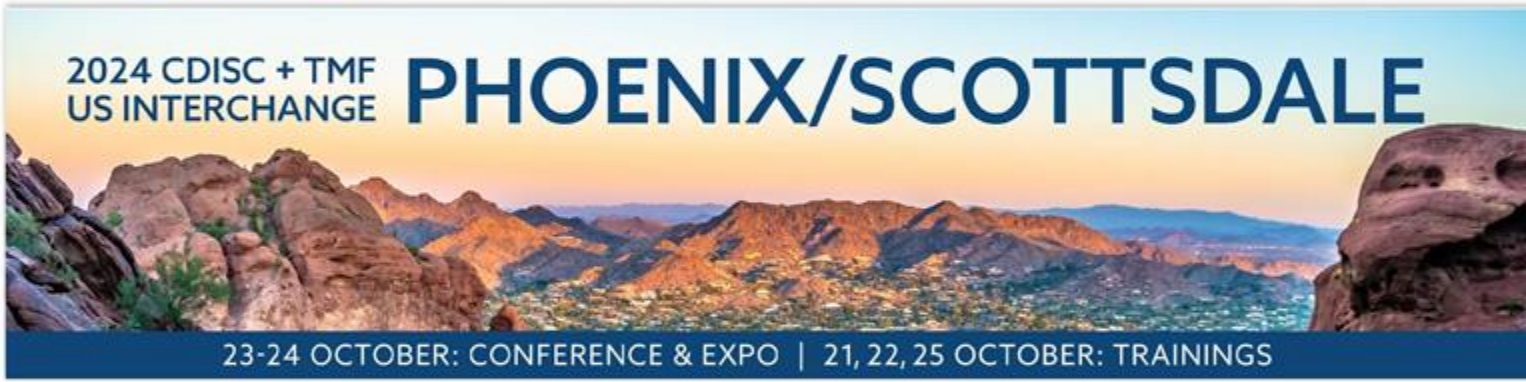

Applying Quality by Design to TMF Risk Management

Michael Agard, Principal Consultant, Epista Life Sciences
Ramya Iyer, Sr. Manager TMF, Regeneron

Meet the Speakers

Michael Agard

Title: Principal Consultant

Organization: Epista Life Sciences

Clinical Operations Consultant specializing in eTMF & CTMS optimization and compliance. I have worked for a pharmaceutical company for 20+ years and have been consulting for 15 years.

Ramya Iyer

Title: Sr. Manager, TMF

Organization: Regeneron Pharmaceuticals

Over 10 years of industry experience, currently serving as a Sr. TMF Manager at Regeneron Pharmaceuticals, where I lead Document Governance, Quality, and Inspection Readiness processes.

Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

- *The author(s) have no real or apparent conflicts of interest to report.*

Agenda

1. Quality By Design Concepts
2. Milestones and Expected Documents
3. Plan, Do, Check, Act
4. Inspection Ready TMF

Quality by Design Concepts

Legos – QbD Example

- **Consistency and Standardization**:
  - Precise specifications, uniformity and consistency
- **Modular Design**:
  - Modular, flexible and maintaining structural integrity
- **Risk Management**:
  - Rigorous testing and quality control measures to minimize defects and ensure safety
- **Customer Focus**:
  - Meet the needs and expectations of users

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Lego QbD Principles and TMF

Principle	Components	Consistency
Standardization	• TMF Reference Model • Metadata • Document Templates	• Study to Study • Country to Country • Site to Site
Modular Design	• Milestones • Expected Document List	• Documents collected at the right time • Maintain the story of the clinical trial
Risk Management	• Safety & Efficacy • Periodic reviews • Functional QC	• Reports • Risk Communications • Oversight & Escalations
Customer Focus	• Right document & right time • Workflows • Views & Reports	• Patients • Investigators & Site Staff • Auditors & Inspectors

Robust Risk Management

Integrate Risk Management with Strategy

Risk considerations are part of decision-making from the start

Informed Decisions

Understand the potential impacts of risks as they apply to decisions

Risk & Opportunity Plans

An ongoing process, revisited regularly as the project progresses

Prepare for Uncertainty

Backup plans and resources mobilized in response to unforeseen events.

Systematic Approach

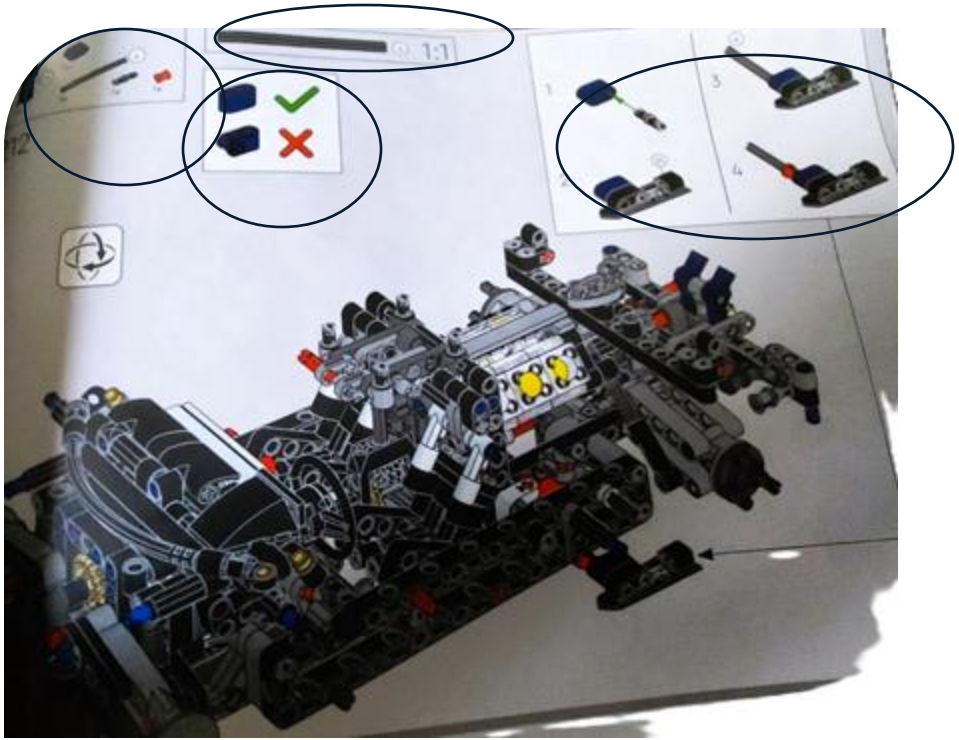
Ensure that strategic risks are systematically identified and managed.

Begin With the End in Mind

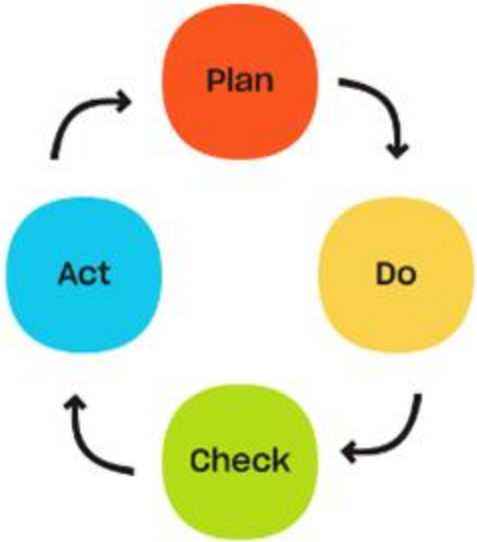
Identify Expected Documents → Follow the Process → Conduct the Trial → Manage the Risks

The end goal is a complete inspection ready TMF that tells the story of the clinical trial

Details Matter



- Identify the documents for each process or milestone
- Provide detailed instructions for critical processes and documents
- Training on correct vs. incorrect + Feedback

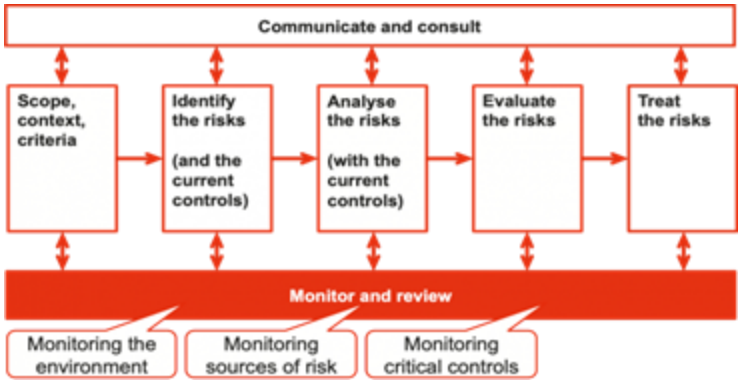


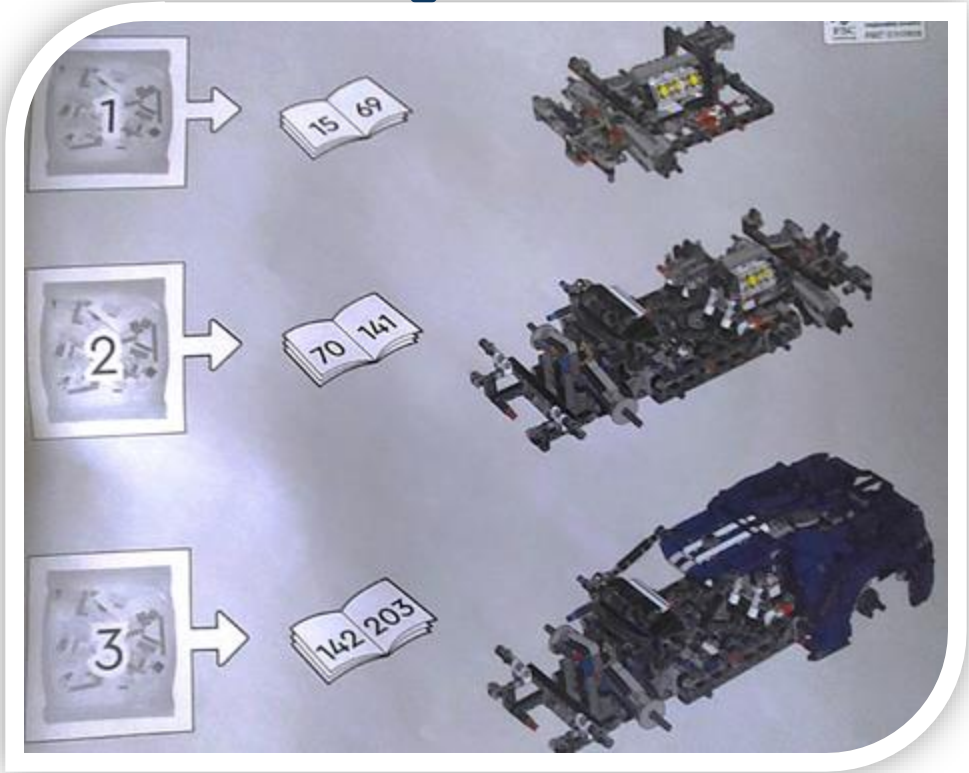
QbD Practical Application for TMF

Where can we apply QbD??

Milestone & Expected Document Management

- Break down the trial to start, middle and end milestones.
- Each phase has specific instructions for TMF documents & risks
- Show the progress towards completion





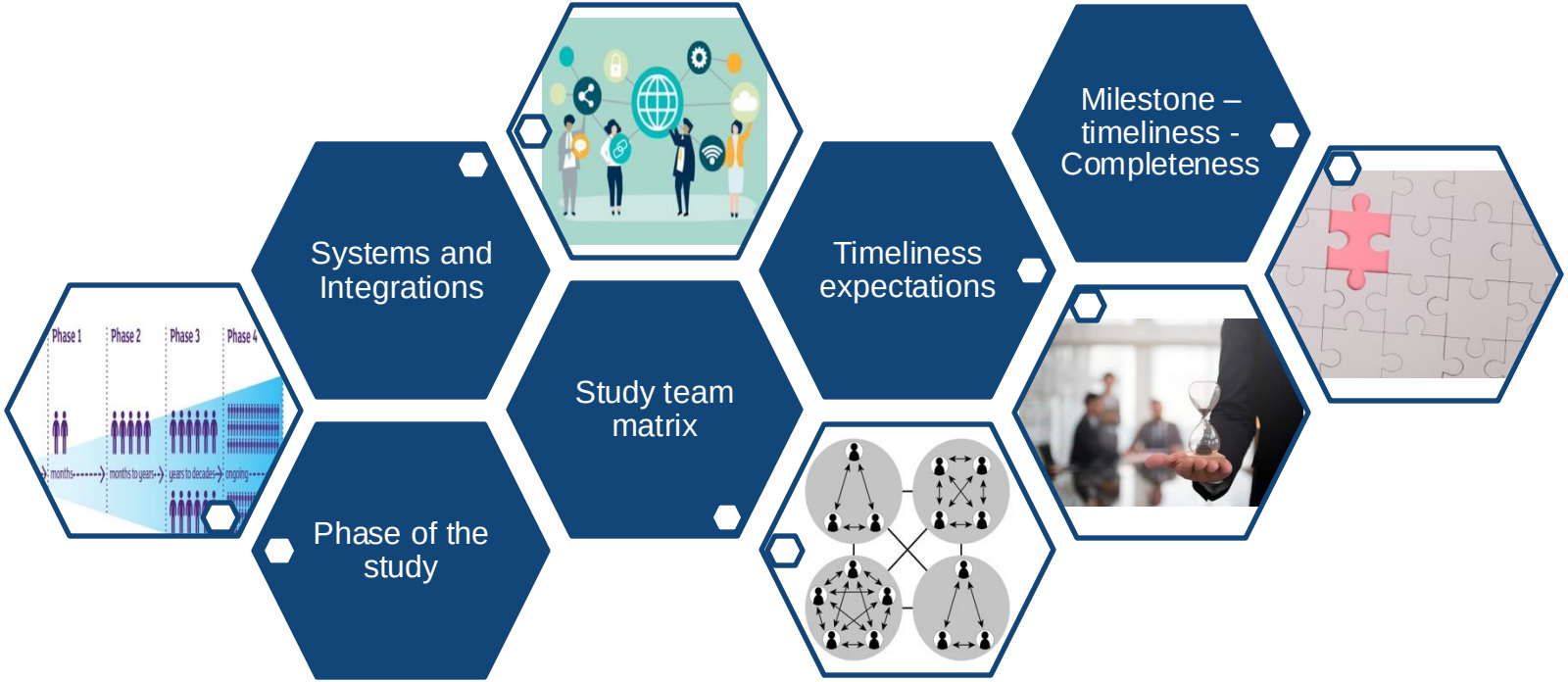
Expected Documents & TMF Reference Model

Leverage the TMF Model features:

- Core / Recommended
- Process Name
- Milestones
- Filing Level
- Add company specifics, for criticality, risk, periodic review and expected document tracking

Artifact name	Core or Recommended for inclusion	Process Nam	Trial Level Document	Trial Level MILESTONE/EVE	Country/ Region Level Docume	Country Level MILESTONE/EVE
List of SOPs Current During Trial	Core	Develop Trial Management Strategy	X	02 Clinical Infrastructure Ready	X	02 Clinical Infrastructure Ready

QbD for Expected Documents



Active TMF

TMF not a final resting place for documents

Part of each process that governs clinical study - the end goal!

Add efficiency to enable an active TMF

Authoring – Review – Finalization within TMF

Role-based access and training to TMF from the start

Keep track of key events for a study – Document it!

A Few Examples -

Database Locks

- Build templates within TMF for the forms required for the various steps for the DBL process
- Author the form within TMF → Send for Review → Obtain esignature approvals
- Audit trail shows beginning to end of the process
- Reviewer can add iterations of the form → quality check being performed real time

Training of Clinical Study Lead vs Stats Lead

- Trigger training based on the level of TMF management activities the role has to perform
- Work with the function to create role-specific training that adds-on the basic TMF training everyone should get.
- Consider aspects of the process that fall under the functional expertise – elevate the training to enable effective functional QC
- Consider team member transition and transfer of historical knowledge!

Integrations

- Multiple Systems in place within a sponsor
- Multiple vendors as well as portfolio vendors use their suite of systems and technology
- Integrations to the final official TMF key to maintaining an informed, real time and active TMF.
- Initiate dialogue and enhance interactions between system for effective transfer of documents at the end of a given process.
- E.g., Visit reports from CRO/vendor's CTMS, Quality or Regulatory docs from function owned system/repository

Credit: Google Images

Conclusion: A Complete TMF

- Increased focus on Quality from start aides Regulators
- Ensure a robust process is in place that minimizes risk and non-compliance – Be Proactive!
- Leverage technology to help with monitoring, compliance and feedback loop for continuous improvement.
- QbD approach ensures robust risk management, streamlined process, and clear responsibility alignment.
- QbD brings moves us closer to achieving a complete TMF!
- Inspectors will be delighted with a complete inspection ready TMF!

Thank You!