Facilitated Clinical Reviews –
An Approach For Better Quality Protocols

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Background

● Focus on Quality Protocols:
  – Subject Safety
  – Right Subjects
  – Data Integrity / Overall Trial Quality
  – Resources (across stakeholders)

● Why are they so complex?
  – Experience
  – Time Constraints
  – Risk Aversion
  – Lack of Downstream Visibility

● Opportunity to Streamline, Improve overall Quality and Minimize Risks
Incorporate Peer Review as part of the protocol process

1. Opportunity to challenge thinking
2. Incorporates best practice considerations
Facilitated Review Objectives – Quality and Efficiency

- Deliver Results for Product Development Strategy
- Reduce unnecessary complexity / mitigate risks
- Prevent avoidable protocol amendments
- Reduced effort, errors and burden
  - Subjects, sites, trial oversight
  - Training, data collection and quality activities
- Increased % of On-time delivery
- Reduced time and expense
Review Format

- Team gather for 3-4 hours
  - Broad functional representation
  - Establish – “safe environment”

- Semi-structured discussion led by trained facilitator
  - Facilitators are experienced drug developers – not involved with team
  - Leads team through discussion, where team engage in dialogue and find answers for themselves

- Planned in advance
  - ~1 month to schedule
  - Conducted when objectives, endpoints, inclusion/exclusion criteria and time & events outlined

- Team accountable for actions
Study Alignment

- Goal of study clear
- Aligned with established Plans
- Objectives and Endpoints

Study Design

- Inc / Exc criteria – rationale for each, clarity of wording
- Time & Events
- Discussion of end product
- Review of data needs
- Investigator feedback

Operational Best Practice

- Data Quality Plan including data review & monitoring
- Site selection criteria
- Recruitment strategies
- Central lab considerations
- Investigator training strategy

Value vs Cost vs Time vs Risk trade-offs
Facilitated Clinical Review Session

- Reduced frequency of ECGs time points without impacting safety monitoring or scientific merit
- Did not collect pharmacokinetic blood samples from every patient – the population PK model would not be compromised
- Reduced full blood haematology and biochemistry monitoring to once per month, while still maintaining liver monitoring at every visit
- Removed one Patient Reported Outcome questionnaire in the absence of wide regulatory acceptance

Reduced cost, patient & site burden

A Changed Attitude to Value Based Decision-Making

- Focus on value-adding training at F2F Investigator Meeting – routine training delivered on-line - drives quality in primary end-point
- Packing drugs into 4 week bottles vs 1 week bottles – reduced complexity for patient at home and Global Supply

Team went on to identify further operational efficiency savings and quality opportunities
FACILITATED CLINICAL REVIEW SESSION

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REDUCED COST, PATIENT & SITE BURDEN

A CHANGED ATTITUDE TO VALUE BASED DECISION-MAKING

- Focus on value-adding training at F2F Investigator Meeting – routine training delivered on-line - drives quality in primary end-point
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TEAM WENT ON TO IDENTIFY FURTHER OPERATIONAL EFFICIENCY SAVINGS AND QUALITY OPPORTUNITIES

“An outsider’s perspective was critical to helping us examine our decisions and our assumptions. Once the facilitators had encouraged us to question our decisions, a whole variety of opportunities opened.”

– Lead for Phase IIb COPD study
Example 2 – Part of Broader Efforts

<table>
<thead>
<tr>
<th>VALUE-BASED STUDY DESIGN</th>
<th>EARLY ENGAGEMENT WITH Central Lab</th>
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<tbody>
<tr>
<td>• Focused Global Health Outcomes endpoints</td>
<td>• Switch from individual tests to IgG panel</td>
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<tr>
<td>• Simplified PD endpoints</td>
<td>• Consulted on PD testing strategy</td>
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<td>• PK sampling from subset vs all patients</td>
<td>• Optimisation of frozen sample shipping</td>
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• Simplified PD endpoints
• PK sampling from subset vs all patients

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IMPROVED ELIGIBILITY, AVOIDING AMENDMENTS, REDUCED PATIENT BURDEN, IMPROVING QUALITY

“It was extremely useful having an extra pair of eyes look over the study with us; myself and the study leader had reviewed the protocol on several occasions streamlining the procedures, yet we still found more as a result of the session.”
GSK Experience to date

- Over 100 Protocols through the Process
- Some initial resistance to external peer review
  - Sessions conducted in the “right” environment
  - Quality facilitator is a must
- Management support / prioritization helps
- Teams going through 2nd time are incorporating lessons
- Significant Benefits and growth of the practice as more examples are shared
Thank You