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Elevate the Inspection Readiness of your TMF through an Agile methodology

Presented by Donatella Ballerini, Head of eTMF Services, Montrium
Paul Fenton, CEO, Montrium

Meet the Speakers

Donatella Ballerini

Title: Head of eTMF Services

Organization: Montrium



16 years of experience in the pharma industry. Gained experience at Chiesi Farmaceutici in the Global Clinical Development Department and Global Rare Disease Department as a Document & Training Manager. Developed and implemented documentation management processes and led the transition from paper to eTMF. Became Head of GCP Compliance and Clinical Trial Administration Unit at Chiesi in 2020. Charged with ensuring compliance of all ClinOps processes with ICH-GCP and maintaining inspection readiness. Became Head of eTMF Services at Montrium in 2021. Joined the CDISC TMF Reference Model Education Governance Committee in 2023 and the CDISC Risk White Paper Initiative in 2024.



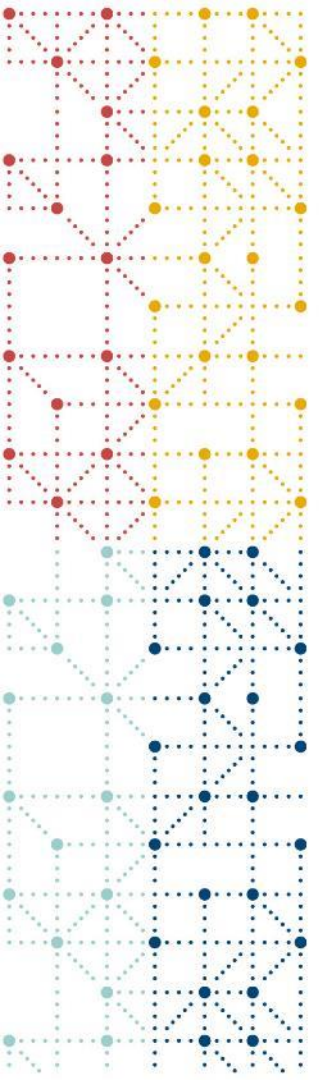
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Agenda

1. Introduction
2. Key Principles of Agile TMF Management
3. Agile Methodology for measuring Inspection Readiness
4. Practical Examples
5. Take Home message



Introduction

Introduction



Generally the common thinking is to associate the TMF to a passive archive, where all the documents of the clinical trial are filed to be accessible in case an Inspector knocks to our door.



What if we stop to think about the TMF as a document collector and start to consider it as a precious source of data like other clinical system?



By applying an Agile methodology, our TMF becomes an active and powerful tool that enables us to prevent issues rather than just correct them, focusing resources and time in a more effective way.

The Agile (Force) Methodology for TMF

Much like the Jedi mastering the Force in Star Wars, we aim to unleash the power of agility in our TMF management. In the Star Wars universe, the Jedi are known for their adaptability, quick reflexes, and ability to navigate unforeseen challenges. Similarly, in our TMF journey, we strive to be TMF Jedi, mastering the art of agility to ensure inspection readiness.

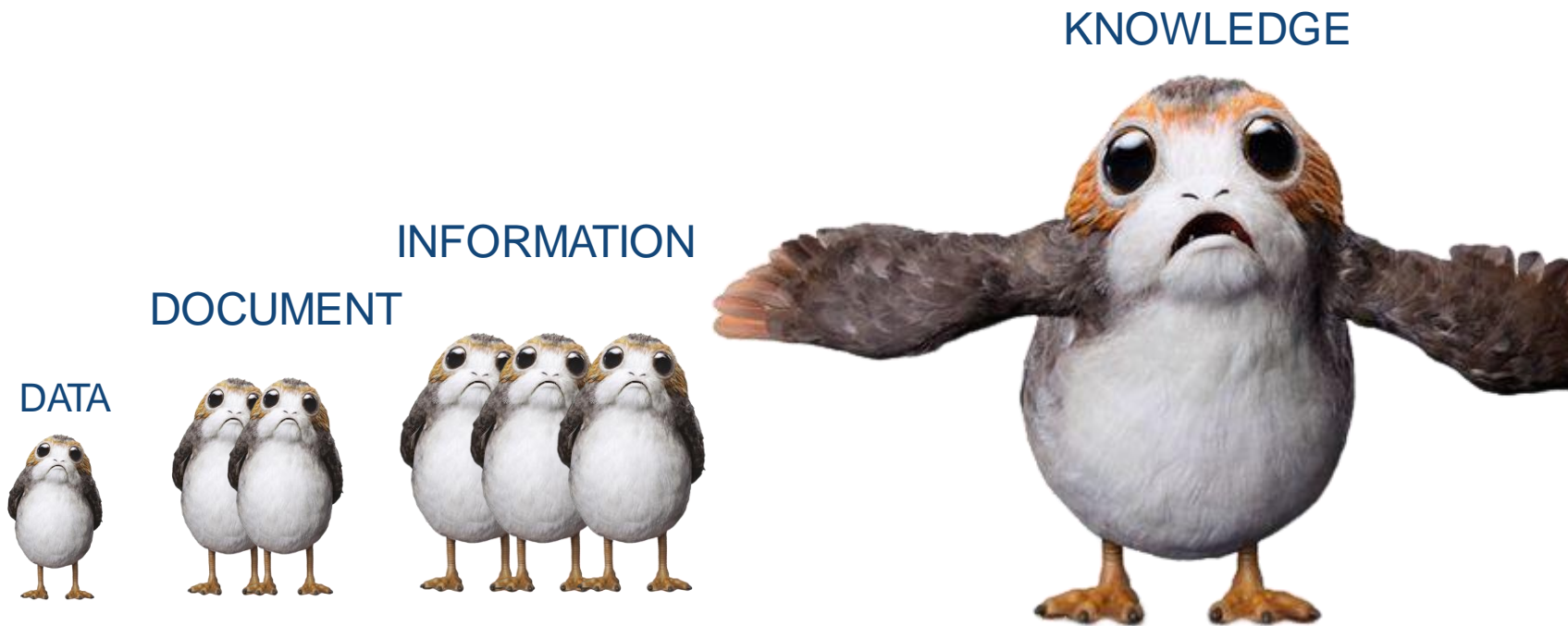


Objective

By applying an Agile methodology, we break free from traditional, old and passive approach to TMF management. Agile means to look at the TMF as a source of data and **proactively maintaining a state of inspection readiness.**



TMF as a Source of Data



Several Types of Data within the TMF

10	Data Management	10.01	Data Management Oversight	10.01.01	Data Management Plan	To identify the overall trial; a compilation of amendments/appendices, Guidelines, Data Quality (build) Specification, E
10	Data Management	10.02	Data Capture	10.02.01	CRF Completion Requirements	To provide detailed instructions to be completed; how to enter data into the system.
10	Data Management	10.02	Data Capture	10.02.02	Annotated CRF	To assign variable names to link the variables to

Compliance

IP Dispensing

Timeliness, quality and completeness

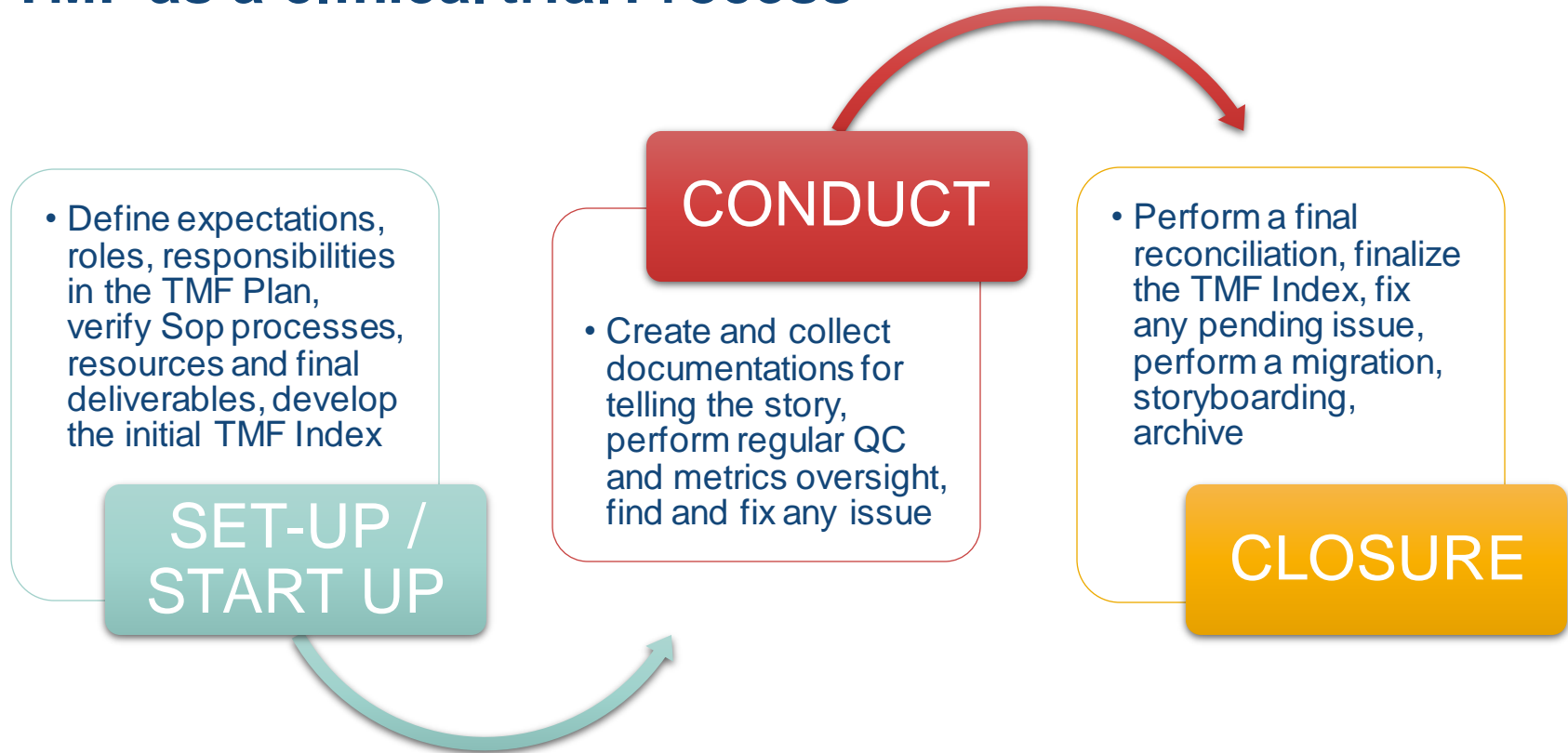
Recruitment

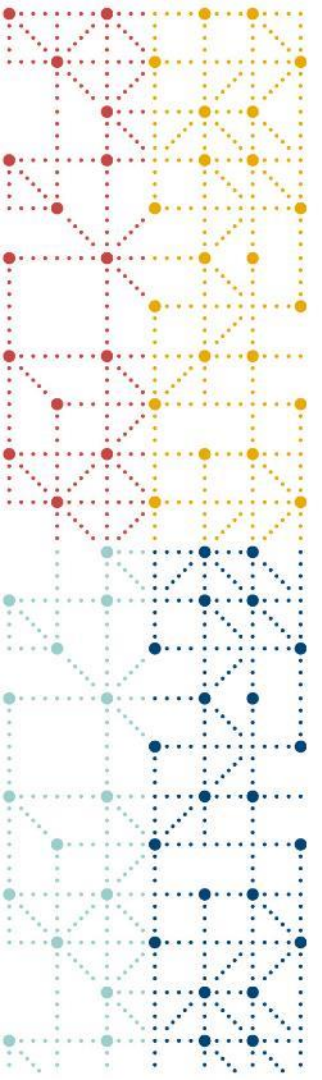
Protocol Deviations

Milestones

Users Performances

TMF as a clinical trial Process





Key Principles of Agile TMF Management

Agile means...Data driven

The Agile Force: Agility acts as the Force in Star Wars that guides us through TMF challenges.

Adaptive Metrics:

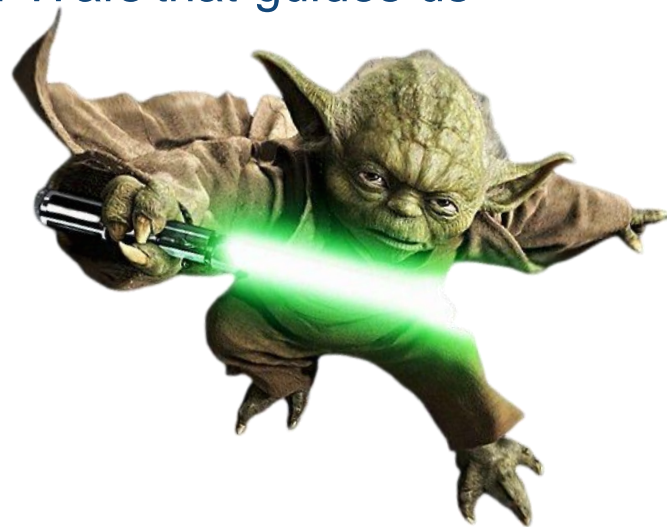
Define metrics that provide real-time insights into the health and readiness of the TMF. Adapt metrics based on changing trial dynamics and evolving needs

Measure progress towards TMF business goals

KPI (keep people involved/interested/inspired)

Identify key parameters that have an impact on TMF quality and its risks

Monitor those parameters



Agile means...a risk based approach

Jedi is Force-sensitive, able to sense disturbances, anomalies in the currents of the force...

Risk-Based Quality Checks:

- Implement risk-based quality checks for TMF documents, focusing efforts on critical areas that could impact inspection readiness.
- Regularly review and adjust quality check processes based on ongoing feedback.

TMF as an ongoing process:

- Respond quickly to changes in TMF risks
- Adjust TMF strategies promptly to meet evolving needs, ensuring that documentation remains aligned with the current trial status.



Agile means...TMF Jedi mindset

Jedi Mindset: adopting a Jedi mindset in TMF teams means being adaptable, responsive, proactive and quick to embrace changes.

Embrace Change Management:

Adapt team members to an Agile mindset.

Address resistance by emphasizing the benefits of flexibility and responsiveness in TMF management.

Continuous Collaboration:

Encourage cross-functional collaboration within TMF teams.

Develop open communication to ensure all stakeholders are involved in decision-making processes





Agile Methodology for measuring TMF Inspection Readiness

WHAT IF I treat my TMF like a passive repository???

There were many documents missing from the eTMF, for example, signature sheets, correspondence, emails and previous versions of documents.

There was a lack of effective oversight QC of an eTMF by the sponsor.

Source: MHRA GCP Inspections Metrics

The TMFs selected for inspection were found to be significantly incomplete, to such an extent that the trial conduct could not be reconstructed, and the inspection had to be extended. This was found to be a systematic issue, with the eTMF being considered and used as a final document repository rather than a contemporaneous system used to manage the trial.

The paper TMF was used as a document archive rather than a working TMF and trial team members did not have access to the paper TMF, but instead used an electronic “shadow TMF” during the trial. Upon review, it was found that there were a large number of documents in the “shadow TMF” which were not filed in the paper TMF.

Define your TMF fears...

DEFINE COST OF INACTION

All the negative aspects to treat your TMF as a passive repository

Lack of oversight/Control

Lack of quality

Lack of completeness

Lack of Inspection Readiness

Lack of awareness of quality issues

Lack of information

.....



PREVENT

what could I do to prevent those bad things to happen?



WHAT MIGHT BE THE BENEFITS OF AN AGILE APPROACH

Prevent

Perform regular QC

Develop an effective TMF management process

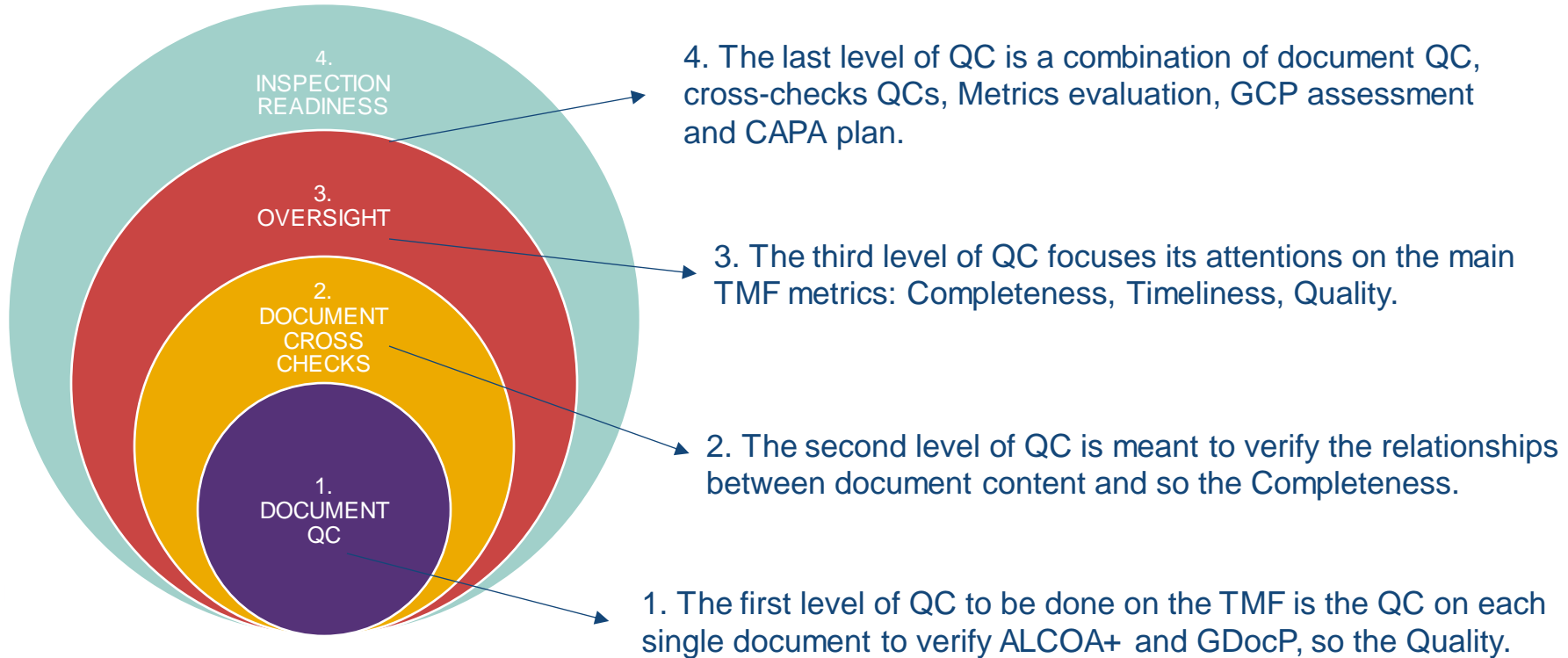
Establish roles and responsibilities

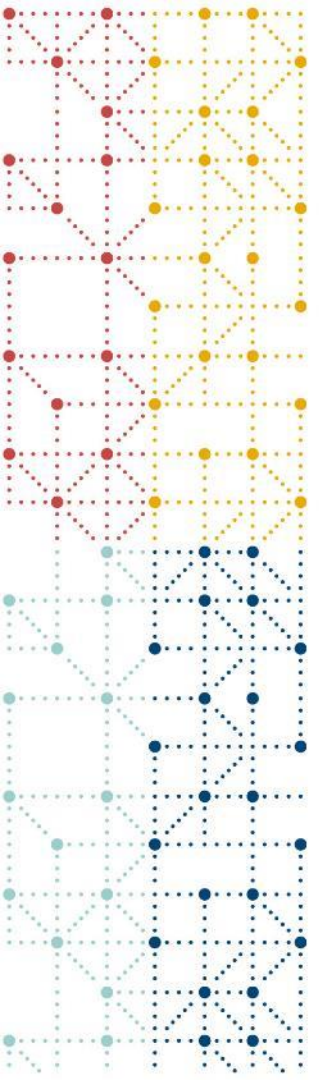
Implement Metrics and KPIs

Develop and implement a risk based approach

Understand the Inspection Readiness status of your TMF...

Understand your TMF Inspection Readiness





Practical examples

1) Single Document QC

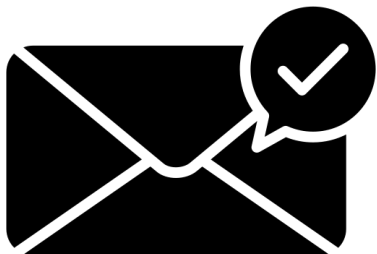
- ✓ Accessible
- ✓ Legible
- ✓ Contemporaneous
- ✓ Original
- ✓ Accurate

- ✓ Complete
- ✓ Consistent
- ✓ Enduring
- ✓ Available

[Insert Name of Department/Group Responsible for Monitoring Trial] MCRI, The Royal Children's Hospital Flemington Road, Parkville, VIC 3052 Phone: (+61) 3 9936 6328		MONITORING VISIT REPORT	
Site Principal Investigator: [Insert full name]			
Study Site: [Insert full name of organisation, City and State]		Date: [Insert date(s) of visit]	
Protocol: [Insert official title of the protocol]			
Monitor(s): [Insert Monitor name and affiliation]			
			Check if present
Principal Investigator: [Insert full name]			<input type="checkbox"/>
Sub-investigator: [Insert full name]			<input type="checkbox"/>
Research Nurse: [Insert full name]			<input type="checkbox"/>
Study Coordinator: [Insert full name]			<input type="checkbox"/>
Data Coordinator: [Insert full name]			<input type="checkbox"/>
Pharmacist: [Insert full name]			<input type="checkbox"/>
Other: [Insert full name and role]			<input type="checkbox"/>
Clinical Site	Yes	No	Comments
<i>Have there been any investigator/sub-investigator changes since the last visit? (If yes, ensure CV on file and HREC notified)</i>	<input type="checkbox"/>	<input type="checkbox"/>	
<i>Have there been any changes in other staff members since the last visit? (If yes, have the new staff members been trained? Are tasks appropriately delegated?)</i>	<input type="checkbox"/>	<input type="checkbox"/>	
<i>Does the facility remain adequately staffed?</i>	<input type="checkbox"/>	<input type="checkbox"/>	

2) Document Cross-Check

Monitoring Visit Confirmation Letter + Follow up Letter

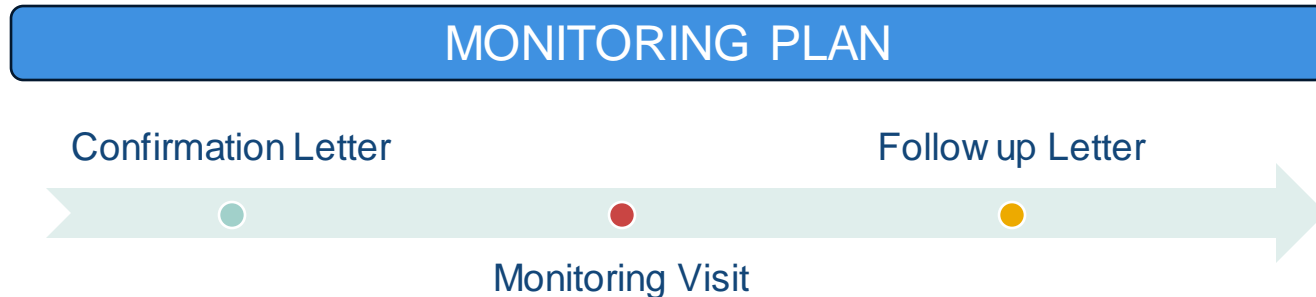


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Sub-investigator: [Insert full name]		<input type="checkbox"/>	
Research Nurse: [Insert full name]		<input type="checkbox"/>	
Study Coordinator: [Insert full name]		<input type="checkbox"/>	
Data Coordinator: [Insert full name]		<input type="checkbox"/>	
Pharmacist: [Insert full name]		<input type="checkbox"/>	
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Does the facility remain adequately staffed?	<input type="checkbox"/>	<input type="checkbox"/>	



3) TMF Oversight

To verify if compared with Monitoring Visit log, all the Monitoring Visit reports have been filed (**Completeness**); if they have been filed in a timely manner as per Monitoring plan (**Timeliness**) and if they are accurate (**Quality**).



4) Inspection Readiness



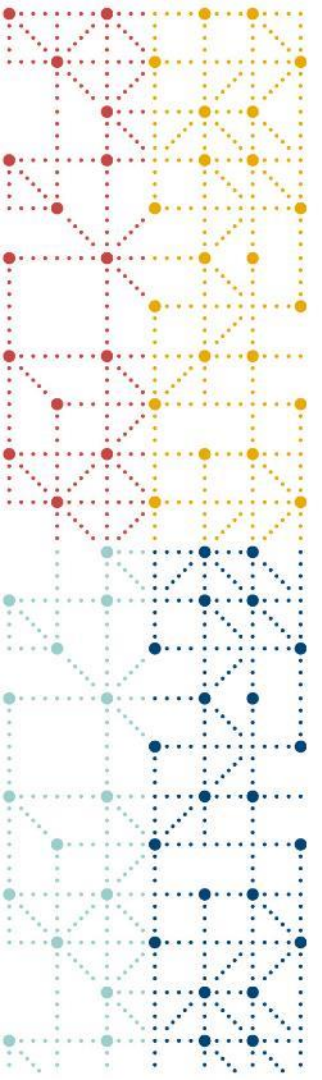
The document is in compliance with ALCOA ++ and GDocP
The linked documents are all there and they are good
The process agreed in the Monitoring Plan has been followed



The document is not readable and the signature is missing
Some follow up letters are missing
The Monitoring visit happened late

GCP FINDING LOG

CAPA PLAN



Take Home message



Agile TMF means...

TMF as source of data to develop preventive action

TMF as a source of data to make informed decision

TMF to plan the future process model

TMF as source to detect deficiencies and improve the process

TMF to identify trends

TMF to share knowledge

Awake your inner TMF Jedi for TMF readiness

The TMF Jedi's Code:

“Always ready for inspection we must be, agile in our ways, complete, timely, and high-quality our TMF stays.”



Thank You!

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