Managing Risk in Clinical Development

"Medical Quality by Design"

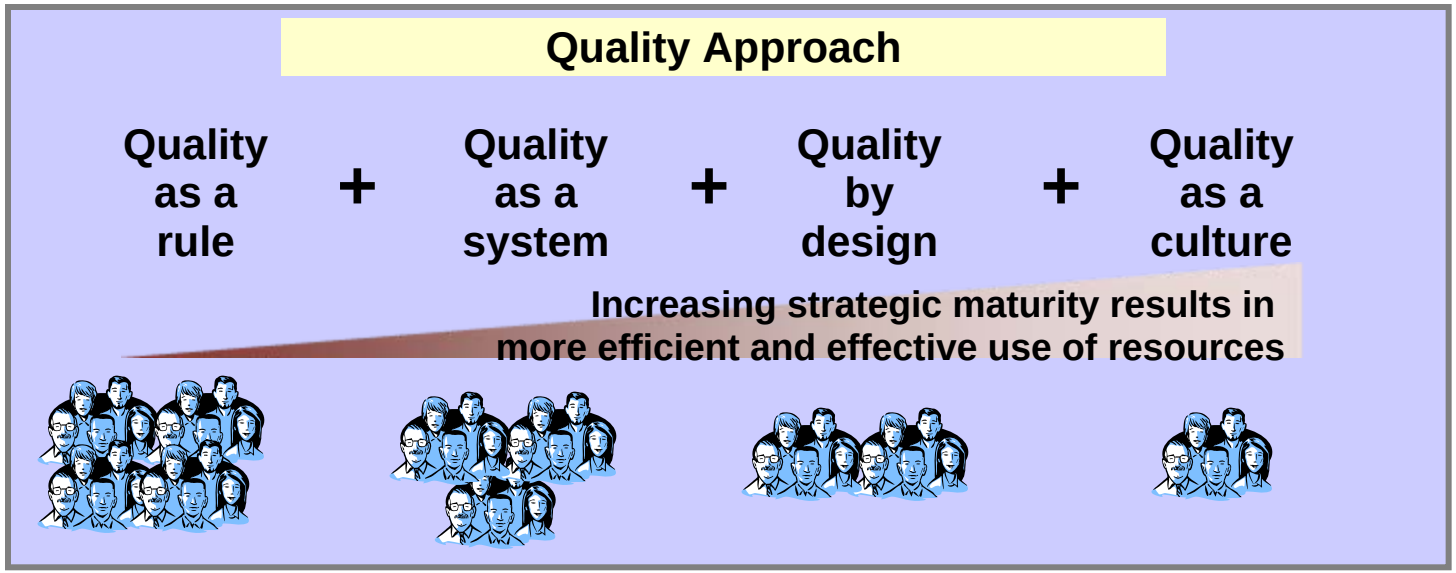
Jeff Kasher

VP Clinical Development, Eli Lilly & Company

11 – 03– 2011

Answers That Matter.

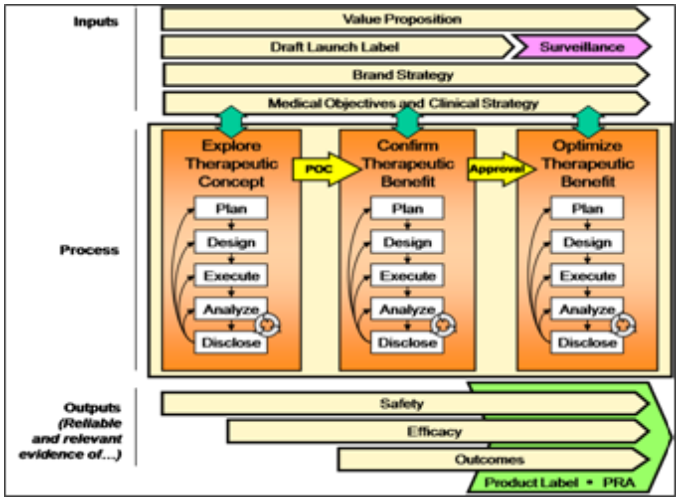
Quality as a Culture



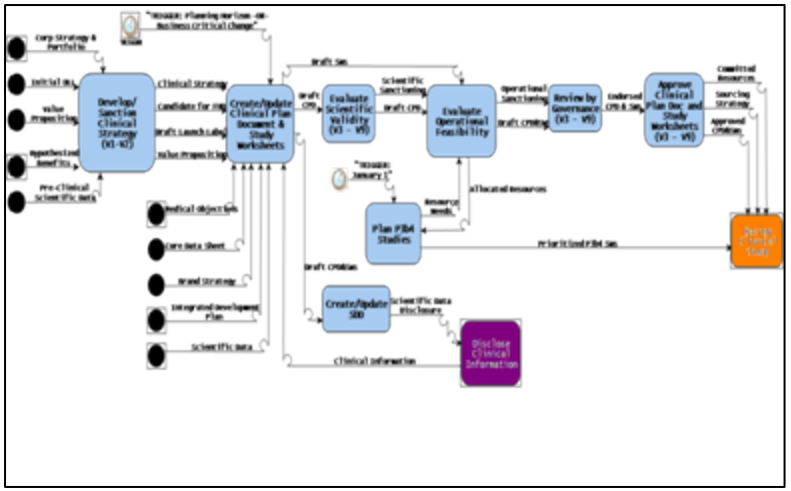
The Road to Quality as a Culture.

Establishing a Quality Foundation

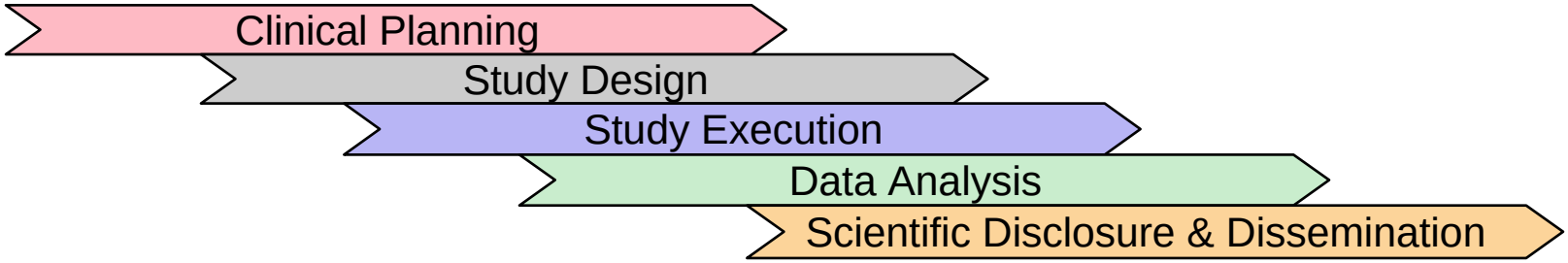
Medical Single Process Map



Business Process Management



Building Quality into Clinical Trials



Clinical Planning
- Approved Clinical Plans
- Medical/Scientific Validity Reviews
- Operational Reviews
- Annual Clinical Plan Reviews
- Chief Medical Officer Oversight

Study Design
- Approved Study Protocols
- Protocol Review Committees
- Change Management

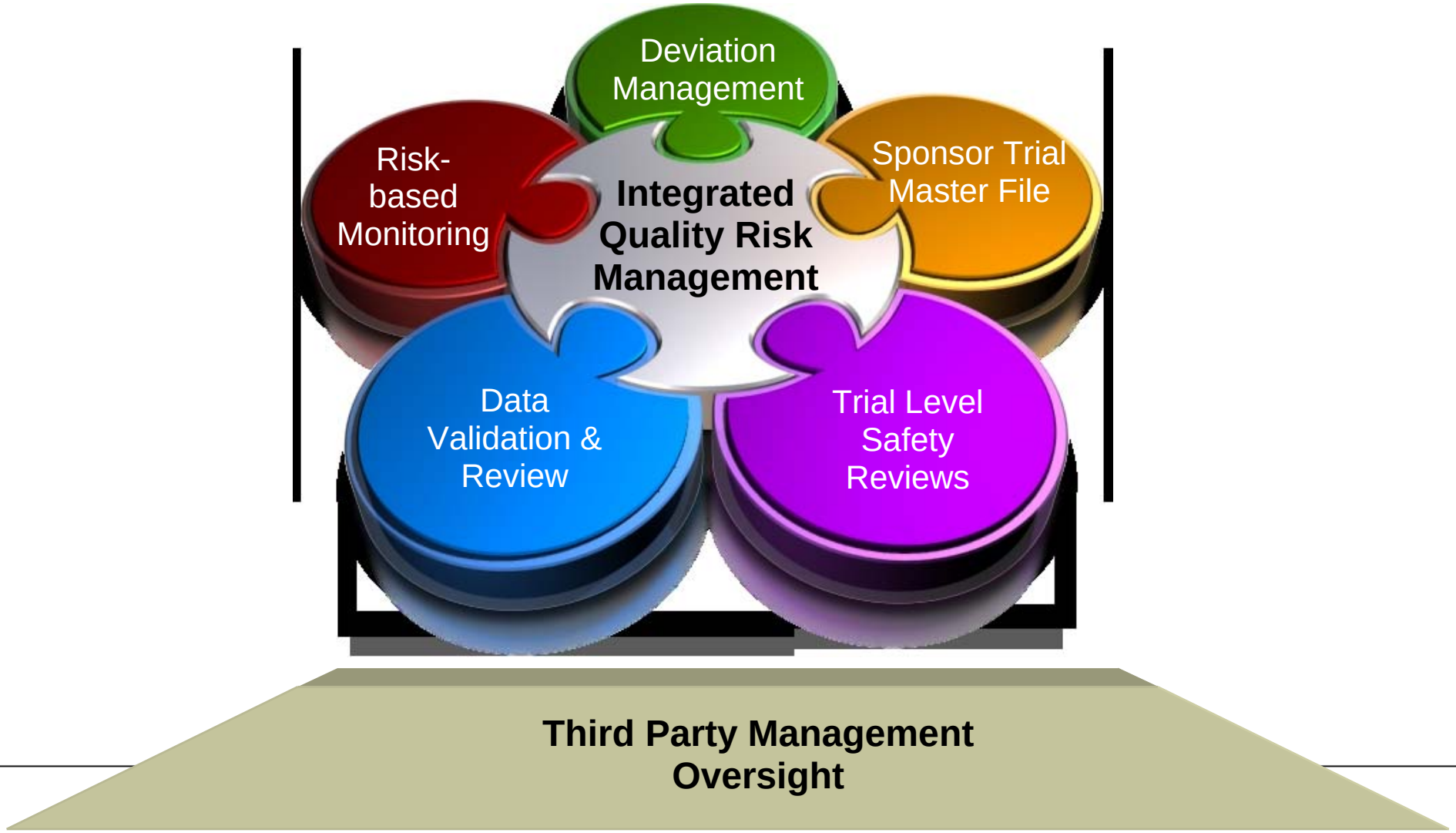
Study Execution
- Investigator Site Selection
- **Risk-based Monitoring Program**

Data Analysis
- Approved Plans of Analysis
- Analysis Program Validation
- Approval of Analysis Output

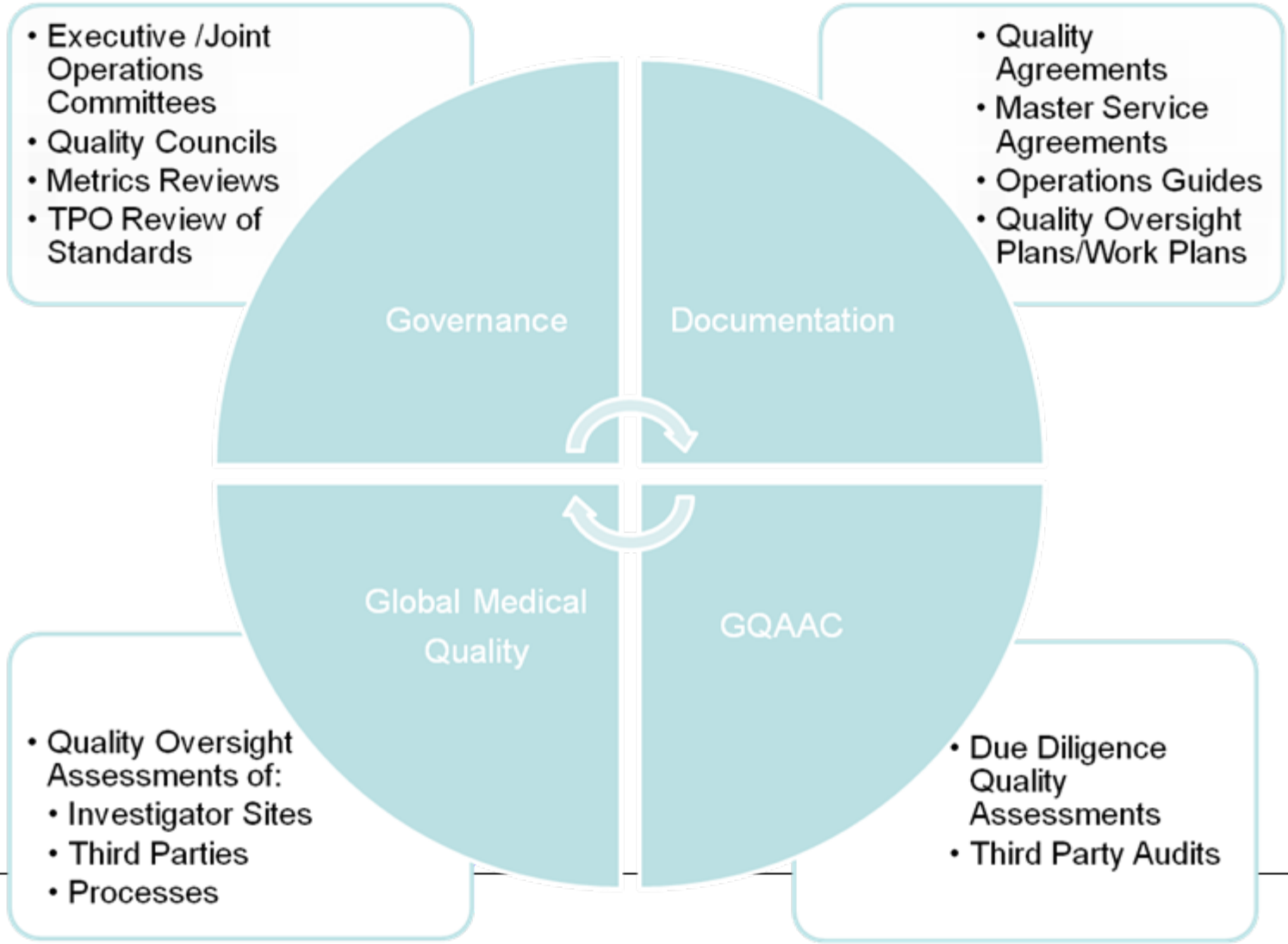
Scientific Disclosure & Dissemination
- Disclosure Approvals

Quality Governance
- Deviation Management
- Quality Plans
- **3rd Party Management Program**
- Trial Master File Periodic Reviews
- Quality Audits & Assessments
- Quality Lead Teams
- Metrics Review

Integrated Quality Risk Management



Oversight of Strategic Third Parties



Quality Oversight Assessment Metrics

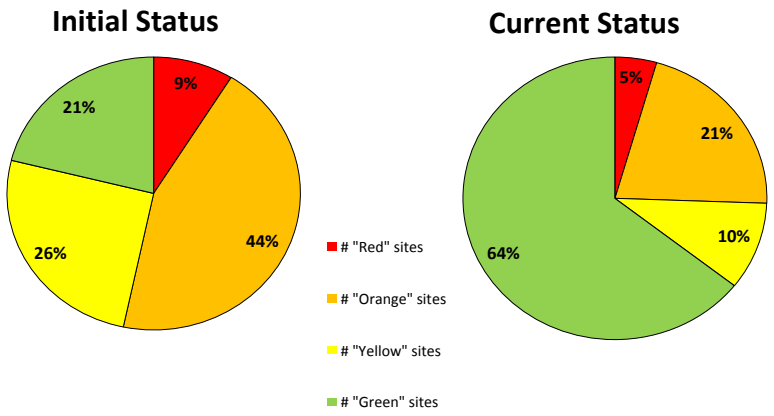
Summary – June 2012

Accomplishments

- 107 assessments have been performed year to date.
  - June 2012: 17 assessment performed globally (no critical observations).
- Trends identified in the following areas (further evaluation and response plan needed):
  - Study Documentation (especially site delegation log not available / inaccurate / incomplete)
  - Monitoring / Issue Resolution (especially issues not identified / escalated and / or resolved appropriately)
  - Training / Personnel Qualification
  - Source Document / Data Accuracy

Improvement Opportunities

- January through May 2012:
  - Of the 8 red sites identified from January through May 2011, 2 sites have moved to orange status and 2 have moved to green status. The remaining 4 red sites remain red.



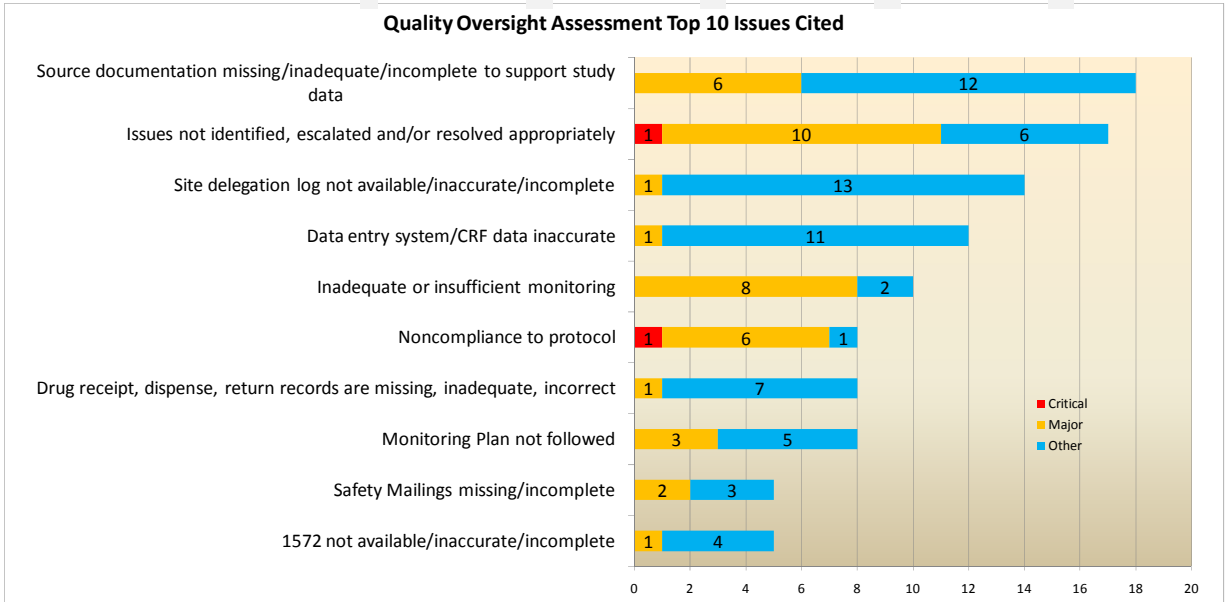
Lilly Answers That Matter.

Strategic Third Party Assessment Metrics
Summary – Q2 2012

Critical Issues
ICD current version not signed and/or signage incomplete
Lack of adequate management control to ensure clinical study services are performed by appropriately qualified personnel and conducted in accordance to defined SOP/guidelines/Clinical Management Plan (CMP)
Issues not identified, escalated and/or resolved appropriately
Noncompliance to protocol

Only assessment findings owned by the TPO are included in the status. Findings owned by Lilly are not included in the TPO assessment summary.

	#1	#2	#3	#4	#5
Number of assessments	19	9	0	1	10
Total number Critical Issues	2	1	0	0	1
Total number Major Issues	53	22	0	1	21
Total number Other issues	134	39	0	0	34
Total Number of issues	189	62	0	1	56



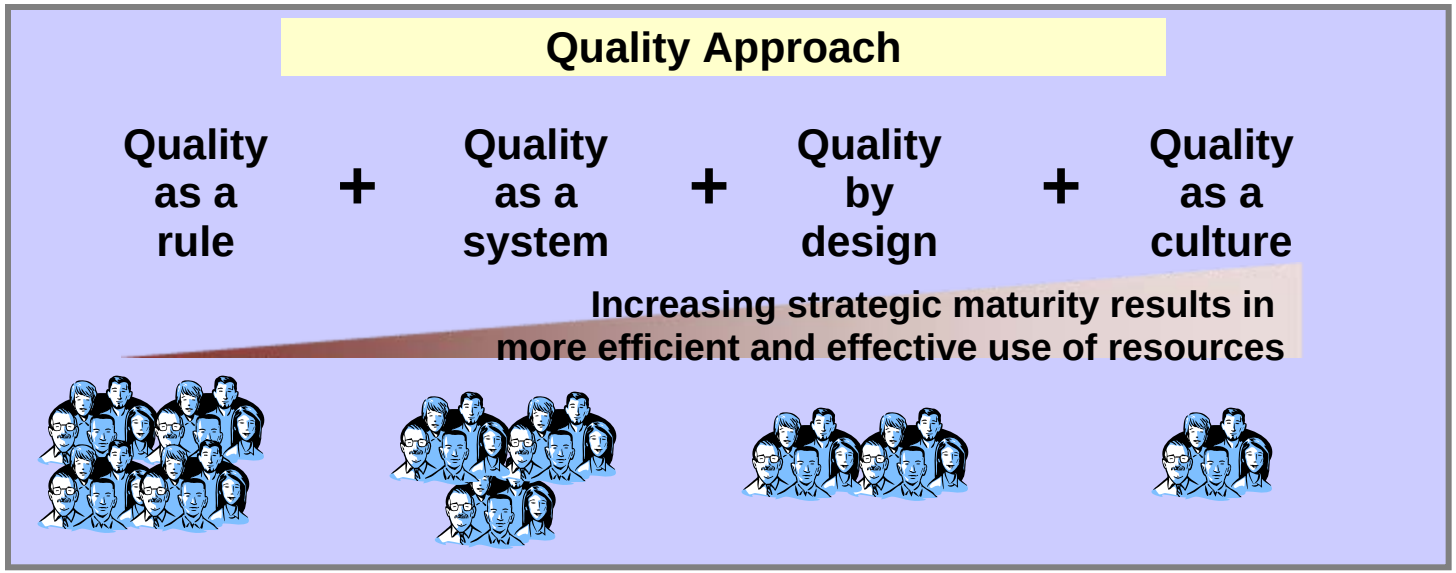
Risk-based Monitoring

Clinical trial monitoring must be driven by: scientific analysis, protocol objectives, and trial data

- Planning: Clinical trial monitoring plan which is based on statistical /scientific data elements in the protocol
  - Prioritization of data and processes critical to data integrity and subject protection
  - Development of adaptive study specific monitoring requirements
- Execution: Ongoing trial monitoring activities include:
  - Traditional on-site monitoring
  - Statistical data monitoring to assess data trends across sites and trials
  - Internal monitoring of key internal processes
- Risk-based monitoring benefits:
  - Enables the proactive identification of areas/sites of risk
  - Establishes the foundation to respond to real-time study data
  - Ultimately ensures that:
    - Clinical data answers the scientific questions/objectives outlined in the protocol
    - Meets regulatory and quality requirements for the safety of study subjects

"Sponsors must be able to answer why they are monitoring what is being monitoring"
– Leslie Ball, MD, Director, Office of Scientific Investigations, FDA

Quality as a Culture



The Road to Quality as a Culture.