CRO Model in the Changing R&D World

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Discussion Topics

- Pressures in Research and Development
- Changes to the Current Environment
- Changes in the CRO Model
- Effect on the Investigative Site
- Changes to the role of the Monitor (Risk Based Approach)
- Additional things to consider
Drug Development Today has:

**Regulatory Pressures:**
- Complexity
- Approval Times
- Intense FDA/EMA Scrutiny
- Ethical Concerns

**Financial Pressures:**
- Costs
- Capital Constraints
- Demand for Value
- Payer Pressure
- ROI

**Development Pressures:**
- Stakeholders Scrutiny
- Patient Access Demands
- Commercialization Stakeholders
- R&D Timelines
- Productivity
- Patent Cliff
- Product Pipelines

**HIGH PRICE TAG:** Current estimates for bringing a drug to market in the U.S. and E.U. exceed $1 billion. *Health Economics, February 2010*
Environment Changes

Reacting to the Pressures and Current State of Technology

• Need to change the R&D Model to bring costs down
  > Pharma moving to a more streamlined infrastructure leveraging CROs in different ways
    - Programmatic Outsourcing – Using CROs for the execution expertise to drive efficiencies in the R&D space
    - Functional Outsourcing – Using CROs as a flexible model for staffing of trials. Mainly partnering in the hands and feet space (data management, Clinical Monitoring, etc)
  > Access to Data driving decision making processes
    - Using Data to drive drug development plans
    - Immediate access to data real time to decrease the R&D risk by cutting programs earlier, running adaptive trials, etc
    - Country and site selection becoming an evidence based approach which drives the timelines and milestones for project/program execution
  > EHR, EDC, Data visualization tools leveraged to keep on site monitoring to a targeted focused visit
    - Moving more work effort in house to a lower cost resource
    - Decrease overall trial costs (on site monitoring ~60-70% of labor budget of a trial)
CRO Model Changes

Reacting to the Changing Market Pressures

<table>
<thead>
<tr>
<th>Traditional Project/Program Outsourcing</th>
<th>Functional Service Providers</th>
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<tbody>
<tr>
<td>• Risk Share Models</td>
<td>• Commoditizing the CRO traditional project model</td>
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<tr>
<td>&gt; ‘Skin in the Game’</td>
<td>• More control moving back into the Pharma company (Project Leadership)</td>
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<tr>
<td>&gt; Country/Site Decision</td>
<td>• Silo’d approach (Many vendors)</td>
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<td>• Accountability for Outcomes</td>
<td>&gt; Spreading the risk out across vendors</td>
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<td>&gt; Milestones set and owned by the CRO</td>
<td>&gt; Using best in class vendor for each function</td>
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<td>&gt; Penalty/Incentive programs</td>
<td>&gt; Loosing consistency of process – too many touchpoints</td>
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<td>• Turnkey Program Development</td>
<td>• Driving cost of services down through use of staffing agencies</td>
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<td>&gt; Little to No oversight from Sponsor</td>
<td>&gt; CROs have troubling in the low margin environment but are trying to compete</td>
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<td>&gt; Fixed Budgets</td>
<td>• Maintain control of data (Pharma systems and processes used)</td>
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<td>• Risk Based Monitoring</td>
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<tr>
<td>&gt; Triggered Visits (workload, quality)</td>
<td></td>
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<tr>
<td>&gt; &lt;100% SDV</td>
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<tr>
<td>• Adaptive Trial Design and Execution</td>
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<tr>
<td>• Planning and Design moving to the CRO</td>
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Driving to a lower cost hybrid delivery model
What does this mean for the Investigative Site?
Changing the Investigative Site

\textit{Trial participation becomes driven on performance, patient access, and quality}

- Selection to participate is evidence based
  - Access to the right patient population
  - Experience conducting research with proven staff / resourcing
  - Previous performance as measured by start up, enrollment, patient retention, and overall quality
- Number of sites participating in a trial decreases as the patient enrollment projections and site performance become more predictable
- Process changes as life goes electronic
  - Workload moves from CRO to Investigative Site (data entry)
  - EDC changes based on pharma
  - Number of additional vendors and interactions increase
- Protocol complexity increase
  - Bigger bang for the buck….Pharma trying to answer more questions in one protocol
  - Workload at the investigative site increases as procedures increase
  - Patient recruitment becomes a larger challenge as patients are more difficult to find to meet the more complex protocol
- Expectation for immediate data access and higher quality add additional pressures
What does this mean for the Site Monitor?
Changes to Monitoring

An approach to managing clinical trials optimizes the monitoring strategy for each clinical study by leveraging our knowledge systems, data analytics, clinical study indicators and on-site/centralized monitors to deliver studies with the highest level of quality, patient safety and regulatory compliance.

*Centralized Monitoring consists of clinical operations, data management and medical surveillance.
Quintiles Approach is an Integrated Monitoring Strategy

**Regional CPM/CRS:**
Manage team, issues, trend analysis via Infosario, operational quality

**In-house CRA (iCRA):**
- Manage site documents
- Site supply management
- Consistent site management via Infosario dashboard
- Primary contact for sites – regular interaction
- Site training and structured calls
- Data cleaning support

**On-site CRA:**
- Site selection, initiation, interim and closeout visits
- SDV % adjusted per protocol, linked via EDC platform & Infosario
- Agrees Recruitment Targets in the Site Recruitment Action Plan
- SDV, ICF review and Drug Accountability

**Recruitment/Retention**

**LOW**

**RISK**

**HIGH**

**Site**
Monitoring Triggers

Workload and Risk based Triggers for Risk Based Monitoring
Predetermined Upfront Monitoring Plan

- In current practice, many clinical monitoring plans require site visits to take place based on cycle times.
- Models have become more sophisticated over time with site visits being pooled for use across the study and scheduled based on work volume triggers.

Triggers may be work volume based or risk management based.

Triggers are defined based on specific protocol features and requirements.

This model allows for a more dynamic management of monitoring resources by scheduling visits based upon an algorithm of pre-determined “triggers” that initiate a monitoring visit only when there is a need.
**Benefits Resulting from Quintiles Risk Based Monitoring Model**

<table>
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<tr>
<th>Benefit</th>
<th>Description</th>
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<tr>
<td>CRA Productivity</td>
<td>More frequent interaction, ensures sites are better prepared for CRA visits, and CRA time on-site may be decreased</td>
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<tr>
<td>Data Quality</td>
<td>Increased frequency of site contact, including on demand access to PCC iCRAs, leads to fewer data queries</td>
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<tr>
<td>Time to Data Lock</td>
<td>The addition of centralized monitoring in between CRA visits resolves queries on an on-going basis, which can decrease time to data lock</td>
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<tr>
<td>Site Relationships</td>
<td>Frequent contact and on-demand iCRA support streamlines site workflow, resulting in a positive site relationship</td>
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<tr>
<td>Cost Efficiencies</td>
<td>Proven, regulatory sound approach to a blended monitoring model results in cost efficiencies</td>
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What do sites need to consider in this changing environment?
## Sites should consider

<table>
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<tbody>
<tr>
<td><strong>Best in Class Recruitment</strong></td>
<td>Innovative recruitment &amp; retention techniques. Reliable performance. Robust feasibility to predict outcome</td>
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<tr>
<td><strong>Metrics</strong></td>
<td>Track and demonstrate performance from CDA to close out &amp; proactively share with CROs &amp; sponsors</td>
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<tr>
<td><strong>Standard Processes</strong></td>
<td>Developing written SOPs showcases standards of clinical research activities and commitment to compliance</td>
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<tr>
<td><strong>Flexible Resources</strong></td>
<td>Flexible resourcing will allow for innovative administrative and recruitment expertise &amp; help staff complex design trials. Robust Training programs ensures integrity of trial</td>
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<tr>
<td><strong>Building Relationships</strong></td>
<td>Proactively seek out relationships with Pharma &amp; CROs to market capabilities &amp; performance. Link with specialists for additional trial opportunities</td>
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<tr>
<td><strong>Proactively Manage Quality</strong></td>
<td>Ensure high quality outcomes through internal QA review. Conduct periodic process assessments to ensure best practices</td>
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How is the CRO model changing to support our sites?
2013 Operating Principles

Focus on Productivity, Delivery, Quality (PDQ)
Introducing Site Management

Our Mission - Best in class site performance

Build Relationships
✓ Tactical to Transformative
✓ Advocacy
✓ Increased access to trials

Provide Operational Expertise
✓ Advice and tools to improve site’s recruitment
✓ Sharing best practices to streamline processes at the site
✓ Sharing of metrics to compare performance to others

Educate
✓ Help Train the investigators of tomorrow
✓ Insight into industry pipeline for key indications

Our Commitment:
✓ High quality customer service around the clock
Partnership, Ownership, Vision

Through integration, commitment, openness, and collaboration.

‘Success is proportionate to the mutual willingness to learn, develop, and deliver across all aspects of clinical trials – from feasibility to database lock WE can do things better, faster, and more efficiently TOGETHER’
Questions?