Medical Quality by Design

"the journey continues"

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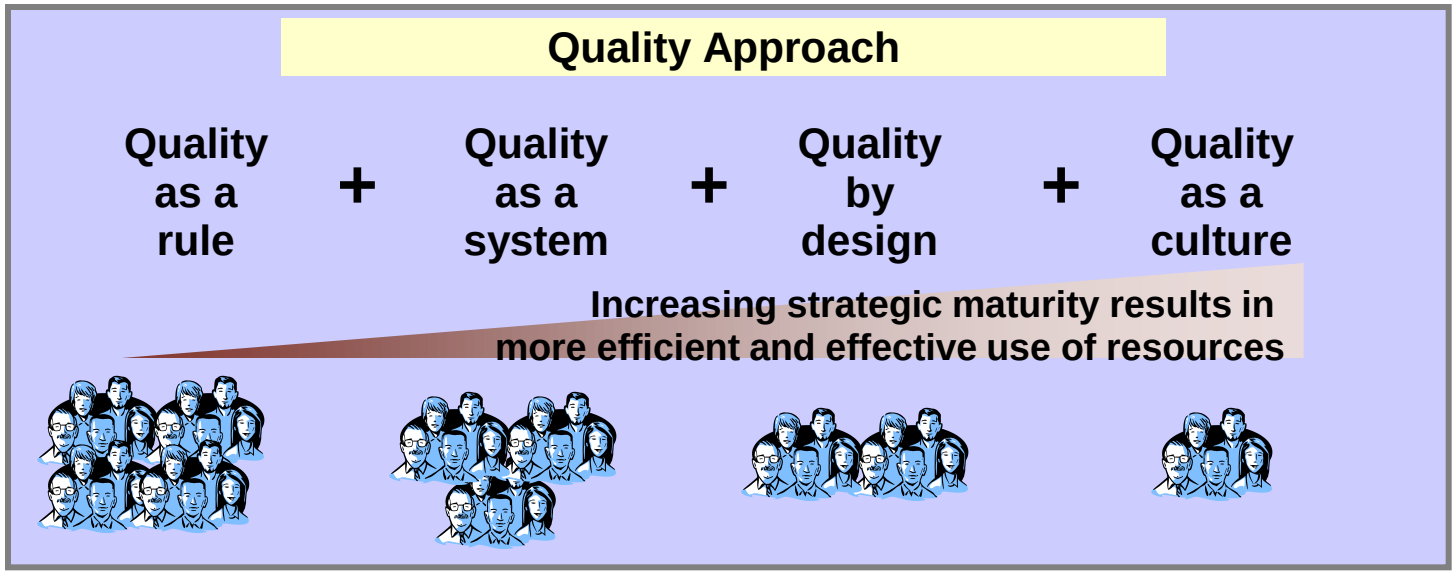
08 – 23 – 2011

Quality as a Culture



The Road to Quality as a Culture.

Vision Statement

The Clinical Development Organization (CDO) will reliably deliver the portfolio with quality, on time, and on budget

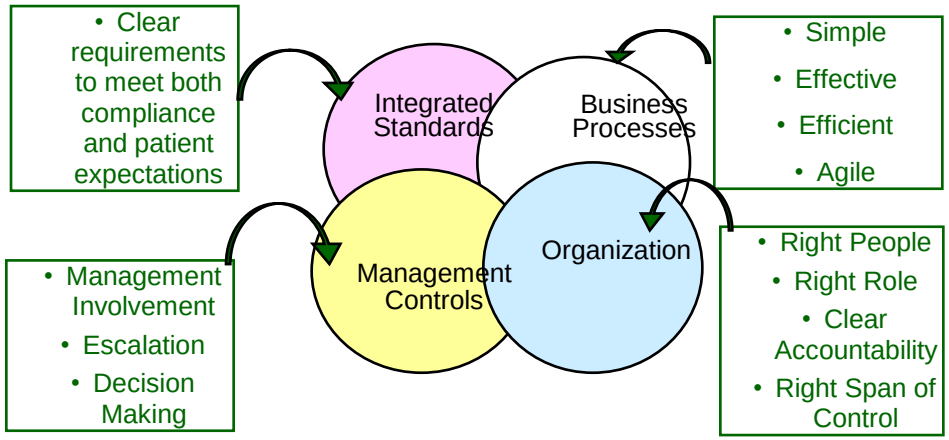
- Critical **processes** are clearly defined and efficient, with single-point accountability for key decisions / process steps
- **Sourcing** and capacity decisions are strategic rather than tactical, and leverage opportunities to increase organizational effectiveness
- Run clinical development with a **business mindset**; measure and track performance with effective metrics
- Clinical **strategy, planning, & execution** activities are tightly linked (clear 'line of sight'). Commitments are made with a full understanding of feasibility

Medical Quality System Redesign

A Single, Integrated Quality System

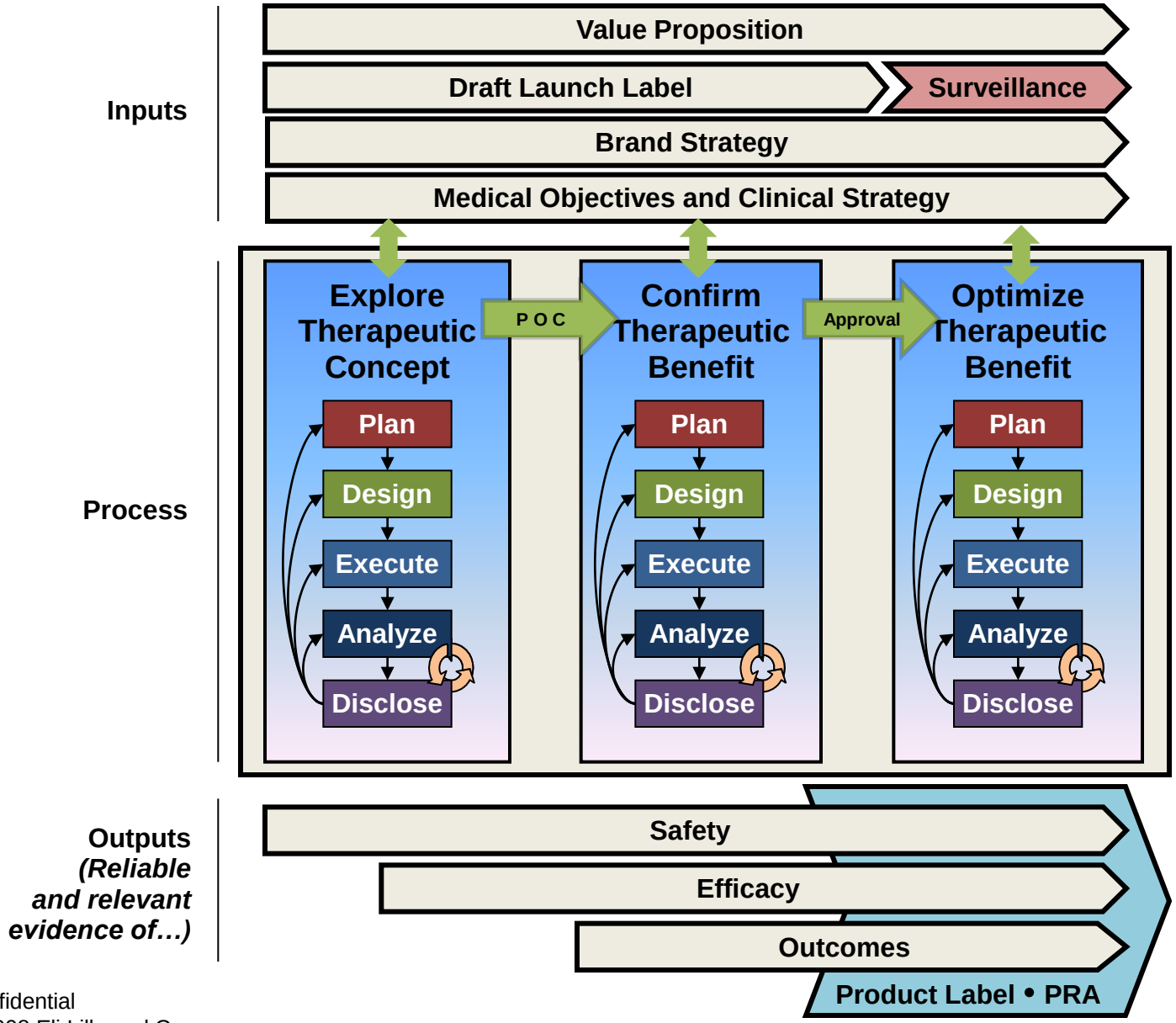
What we've built:

- A streamlined set of global quality system documents (~90% reduction in global documents)
- A comprehensive, process-based approach to support effective implementation - process streamlining, role clarification, and strengthened governance
- Structured to enable FIPNET through requirements applicable internally and externally
- Designed to integrate with other related quality systems (e.g., Lilly Global, Safety, Regulatory, Product Research & Development Quality Systems)



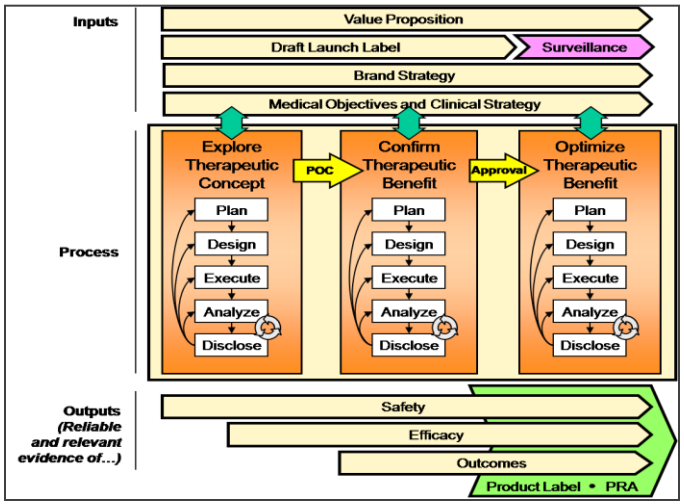
Lilly Answers That Matter.

CDO Single Process Map

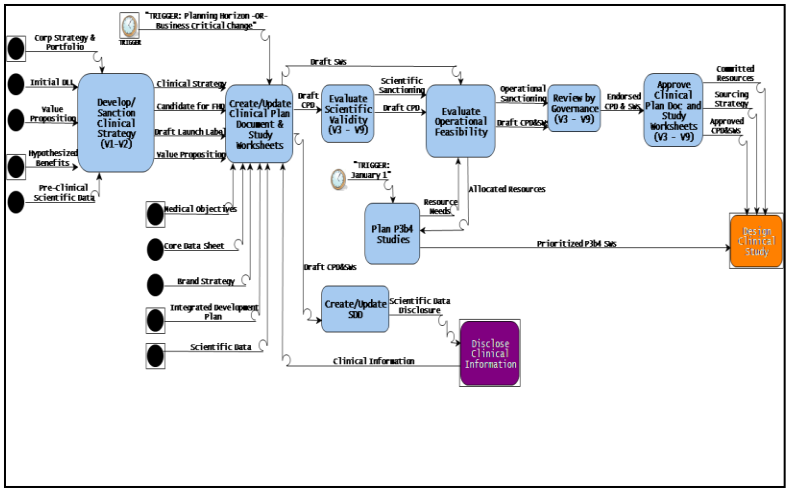


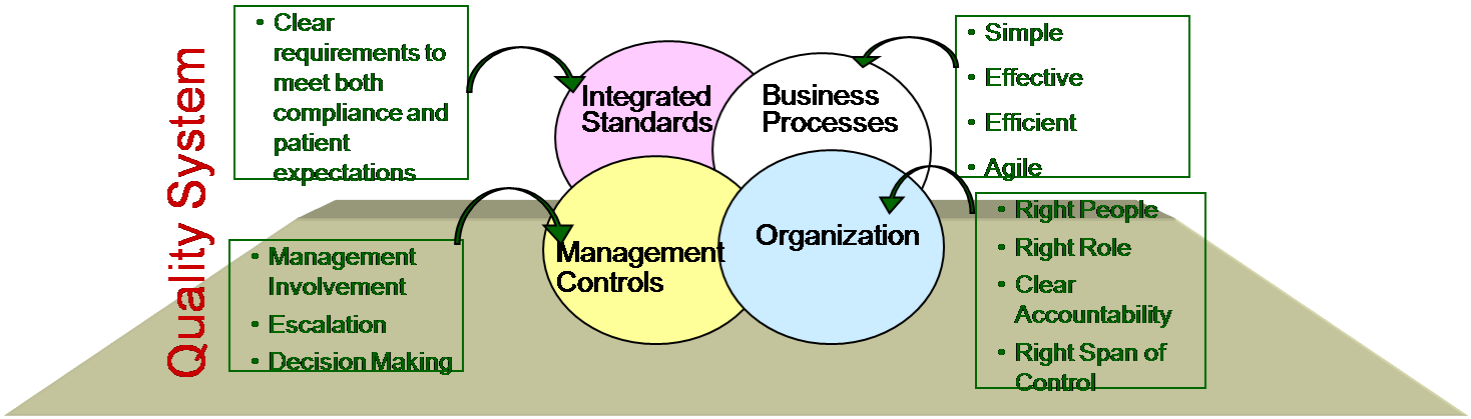
Establishing a Quality Foundation

Medical Single Process Map

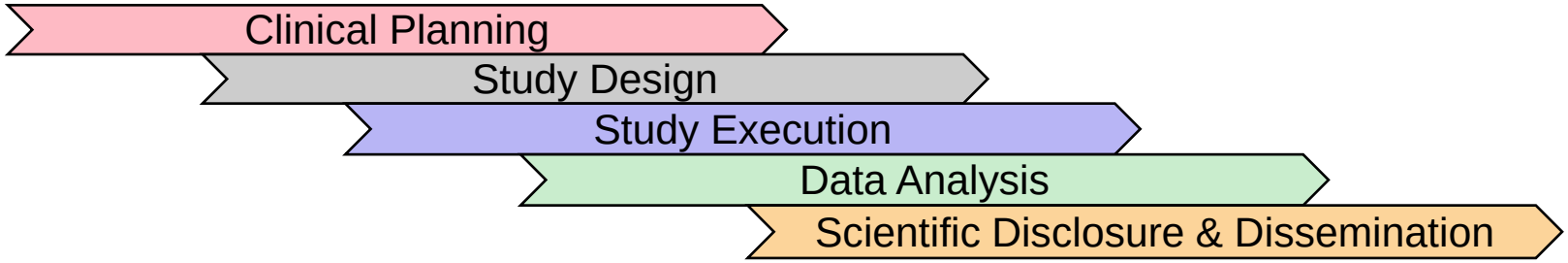


Business Process Management





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

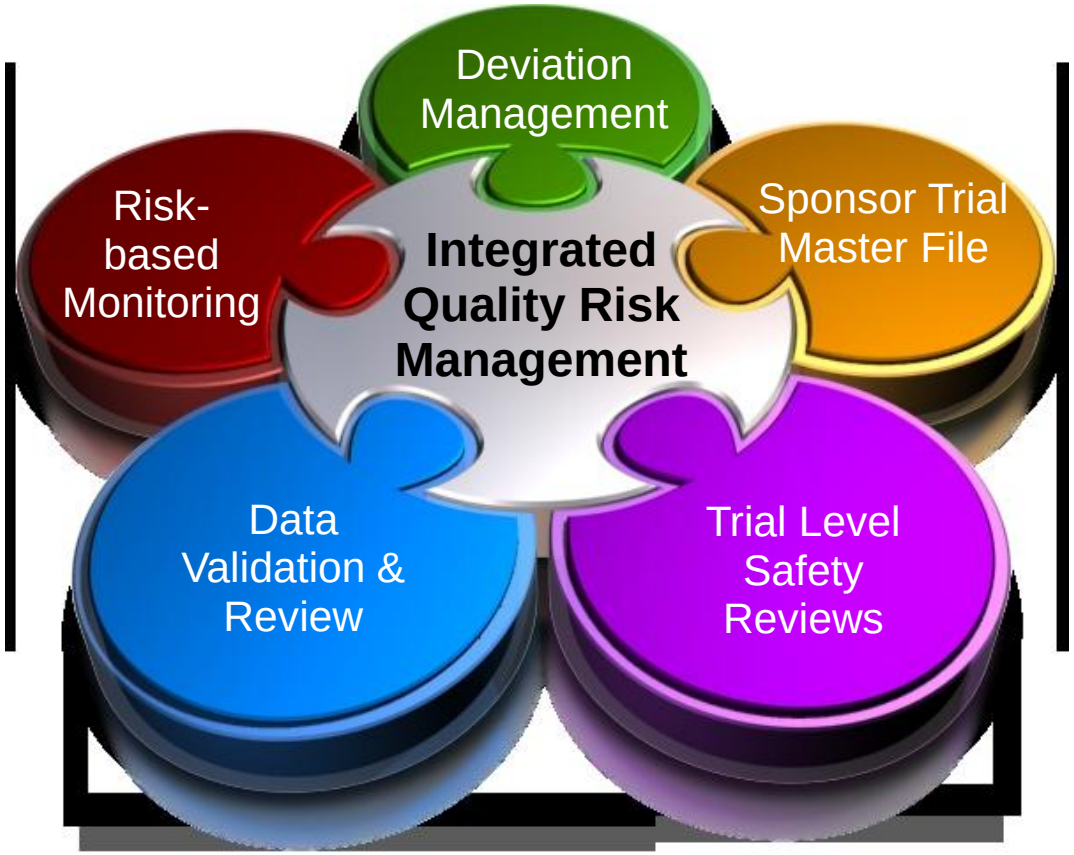
Study Execution
- Investigator Site Selection
- Risk-based Monitoring Program

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

Scientific Disclosure & Dissemination
- Disclosure Approvals

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

Integrated Quality Risk Management



Third Party Management Oversight

Sourcing Model Distinctions

Lean Six Sigma for Service

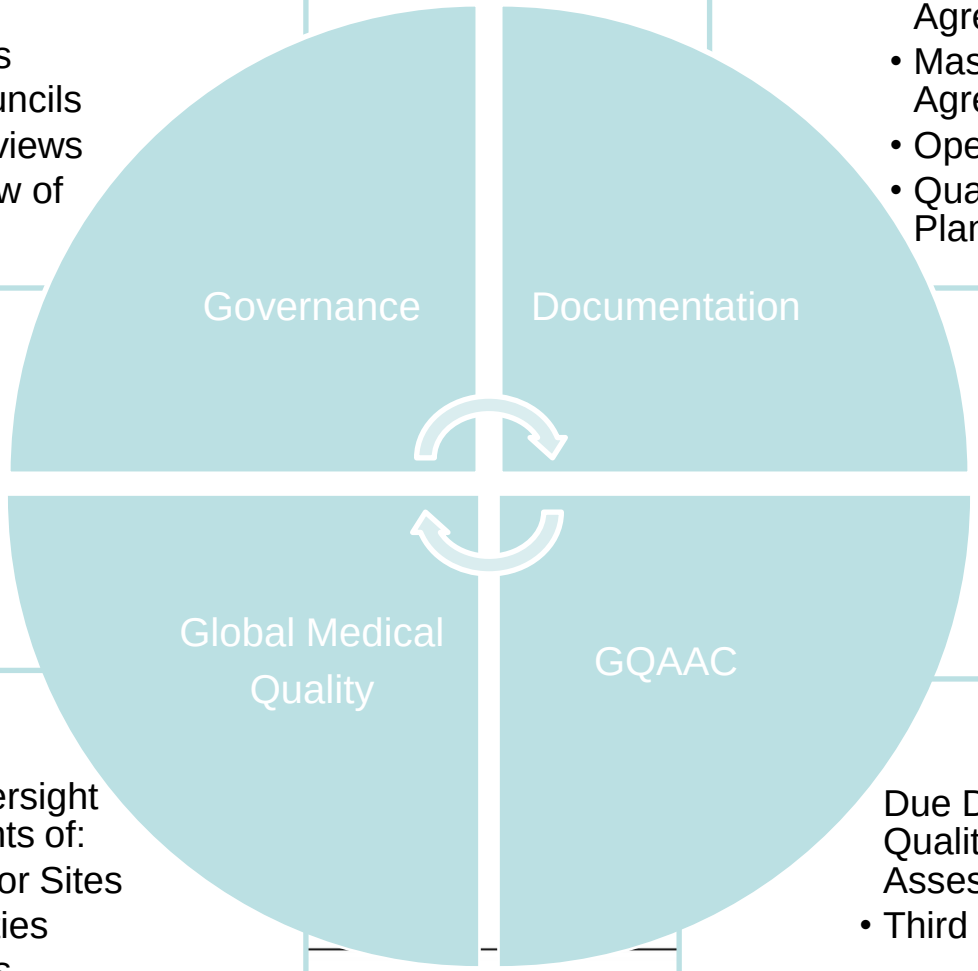
		Functional Sourcing		Project Sourcing
		Role	Process	Project
Quality	Standards	Lilly	Lilly	Lilly
	Procedures	Lilly	TPO*	TPO*
Work	Payment method	FTE rate	Activity or Deliverable unit pricing	Milestones
	Forecast Volume	Lilly Function	Lilly Function	TPO
	Resource Planning	Lilly	TPO	TPO
Integration	PM Accountability	Lilly	TPO – Process, Lilly - Project	TPO
	Data Integration	Lilly	Lilly	TPO*

* In transition to Future State with redesign efforts

Oversight of Strategic Third Parties

- Executive /Joint Operations Committees
- Quality Councils
- Metrics Reviews
- TPO Review of Standards

- Quality Agreements
- Master Service Agreements
- Operations Guides
- Quality Oversight Plans/Work Plans



- Quality Oversight Assessments of:
  - Investigator Sites
  - Third Parties
  - Processes

Due Diligence Quality Assessments

- Third Party Audits

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 Oversight Assessment Metrics

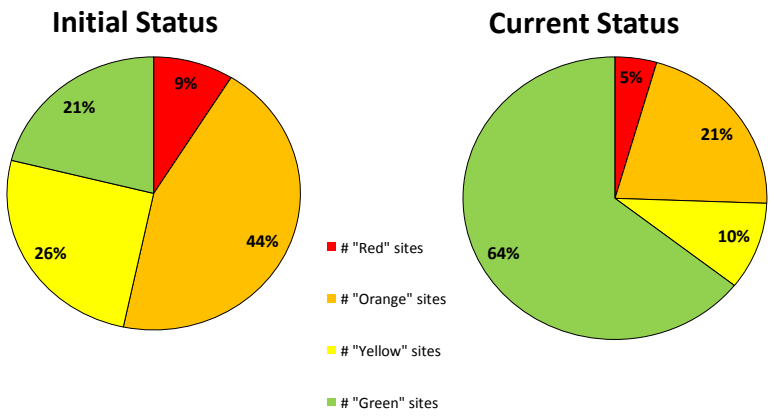
Summary – June 2011

Accomplishments

- 107 assessments have been performed year to date.
  - June 2011: 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 2011:
  - 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.



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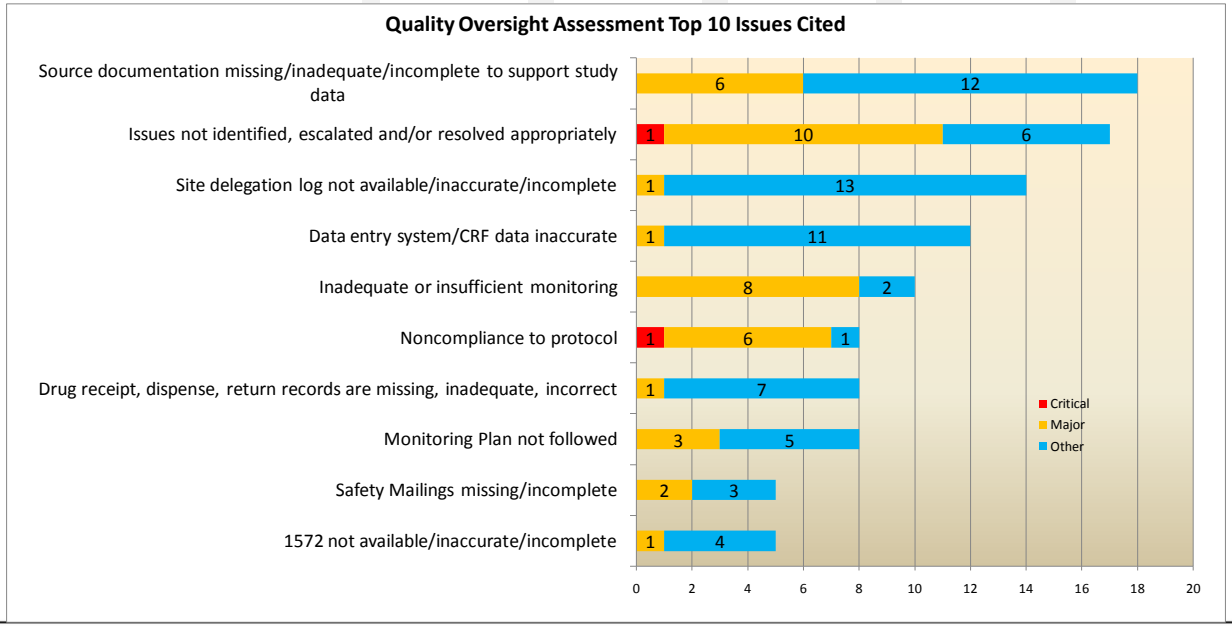
Strategic Third Party Assessment Metrics

Summary – Q2 2011

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

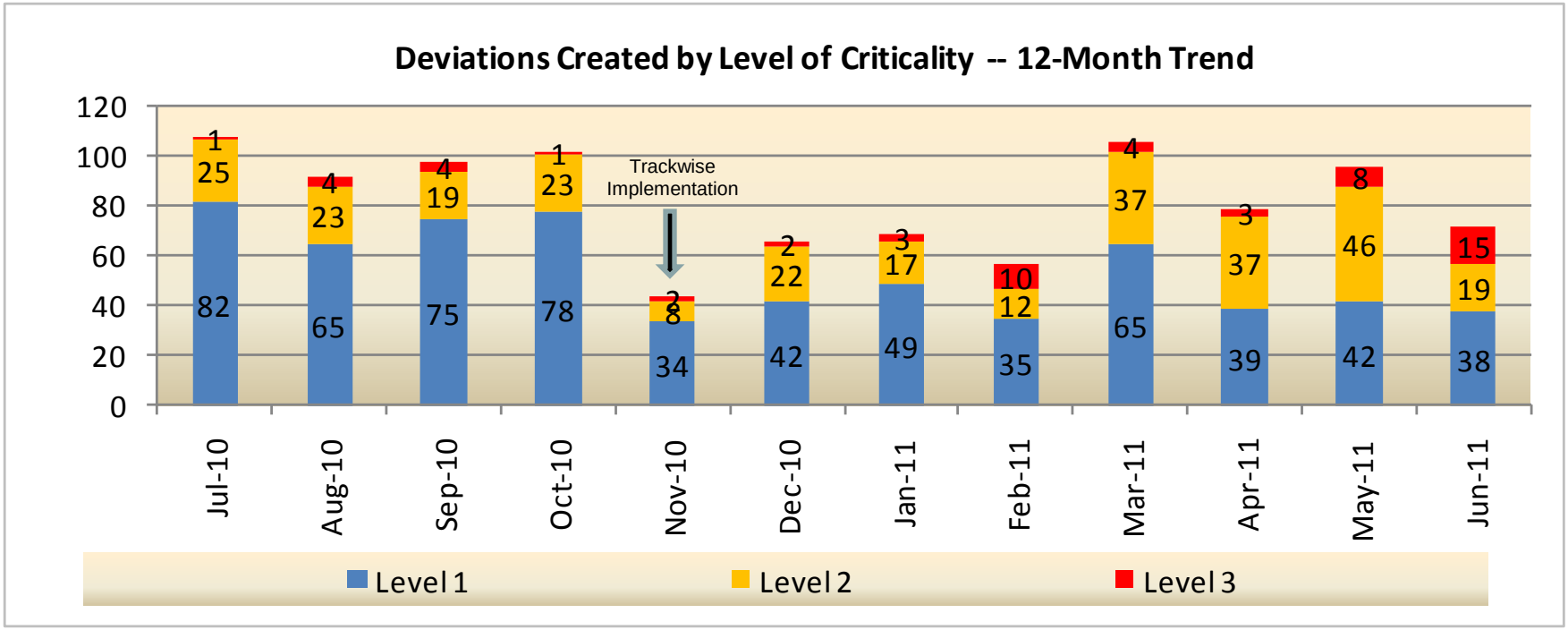
Only assessment findings owned by the TPO are included in the status. Findings owned by Lilly are not included in the TPO assessment summary.

	#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



Deviation Metrics

Summary – June 2011



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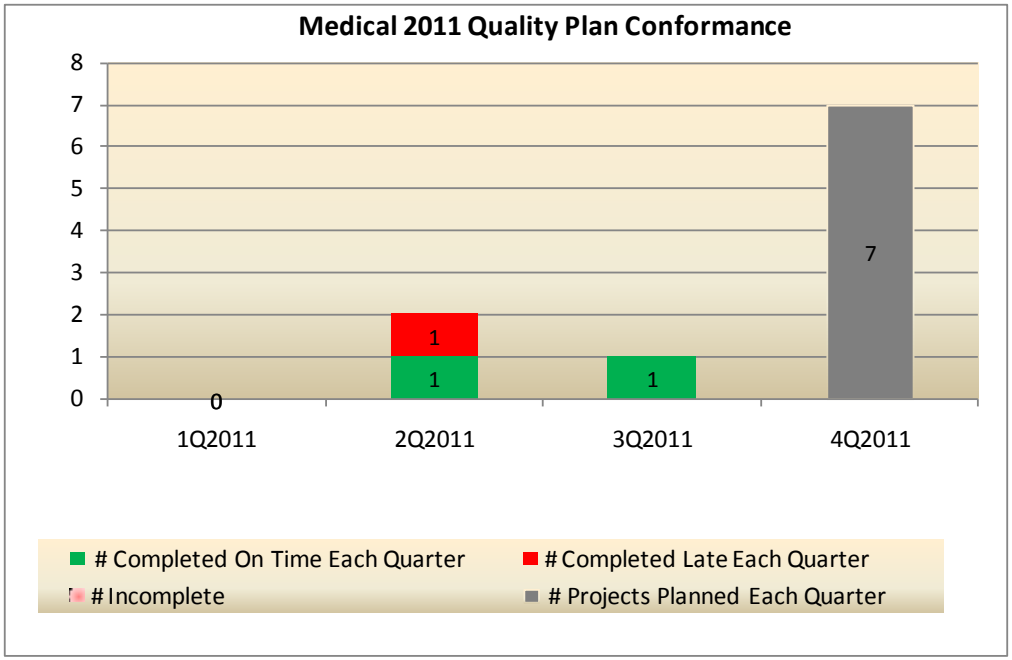
Quality Plan Conformance

Summary – July 2011

Quality Plan Conformance (Metric #9)



Projects Open and Overdue (12 July 2011)

No Global Medical Q Plan projects are currently overdue.

Projects Past Due When Completed (12 July 2011)

Action	Due Date	Completion Date
Release Sponsor Trial Master File procedure and related tools.	01 June 2011	10 June 2011

Projects Completed On Time (12 July 2011)

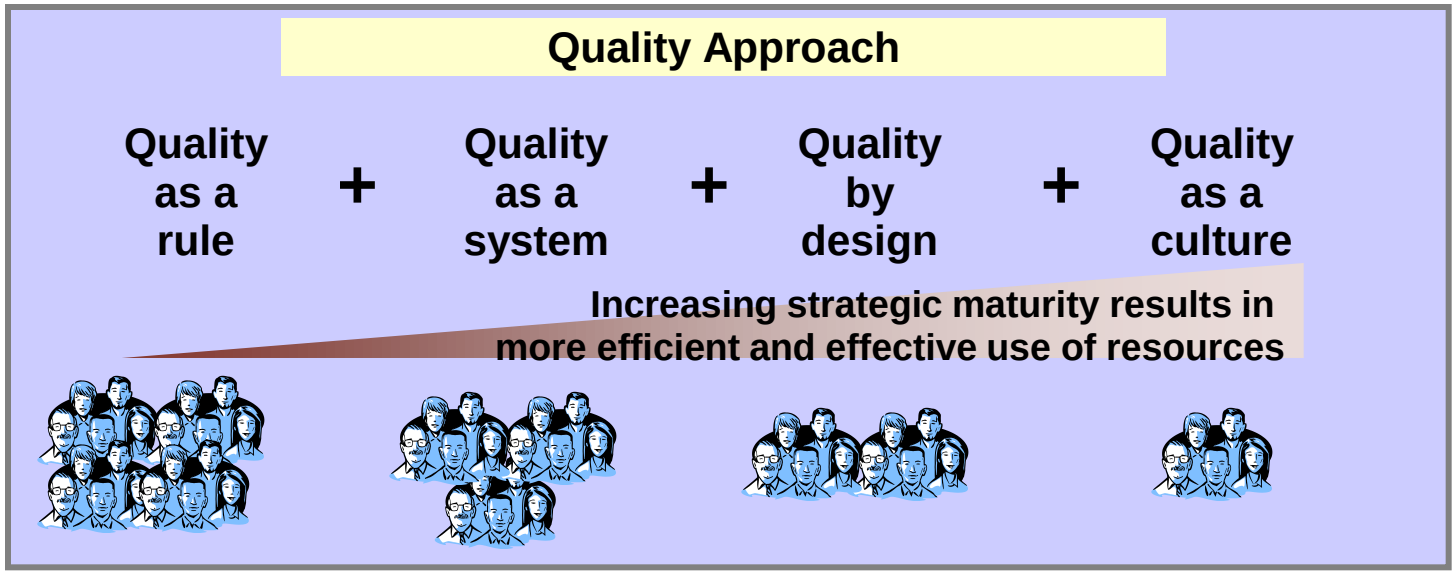
Action	Due Date	Completion Date
Update IMPACT to include missing network investigator site information.	30 April 2011	21 April 2011
Utilize the LQS Inspection Readiness and MQS Inspection Management processes to ensure readiness for an MHRA or FDA Inspection.	01 July 2011	08 June 2011

Ongoing Focus

- Execution Excellence – Right the first time!
  - Internal adherence to MQS
  - Investigator site performance
  - Third party organization performance
- Medical Quality System
  - Streamlining (e.g., Data Management, Statistics)
  - Continued harmonization of Quality System topics across Medical, Regulatory, and Safety
- Asia Pacific support
- Ongoing inspection readiness

We are continuing to progress on our Quality Journey!

Quality as a Culture



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