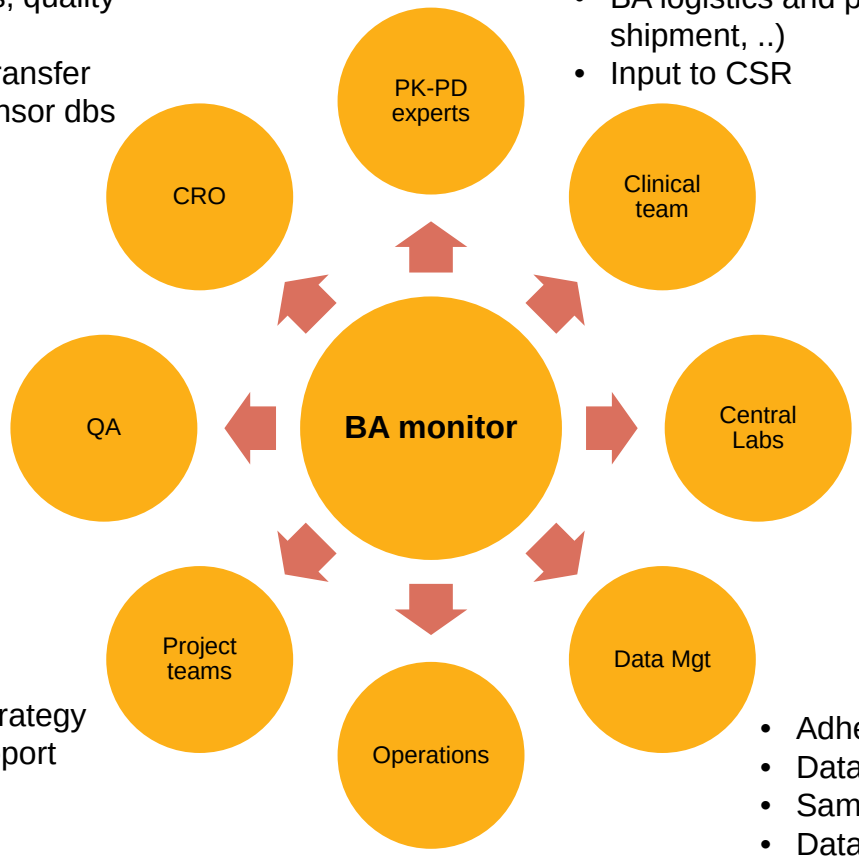
Monitoring of outsourced Bioanalytical activities

Do not underestimate the function

The ultimate responsibility for quality and integrity of the data resides with the Sponsor (ICH E6)

CRO monitoring:
- Adherence to timelines, quality requirements
- Reconciliation / Data transfer
- Data import in the sponsor dbs
- Report review

- Input to Study Protocol, and other clinical doc
- BA logistics and planning (sample labeling, sample shipment, ..)
- Input to CSR



- CRO audits
- Adherence to the Sponsor requirements

- Adherence to the sponsor standards
- BA logistics and planning (sample storage, sample listing, sample shipments, ...)
- Reconciliation

- Development strategy
- Submission support

- Adherence to the sponsor standards
- Data Transfer Specifications
- Sample reconciliation
- Data extraction / integration in the CDB

- Contracts with the CROs
- Invoice endorsement

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DO / DO NOT

DO	DO NOT
Do communicate. Be open, clear, transparent.	Do not underestimate CRO expertise (CROs are much more exposed to other external expertise and opinions).
Do anticipate. Discuss the project as earlier as possible with the CRO.	Do not hide any weakness / complexity of the method to be transferred.
Make sure the differences between the 2 labs are fully identified/understood (technical, operational, cultural, ...)	do not wait to discuss issue.
Ensure non commercial reagent early supply and continuity.	Do not underestimate the required monitoring to get a successful method transfer.
Ensure solved issues go through a closing process.	Do not accept blaming.
Keep in mind outsourcing must be a win-win collaboration. Both parties have the same goals. Build mutual trust.	
Ask for regular feedback (on methods, coordination processes (sample shipment, DM,..) monitoring processes, etc).	
Meet F2F at least yearly.	

Take home message

Technical method transfer difficulties are well recognized for large molecule bioanalytics

For a successful Assay Transfer ensure the technical difficulties are “compensated” by key not technical related aspects:

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