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**

Facilitated Clinical Review

- 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

Review Format (continued)

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

Example 1

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

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"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

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Example 2 – Part of Broader Efforts

VALUE-BASED STUDY DESIGN

- Focused Global Health Outcomes endpoints
- Simplified PD endpoints
- PK sampling from subset vs all patients

EARLY ENGAGEMENT WITH Central Lab

- Switch from individual tests to IgG panel
- Consulted on PD testing strategy
- Optimisation of frozen sample shipping

FACILITATED STUDY REVIEW SESSION

- Streamlined range of disease and PD markers to limited number of visits
- Clarified, simplified inclusion/exclusion criteria wording

PRE Final Protocol INVESTIGATOR MEETING

- Inclusion/exclusion criteria, prohibited meds, study procedure changes adjusted to reflect local medical practice
- Streamlined patient sampling schedules to ease patient & site burden
- Study-specific training adjusted - improving quality and speeding approval

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

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EARLY ENGAGEMENT WITH Cent... Lab

"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."

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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