



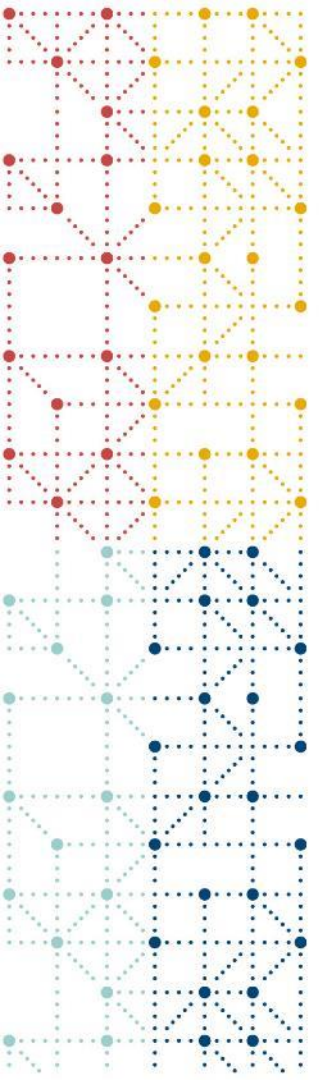
2023 CDISC TMF INTERCHANGE

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Sponsor and CRO: Creating a Sustainable TMF Partnership

Presented by: Annette Bugno, Biomea Fusion
Alex Markiel, TMF Consultant



Meet the Speakers

Annette Bugno

Title: TMF Manager

Organization: Biomea Fusion

Annette Bugno has been working in the Pharmaceutical industry for the past 5 years, beginning her TMF journey as a Clinical Records Technician at Pharmacyclics/AbbVie in 2018 and moving into Clinical Operations as a CTA and CRA where she continued to work closely with the TMF lending a helping hand with multiple migration projects and working closely with the Clinical Records Team. In 2022 she joined Biomea Fusion as the TMF Manager, implementing an eTMF system and establishing robust processes to ensure an inspection-ready TMF. Previous to her experiences in the Pharmaceutical industry, she worked in the clinical laboratory setting for a number of years and attended Veterinary School for her first year before making the career switch into the Pharmaceutical Industry where she gained her love of the TMF. In her free time, she loves traveling, hiking, and photography!



Alex Markiel

Title: TMF Consultant

With twenty plus years of commended performance focused on clinical trial compliance and inspection readiness, Alex has become an expert in multiple aspects of Trial Master File (TMF) management. His passion for TMF excellence has resulted in the successful creation, development, and inspection of TMF's across the industry. Alex is based in San Francisco and has worked for Genentech, BioMarin, AbbVie Pharmacyclics and Nektar Therapeutics along with providing additional consultant services.



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 and Biomea Fusion.*



Agenda

1. Creating a Successful Sponsor and CRO TMF Partnership Framework
2. Defining a Partnership's Operational Parameters
3. Utilizing Communication and Goals to Drive a Sustainable Partnership
4. Questions

Turnover and change inherent to the biotech/ pharma industry can make a successful sponsor and CRO TMF partnership difficult to develop and sustain.



Turnover and change inherent to the biotech/ pharma industry can make a successful sponsor and CRO TMF partnership difficult to develop and sustain.

- *Misunderstanding the goals of your partnership.*
- *Your TMF representative is replaced, repeatedly.*
- *You do not have a TMF specific representative (CRO and/ or Sponsor).*
- *You are new to the study and its TMF.*
- *Your TMF model changed after the study began...*

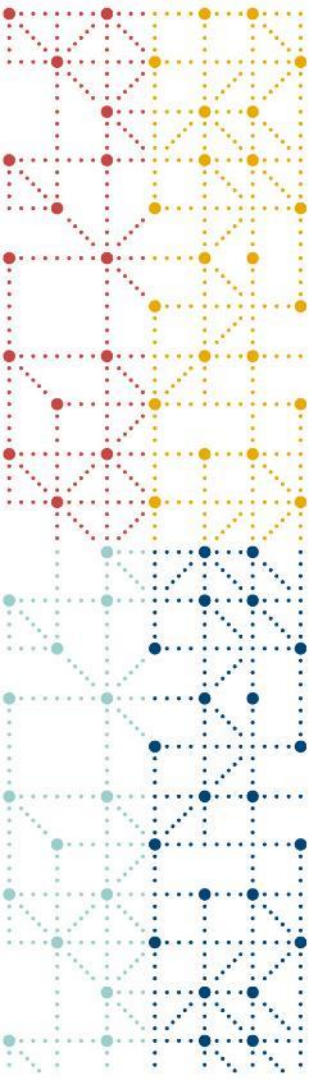




Create a TMF OPERATIONAL* FRAMEWORK in which to collaborate and meet both the sponsor and CRO's TMF goals

** “Operational” Definition:*

*A structure that describes the operations (processes, procedures, actions) regarding the TMF that should be **monitored and measured consistently***



Create an OPERATIONAL TMF SPECIFIC FRAMEWORK in which to collaborate and meet both the sponsor and CRO's TMF goals.

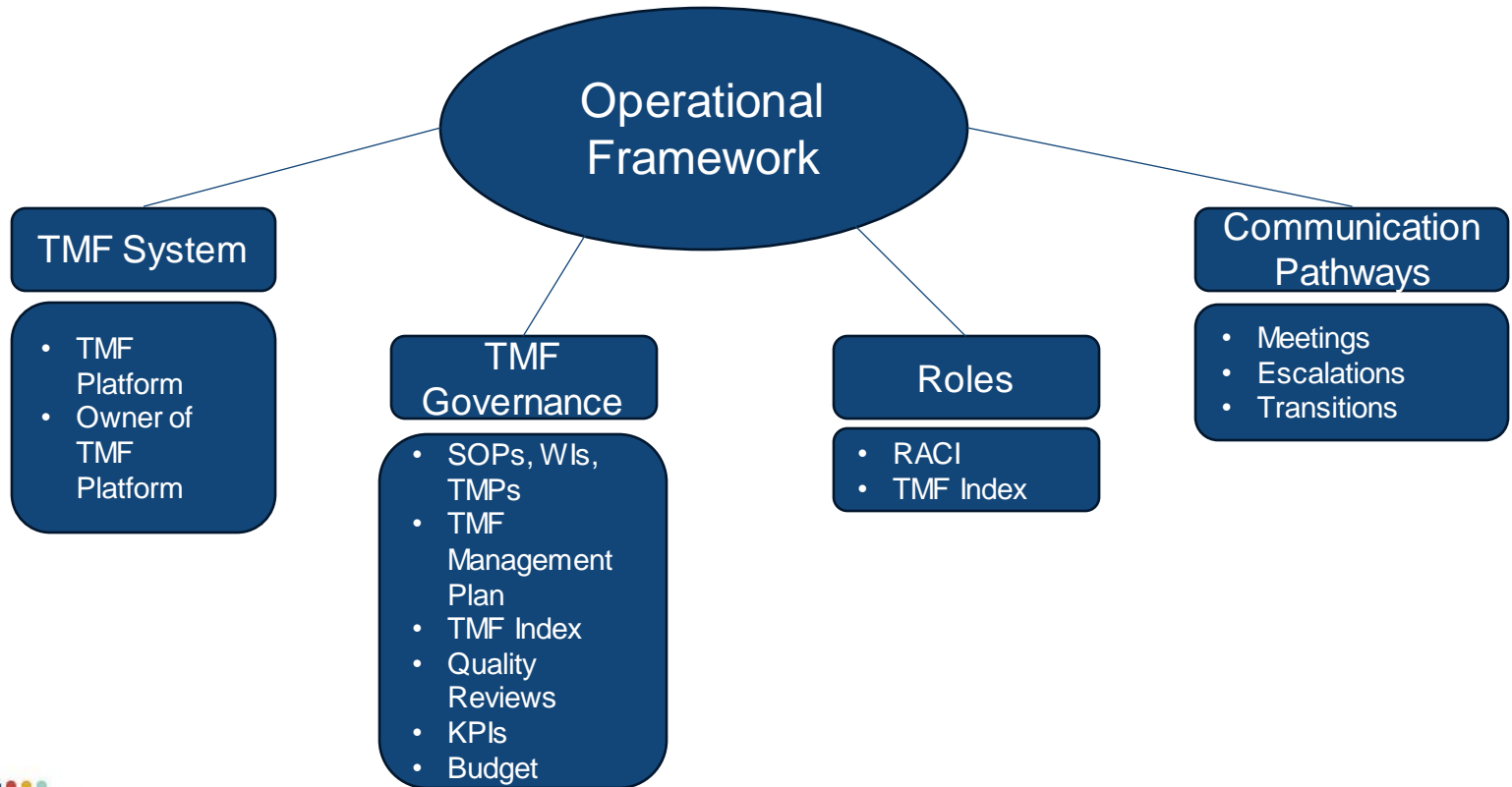
1. **DEFINE** the partnership's TMF management framework
2. **UNDERSTAND** the partnerships management framework and TMF goals
3. **MONITOR** and **MEASURE** (or assess) your TMF partnership against your TMF goals, consistently.

Define Your TMF Management Operational Framework

- Identify your TMF Model
 - In-House Model
 - Sponsor maintains the TMF system with CRO contribution
 - CRO Model
 - CRO maintains the TMF system with Sponsor Contribution
 - Hybrid
 - Both Sponsor and CRO maintains the TMF System with respective contributions

Define Your TMF Management Operational Framework

Consistent reference to and use of the completed framework by both parties will drive the partnership's sustainability.



Defining and Understanding Your TMF Operational Framework: System

Model	TMF System
In-House: Sponsor Maintains the TMF System with CRO Contribution	<ul style="list-style-type: none">❑ Identify TMF System❑ Development of Training Materials – External and Internal partners<ul style="list-style-type: none">❑ Document Uploading, QC Review, Periodic Reviews, Reporting and Dashboards❑ Documentation of training – LMS, tracking system❑ System Access Procedures<ul style="list-style-type: none">❑ Internal, External, Inspector/Auditor❑ Expectations of timeliness for User addition/modification/revocation❑ System Capabilities<ul style="list-style-type: none">❑ Tracking of specific reviews in the system
CRO: CRO maintains the TMF System with Sponsor Contribution	
Hybrid	

Defining and Understanding Your TMF Operational Framework: System

Model	TMF System
In-House: Sponsor Maintains the TMF System with CRO Contribution	<ul style="list-style-type: none"><input type="checkbox"/> Other considerations:<ul style="list-style-type: none"><input type="checkbox"/> Troubleshooting, escalations of system issues<input type="checkbox"/> Electronic signatures (TMF system vs external system)<input type="checkbox"/> TMF Migration capabilities if applicable<input type="checkbox"/> TMF system archive processes
CRO: CRO maintains the TMF System with Sponsor Contribution	
Hybrid	

Defining and Understanding Your TMF Operational Framework: Governance

Model	TMF Governance (TMF SOPs, WIs, TMPs, TMF Plan, TMF Index, Quality Reviews)
In-House: Sponsor Maintains the TMF System with CRO Contribution	<ul style="list-style-type: none">❑ TMF SOPs, Work Instructions, and Templates<ul style="list-style-type: none">❑ Gap-Analysis and mitigation for mis-alignments<ul style="list-style-type: none">* Highly recommend against utilizing 2 sets of SOPs/WIs/TMPs❑ TMF Management Plan<ul style="list-style-type: none">❑ Gap Analysis and mitigation of mis-alignments<ul style="list-style-type: none">* Recommend following one TMF MP and TMF Index if amenable for hybrid models, modify as needed for alignment
CRO: CRO maintains the TMF System with Sponsor Contribution	<ul style="list-style-type: none">❑ Timeliness of filing into the TMF System❑ Periodic Quality Reviews and Completeness<ul style="list-style-type: none">❑ Percentages, error thresholds, evidence of reviews, subsequent reviews, issues reporting and follow up inclusive of timelines
Hybrid	<ul style="list-style-type: none">❑ Relevant Communications, Certified Copy, Translations, Unblinding Procedures, Oversight, Third-Party filing (how are documents being provided and when?)❑ Clearly outlined Transition Plan for team turnover

Defining and Understanding Your TMF Operational Framework: Governance

Model	TMF Governance (TMF SOPs, WIs, TMPs, TMF Plan, TMF Index, Quality Reviews)
In-House: Sponsor Maintains the TMF System with CRO Contribution	<ul style="list-style-type: none"><input type="checkbox"/> TMF Index<ul style="list-style-type: none"><input type="checkbox"/> Identify Artifact Ownership – Who is responsible for this document?<ul style="list-style-type: none"><input type="checkbox"/> Sponsor, Functional Area, CRO, TPV<input type="checkbox"/> Identify Document Uploader – Who is responsible for uploading?<ul style="list-style-type: none"><input type="checkbox"/> Sponsor, Functional Area, CRO, TMF Group<input type="checkbox"/> Identify Document Repository – Where is the document retained?<ul style="list-style-type: none"><input type="checkbox"/> TMF System, alternate Satellite TMFs<input type="checkbox"/> Considerations<ul style="list-style-type: none"><input type="checkbox"/> Translations, wet-ink designations, additional comments
CRO: CRO maintains the TMF System with Sponsor Contribution	
Hybrid	

Defining and Understanding Your TMF Operational Framework: Roles

Model	TMF Roles
In-House: Sponsor Maintains the TMF System with CRO Contribution	<ul style="list-style-type: none">❑ Develop a RACI that includes <u>CRO</u> and <u>Sponsor</u> roles as they pertain to:<ul style="list-style-type: none">❑ TMF System Ownership❑ TMF Governance (SOPs/WIs/TMPs, TMF MP, TMF Index)❑ TMF Quality Reviews (document specific vs Periodic/Overall)❑ TMF Quality Oversight❑ Third Party Contributor Management and Oversight❑ Non eTMF Repository Management
CRO: CRO maintains the TMF System with Sponsor Contribution	<ul style="list-style-type: none">❑ TMF Reporting and Metrics❑ Inspection/Audit Support❑ TMF Meetings
Hybrid	

Defining and Understanding Your TMF Operational Framework: Communication

Model	TMF Communication Pathways
In-House: Sponsor Maintains the TMF System with CRO Contribution	<ul style="list-style-type: none">❑ TMF Meetings (... or equivalent)<ul style="list-style-type: none">❑ Frequency, Type, Meeting Lead and Invitees❑ Agenda includes regular review of TMF goals (monitor and measure), reporting of quality reviews, quality issues (closed vs open statuses), escalations as needed❑ Minutes should be captured and circulated❑ Escalation Pathways<ul style="list-style-type: none">❑ Within organization, external to organization (inclusive of TMF System organization)❑ Transition Process<ul style="list-style-type: none">❑ Captured in TMF MP and to be utilized/referred to when transition occurs❑ CV Review, 1/1 Meetings, Trainings
CRO: CRO maintains the TMF System with Sponsor Contribution	
Hybrid	

Defining and Understanding Your TMF Operational Framework: Communication

Model	TMF Communication Pathways
In-House: Sponsor Maintains the TMF System with CRO Contribution	<ul style="list-style-type: none"><input type="checkbox"/> Communication Style<ul style="list-style-type: none"><input type="checkbox"/> Assess preferred communication style of counterparts<ul style="list-style-type: none"><input type="checkbox"/> Emails, phone calls, formal meetings<input type="checkbox"/> Assess preferred dissemination of information<ul style="list-style-type: none"><input type="checkbox"/> Excel trackers, word documents, table format in emails<input type="checkbox"/> Assess frequency of meetings based on bandwidth
CRO: CRO maintains the TMF System with Sponsor Contribution	
Hybrid	



TMF Goals: Assess TMF Goals Across the Partnership

Before establishing your TMF goals across your Sponsor and CRO partnership:

How do your defined governance procedures guide you in establishing your TMF goals?

- Ensure that your goals do not conflict with your established governance procedures...or with your partners’.
- Review your goals for understanding across the team, including leads and senior management, prior to committing to them.
- Agree to goal tracking and reporting mechanisms.

TMF Goals: Assess TMF Goals Across the Partnership

A sustainable TMF partnership requires

- An understanding from both parties as to how the goals fit within their established framework
- How goals are reported out and frequency
- How unmet or at-risk goals are to be addressed and managed

TMF Goal Examples

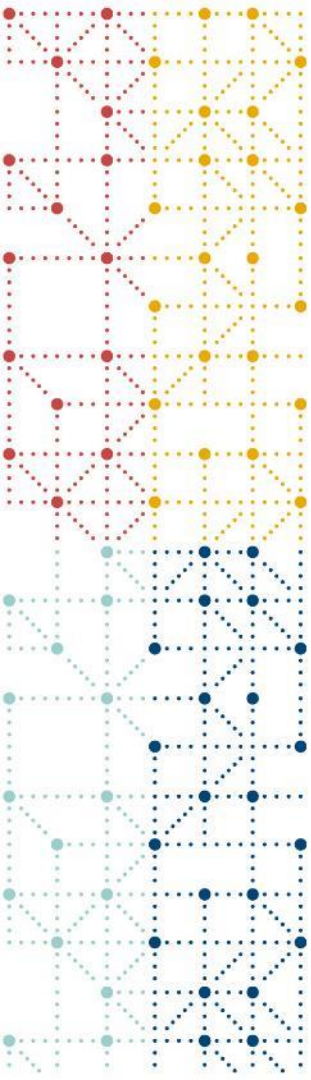
- **TMF Management**
 - Timeliness
 - Contemporaneous document uploading threshold, QC Workflow timeline, Quality Issue Resolution timeline, Periodic Review timeline
 - Quality
 - Percentage of documents rejected in the TMF System
 - Percentage of open Quality Issues
 - Percentage of findings during Periodic Reviews
 - Number of quality issues open, closed, pending
 - Completeness
 - Number of documents uploaded against EDLs and/or expected milestones
- **Audit Goals**
 - Timeliness of Response to Audit Request and Audit Findings
 - Timelines for Close-Out of Audit Findings
- **Goal Reporting**
 - Determine timepoints for reports (weekly, monthly, quarterly, etc)
 - Providing KPIs and metrics on a pre-determined periodic basis - Regular reports, TMF Health Meetings, CRO/Sponsor Call standing Agenda items

Conclusion

Implementation of an operational TMF specific framework that considers both partner's TMF requirements and includes an ongoing monitoring and measurement of a TMF's goals will result in a sustainable, successful partnership.

... and a defined, consistent, **documented** communication pathway between both partners is KEY!





Thank You!

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