Continued Strides to "Get it Right"—Further Tales of True Collaboration in Bioanalysis in the AstraZeneca-Covance Laboratory Partnership

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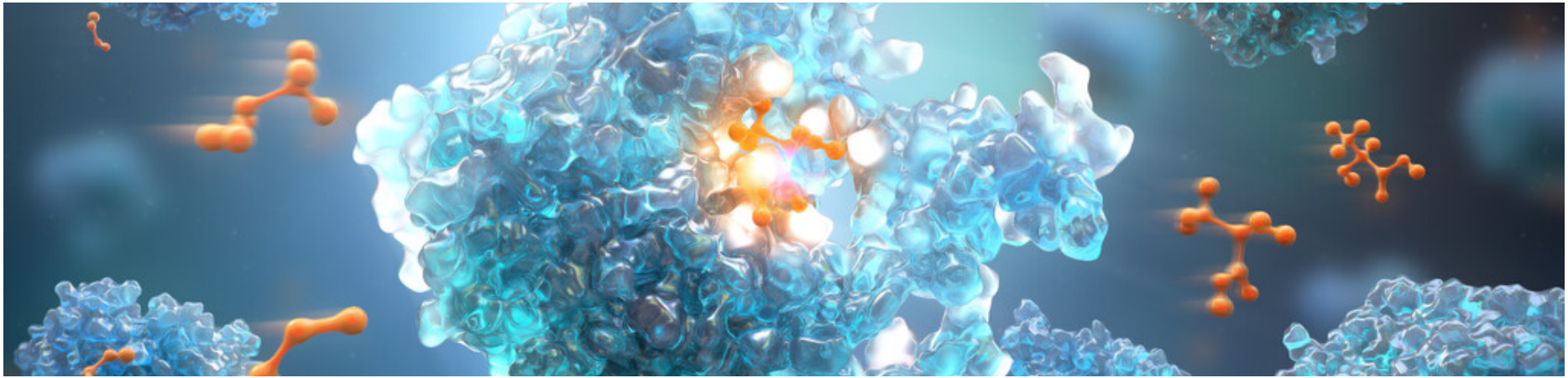


Introduction

Pre Partnership years

- Background
- Drivers for change

Bioanalysis in Partnership

- Early years and implementation
- Clinical Bioanalysis Alliance (CBioA) 2011
- Partnership development

Background: AstraZeneca's early CRO journey

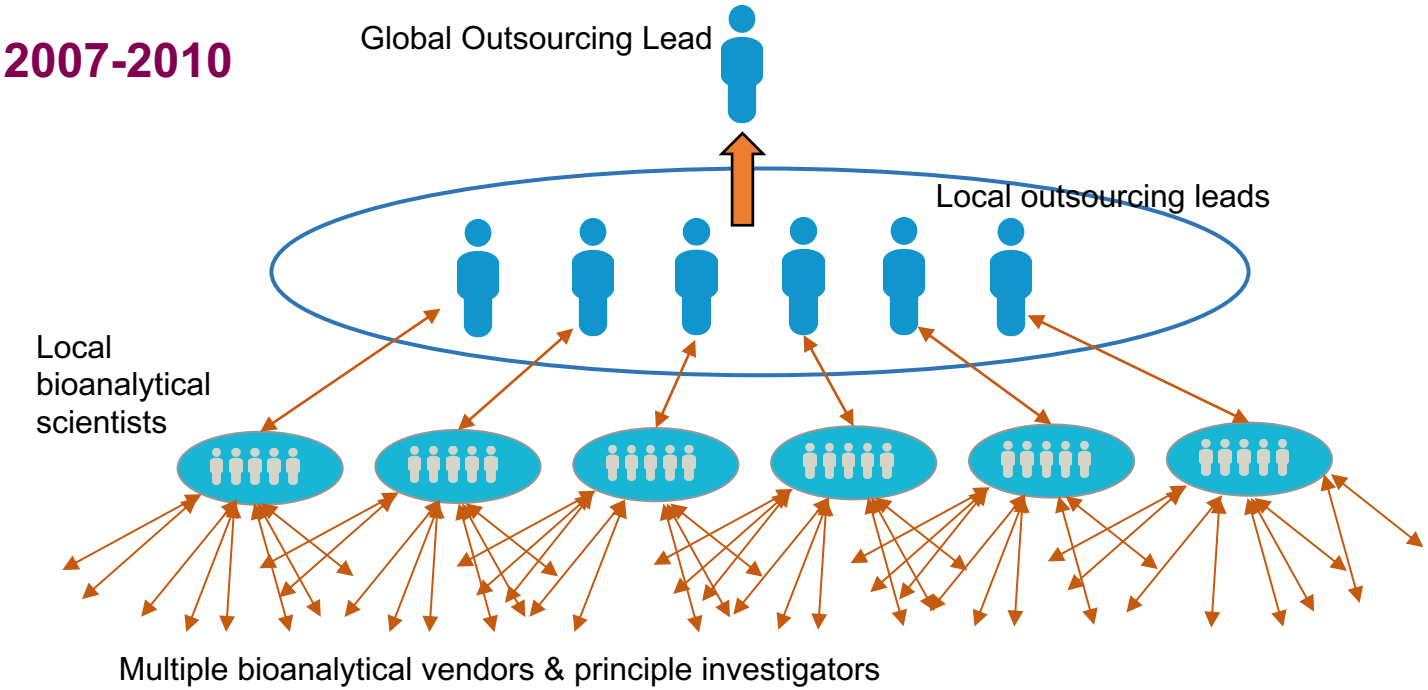
Pre 2007

- Small molecule bioanalysis work was supported by six research sites within AZ (US, UK and Swe)
  - In-house support and outsourced to CROs, tactical delivery
  - Each AZ research site set its own outsourcing strategy
  - Multiple outsourcing models with global and local CROs (>30 CROs)

2007-2010

- A more unified outsourcing model for small molecule bioanalysis
- Global harmonisation and efficiency, more strategic delivery
- Governance process, Global and Local Outsourcing Leads
- Limited number of preferred providers selected (~10 CROs in EU/US)
- 4 out of 6 AZ research sites closed
- Economic challenges

Background AstraZeneca's bioA delivery



Background: a need for change

AZ workstream formed

Evaluate and identify a strategic alliance partner for small molecule clinical bioanalyis globally (primarily LC-MS/MS based)

- ❑ Scientific capability
- ❑ Capacity requirements, company size
- ❑ Strong regulatory compliance
- ❑ Global footprint (EU/US/China)
- ❑ Experienced project management support
- ❑ ’Partnering’ mindset and behaviour

Clinical Bioanalysis Alliance (CBioA) 2011

The partnership was formed to drive efficiency and harmonisation

- Trusted collaboration
- Joint scientific excellence
- Improved competiveness
- Efficient Operating Model

Clinical Bioanalysis Alliance - Early Years
Business as usual

Foundational activities

- Structure
- Roles and responsibilities

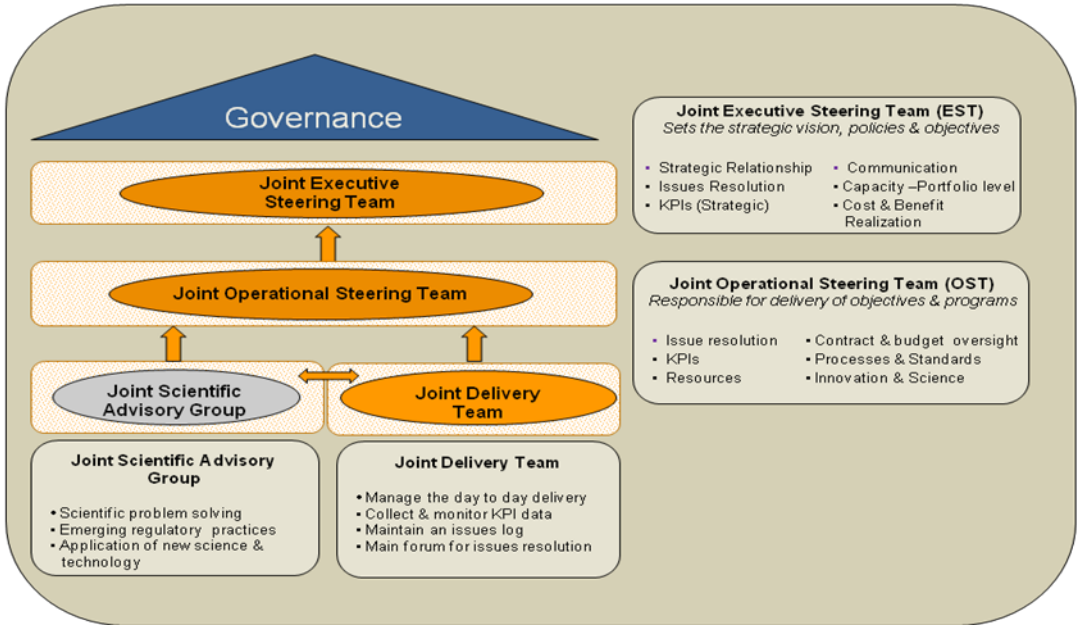
Project activities

- Method transfers and implementation
- Alignment of processes

People

- Training and education
- Communication

Governance


Governance
Joint Executive Steering Team
Joint Operational Steering Team
Joint Scientific Advisory Group
Joint Delivery Team
Joint Executive Steering Team (EST)
Sets the strategic vision, policies & objectives
Strategic Relationship
Issues Resolution
KPIs (Strategic)
Communication
Capacity –Portfolio level
Cost & Benefit Realization
Joint Operational Steering Team (OST)
Responsible for delivery of objectives & programs
Issue resolution
KPIs
Resources
Contract & budget oversight
Processes & Standards
Innovation & Science
Joint Scientific Advisory Group
Scientific problem solving
Emerging regulatory practices
Application of new science & technology
Joint Delivery Team
Manage the day to day delivery
Collect & monitor KPI data
Maintain an issues log
Main forum for issues resolution

Roles & Responsibilities, delivery team

The Covance Program Manager role is accountable for the operational and scientific BioA delivery at a ***study level*** (LC-MS bioanalysis)

Typically the PM represents Bioanalysis at a study level:

- Responsible for bioanalysis, sitting on AZ clinical study teams, covering the entire bioanalytical lifecycle from CSP development to study execution and reporting
- Ensure that the appropriate regulatory and scientific requirements for bioanalysis are implemented within AZ study teams
- Ensure on-going compliance with standards and templates
- Represent AZ within Covance

The AZ Clinical Bioanalytical Scientist is accountable for the scientific BioA strategy and delivery at a ***program level***.

May not be visible on a study but are there for:

- New/updated assay requests
- Escalation/Feedback, Any analytical questions & trouble shooting
- Oversight, ensure high quality and on-time delivery of programs
- Regulatory submission authoring support (NDA/MAA, queries etc)
- Represent Covance within AZ

Scientific collaboration

Scientific advisory group and science forum with representatives from both companies

- Scientific guidance
- Support joint publications
- Proactively evaluate portfolio technology
- Encourage direct communication scientist to scientist
- Access to much larger bioanalytical scientist pool

Shared partnership benefits

- Line of sight of entire AZ portfolio
  - Aids capacity planning
- Process efficiency
  - Global Covance SOPs and templates
- Clearly defined roles and responsibilities, RACI
- Quality and continuous improvement
- Standardised commercial process-straight to PO process
- Two-way/reverse KPIs
- Resource savings
- Collaborative science

Example: Scientific Collaboration

Background

The development and validation of the simultaneous assay for determining concentrations of a drug and two metabolites in pharmacokinetic samples had been completed in spiked samples, to be used in upcoming FTIM study

Challenges

Data from the analysis of samples from preclinical toxicology studies identified a drug related chromatographic peak with the potential to impact the quantification for one of the active metabolites

Results

The regular knowledge transfer teams (preclinical/clinical, AZ/Covance) highlighted this potential issue and Covance were able to quickly redevelop and validate a revised assay to reduce/eliminate the potential impact of the interferent peak on quantification of the active metabolite. The assay was successfully used in the FTIM study

Successes

Early, open engagement ensured the assay did not fail and delay critical decisions for the study and project team. It illustrates the importance of direct communication scientist to scientist, sharing experiences, best practice and even samples in this case - in an open and collaborative way

Example: Visability of Portfolio

Background

Compound in development required new formulation suitable of moving into late stage development

A number of studies were pending the decision on the solid dosage form

Plan and budget were pending the results of Relative BA PK data

Challenges

Study required a relative bioavailability arm with quick turnaround data in order to determine if formulation was suitable or if additional data was required

Study requirements exceeded alliance agreement for quick turnaround studies

Last PK samples for interim analysis needed to be received before Christmas holiday; analysis had to be performed between Christmas and New Year Holiday season

Successes

Early engagement via alliance allowed for advanced notification of this study and strategic planning with site operations within Covance

Advanced planning with Operations enabled adequate staffing over the holiday period

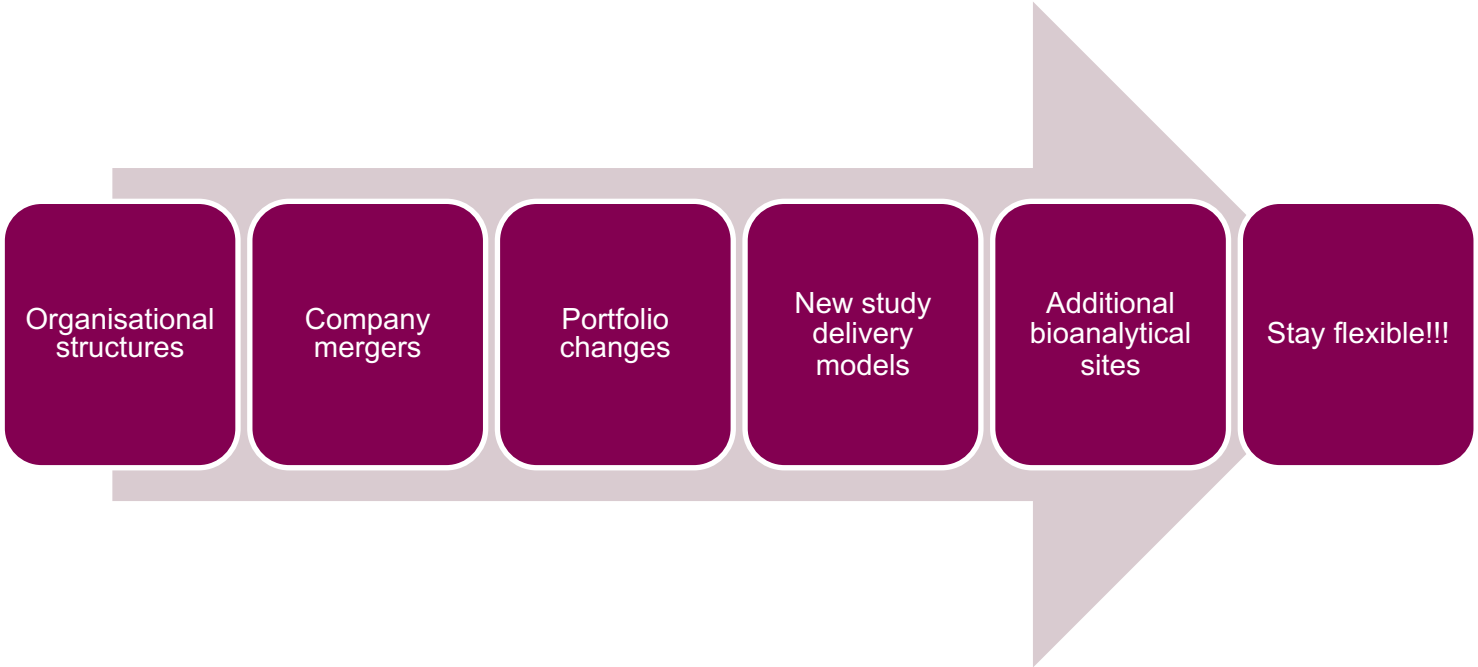
Results

Data delivered on time

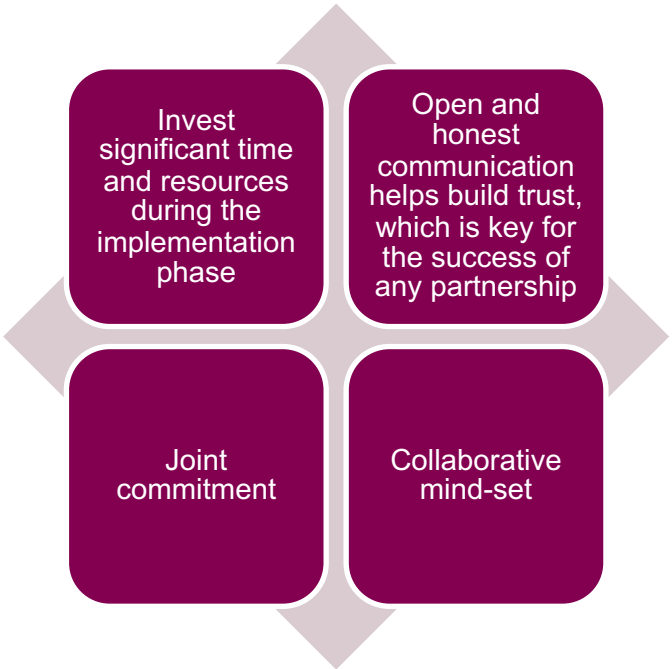
New dosage formulation identified to enable future clinical studies

AZ management endorsed future clinical plans

Partnership development



Conclusion: Key for success



Any Questions?

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Confidentiality Notice