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WEBINAR

Solving the eTMF Conundrum: Strategies for TMF Success

August 10th 2017

Presented by
Paul Fenton – President & CEO, Montrium

About Montrium

Connecting **People**, **Processes** and **Technology**

Focused on providing content and quality management solutions to the life sciences

- Founded in 2005
- Working Exclusively in the Life Sciences
- Headquartered in Montreal
- Clients in North America and EU
- Focused on ECM Solutions
- Experienced Professional Services Group

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What We Do

We provide cost effective solutions to the Life Sciences

Clinical Solutions

Electronic Content Management Tools for Clinical Trials

Regulatory Solutions

Regulatory Document Management for Life Sciences

Quality Solutions

Integrated Quality Management for Life Science Organizations

Professional Services

A Range of Professional Services from Life Science Experts

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Our Presenter

Paul Fenton
CEO & Founder
Montrium

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Today's Agenda

What we'll be covering today

- Evolving Expectations of the Regulators
- Trial Master File (TMF) Planning to Ensure Timeliness
- Centralizing Content Through Technology
- the 5Ws of TMF Planning
- Challenges of calculating TMF completeness
- Features of your eTMF needs to facilitate inspections

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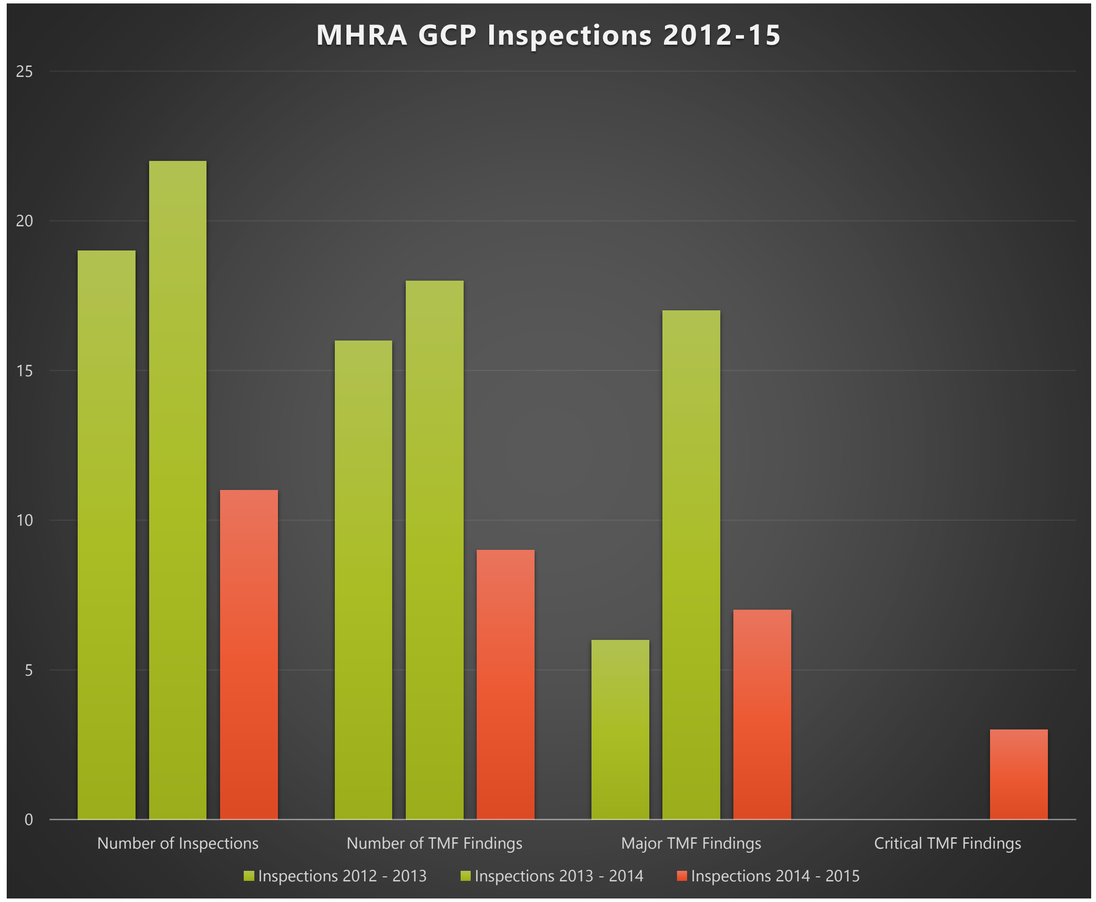
1 Evolving Expectations of the Regulators

Did you know….

- Between 2012 and 2015, MHRA conducted 52 GCP Sponsor Inspections
  - **82%** of these inspections had **TMF** findings
  - 58% of the findings were major
  - 22% of the findings were critical*
  - 20% of the inspections needed extra days due to the TMF



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New guidance - EMA

- EMA - Guideline on GCP compliance in relation to trial master file (paper and/or electronic) for content, management, archiving, audit and inspection of clinical trials - Public consultation finished in July
- Expected to become a final guidance document towards the end of 2017
- Key points within the guidance:
  - Provides clear guidance on how inspectors want to access eTMF – direct access to complete eTMF as well as access to data contained within other systems
  - Provides data integrity requirements for eTMF systems
  - Discusses multiple systems and outsourced activities including sponsor access to eTMF
  - Provides guidance on destruction of paper records (certified copies)

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New Guidance - FDA

- Use of Electronic Records and Electronic Signatures in Clinical Investigations Under 21 CFR Part 11 – Questions and Answers
- Not specific to TMF but relevant
- Key Points within guidance:
  - Provides guidance on destruction of paper records (certified copies)
  - Requires a signature on certified copies
  - Discusses use of external vendors to manage records and cloud computing

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POLL

Q: Have you been involved in a regulatory inspection utilizing an eTMF in the past 12 months?

A: Yes
B: No

2 Centralizing Content Through Technology

eTMF is decentralized..

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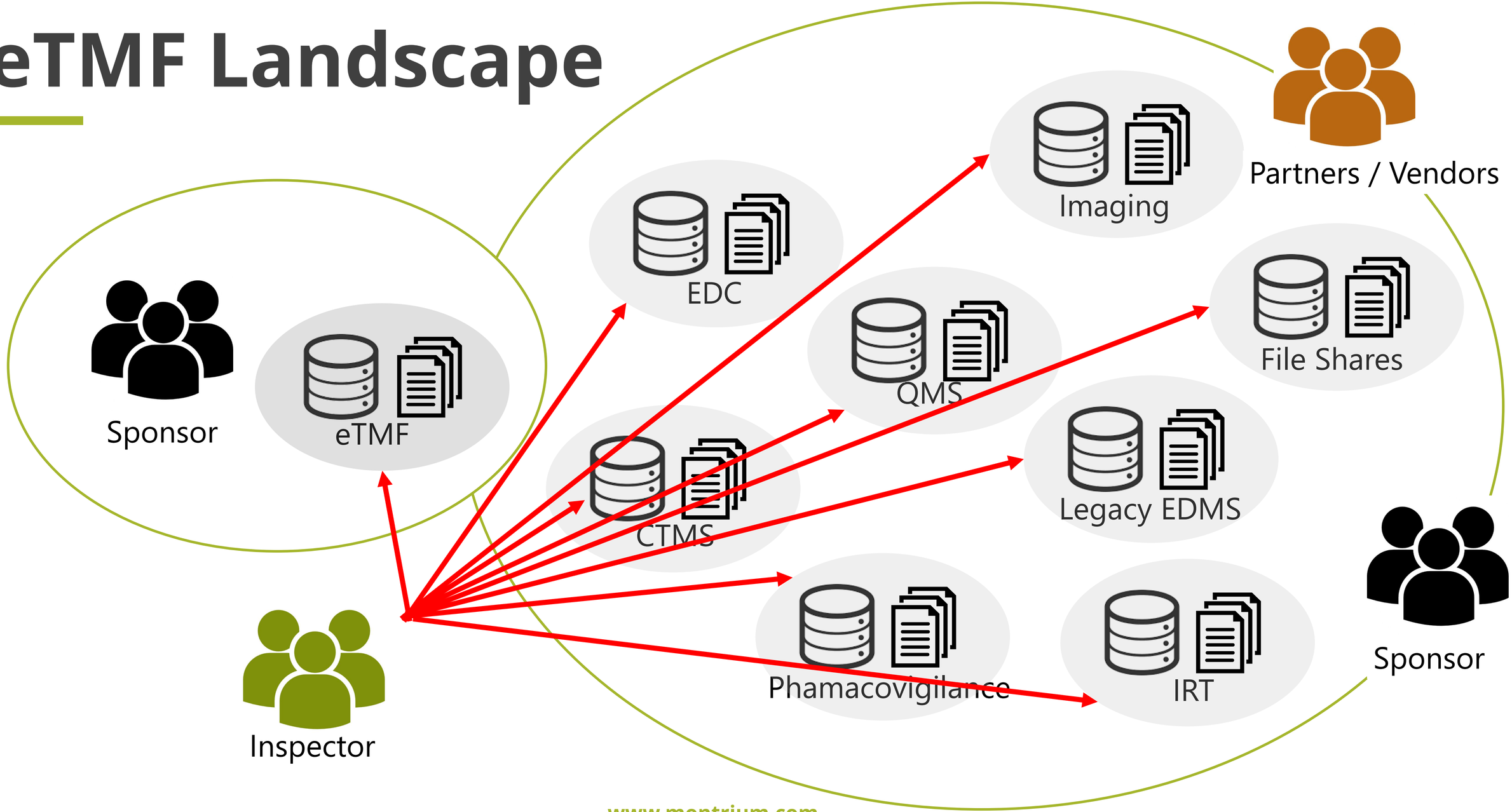
eTMF Landscape



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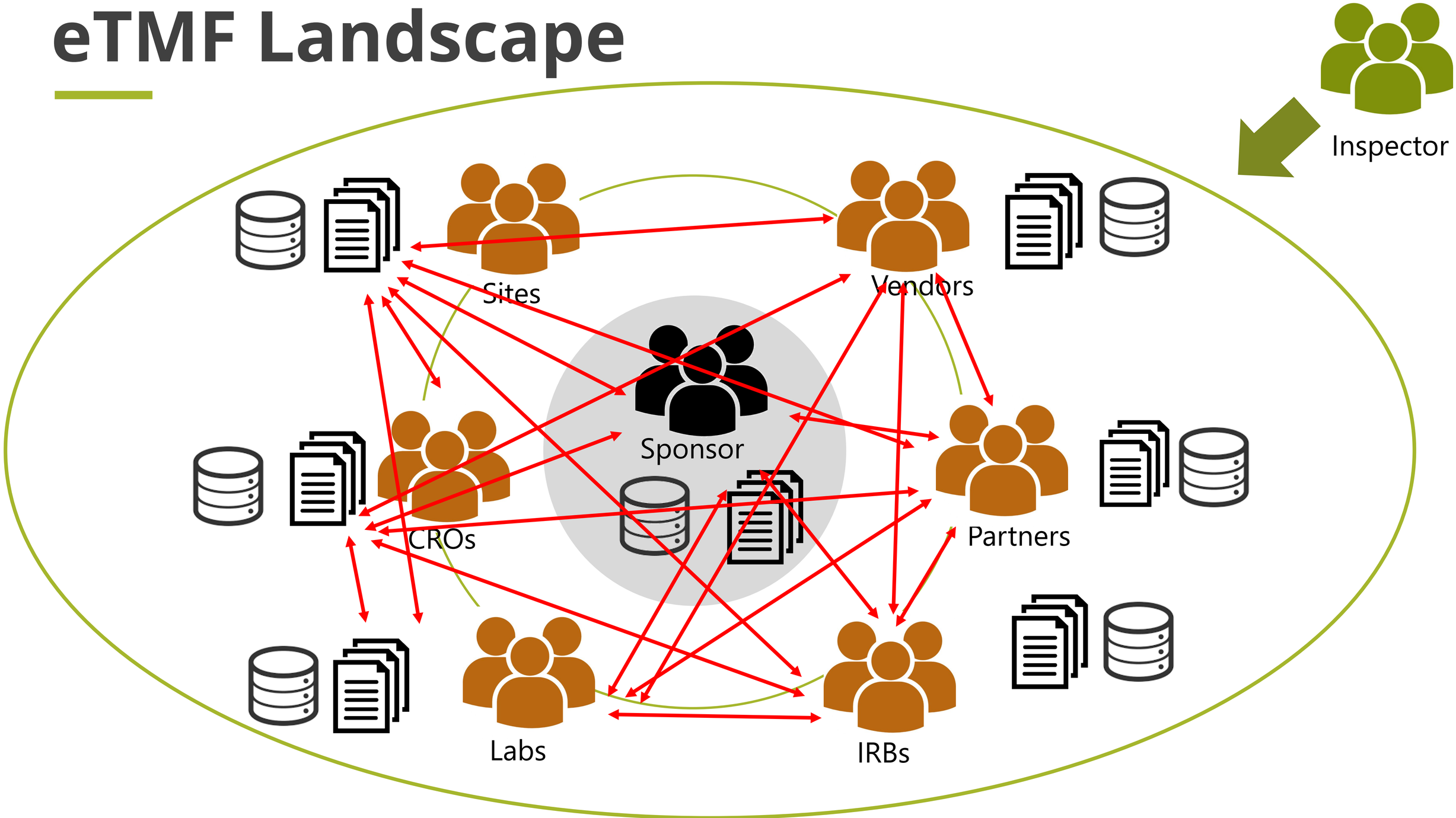
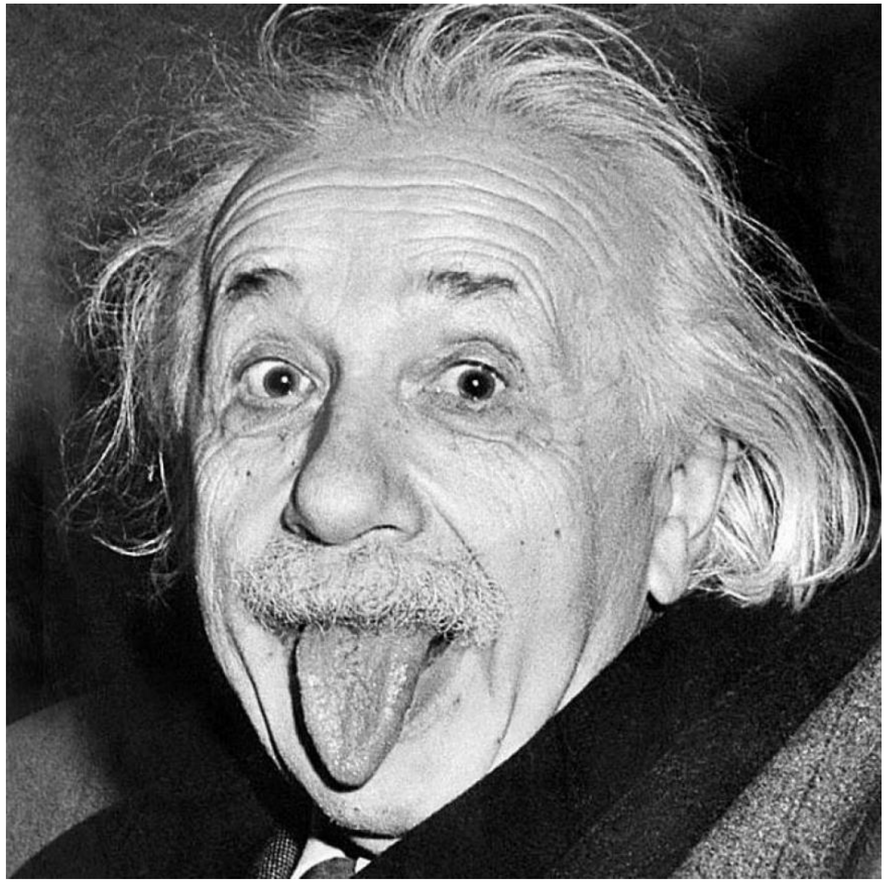
eTMF Landscape





“We cannot solve our problems with the same thinking we used when we created them.”

-Albert Einstein

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Not a new problem...
but still a problem...

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POLL

Q: What is your biggest challenge when preparing an eTMF for inspection?

A. Identifying where all content is
B. Getting system access for inspectors
C. Copying all content to the primary eTMF
D. Printing out the eTMF

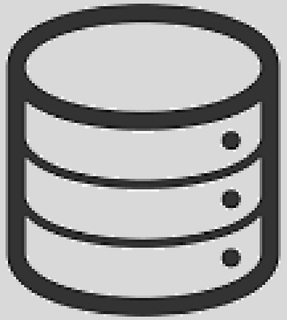
Centralizing Content – Identify

eTMF Plan

1

Identify what you consider to be TMF content

+



2

Identify which systems hold eTMF relevant content

3

Identify what content is being held in which systems

The 5 Ws

eTMF Plan

- Same principle as a TMF plan
- Electronically held within the primary eTMF system
- Provides an eTMF plan with

What: Expected artifacts

Who: Roles and responsibilities

When: Milestones, Events, timeliness standards

Where: Systems that hold the authoritative source

Why: Processes and events

- Can be used to calculate completeness and timeliness?
- Can be used to allow the inspector to more easily navigate the eTMF

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What – Expected artifacts

- Remember that the TMFs primary use is to tell a story
- Define what needs to be collected based on this assumption (not just ICH E6 8.x)
- Expected artifacts form the basis of system configuration for a study
- Remember artifacts may also be data, not just documents
- Look for systems that allow you to define your own standards based on study design
- Identify what is inspectable and in what state

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Who – Roles and Responsibilities

- Define internal and external organizations and roles
- Associate these to artifacts within the system
- It should be clear to the inspector who is responsible for providing what

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When – Milestones, events and timeliness

- Define different milestones at study, country and site levels and associate with artifacts
- Identify events and what information should be available in the TMF to support and document these events
- Ensure that you have a clear system for measuring and demonstrating timeliness – identify the key dates that will be used and establish a standard
- Associate timeliness calculation method to artifacts
- Ensure the system is able to calculate and show timeliness during an inspection

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Where – Identifying authoritative source

- Clearly identify which system holds the authoritative source for each artifact
- If shadow copies are being stored in the primary eTMF then this should be clear in the eTMF plan
- Ensure that placeholders are present for artifacts being maintained outside of the primary eTMF
- Better still provide hyperlinks if possible
- Determine how you will integrate with 3rd party systems to present information in one place or
- Determine how you will provide access to the information

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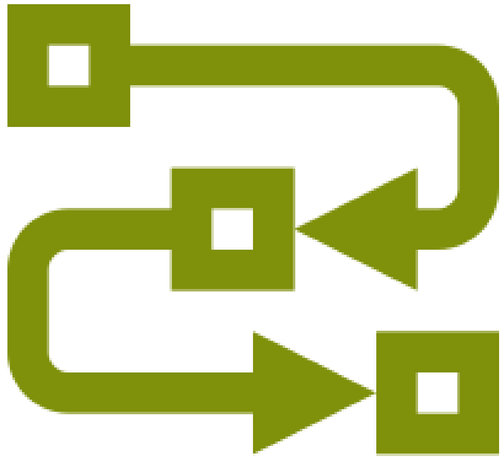
Why – processes and events

- Ideally associate which process or event generates which artifact
- You should indicate where an artifact is mandatory or not
- The ideal system will allow the inspector to navigate within and across processes or from a specific event
- **VERY CHALLENGING** to put in place – very different approach to the current way of presenting an eTMF



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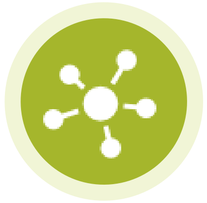
3 Models for Centralization



The Cross Referenced

The All-in-One

The Clone

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System Model 1 – The Cross Referenced

Multiple systems with placeholders in primary eTMF to cross reference artifacts	
Pros	**Cons**
• Easy to setup and manage from an individual system standpoint • Less training and user management	• Challenging to provide access to inspectors if many systems involved • Can be labor intensive to cross reference artifacts and maintain consistency between systems • Long term archiving can be difficult

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System Model 2 – The All-in-One

All stakeholders work in one system	
Pros	**Cons**
• All content in one place – easier to inspect • All content within the system is authoritative • More consistent inspection process • Easier archiving	• Some content contained in other systems i.e. CTMS cannot be managed within the eTMF without copying • Not all study stakeholders will be able to or want to use the system

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System Model 3 – The Clone

Primary and shadow copies in multiple systems	
Pros	**Cons**
• A complete copy of the eTMF present in all systems • Easy to inspect • Better able to meet timeliness requirements	• Requires integration with systems or manual processing • Difficult to transfer and reconcile • Expensive to maintain ***TMF RM Exchange Standard could help…***

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TMF RM Exchange Standard
The Initiative

- A **technical sub-committee** composed of sponsors, CROs and vendors was established
- **Objective: To define a standardized and simple mechanism for transfer of eTMF content**
- Used existing standards such as **eCTD** and **CDISC** as inspiration
- **Work in Progress….**

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How could it be used?

- **Final eTMF transfer** to sponsor from CRO for filing
- **Interim transfer of eTMF** content to central eTMF or other trial management systems
- **Migration of eTMF** content following **merger and acquisition**
- **Migration of eTMF** content following **upgrade** or change of eTMF system
- **Long term archiving** of eTMF content and associated metadata

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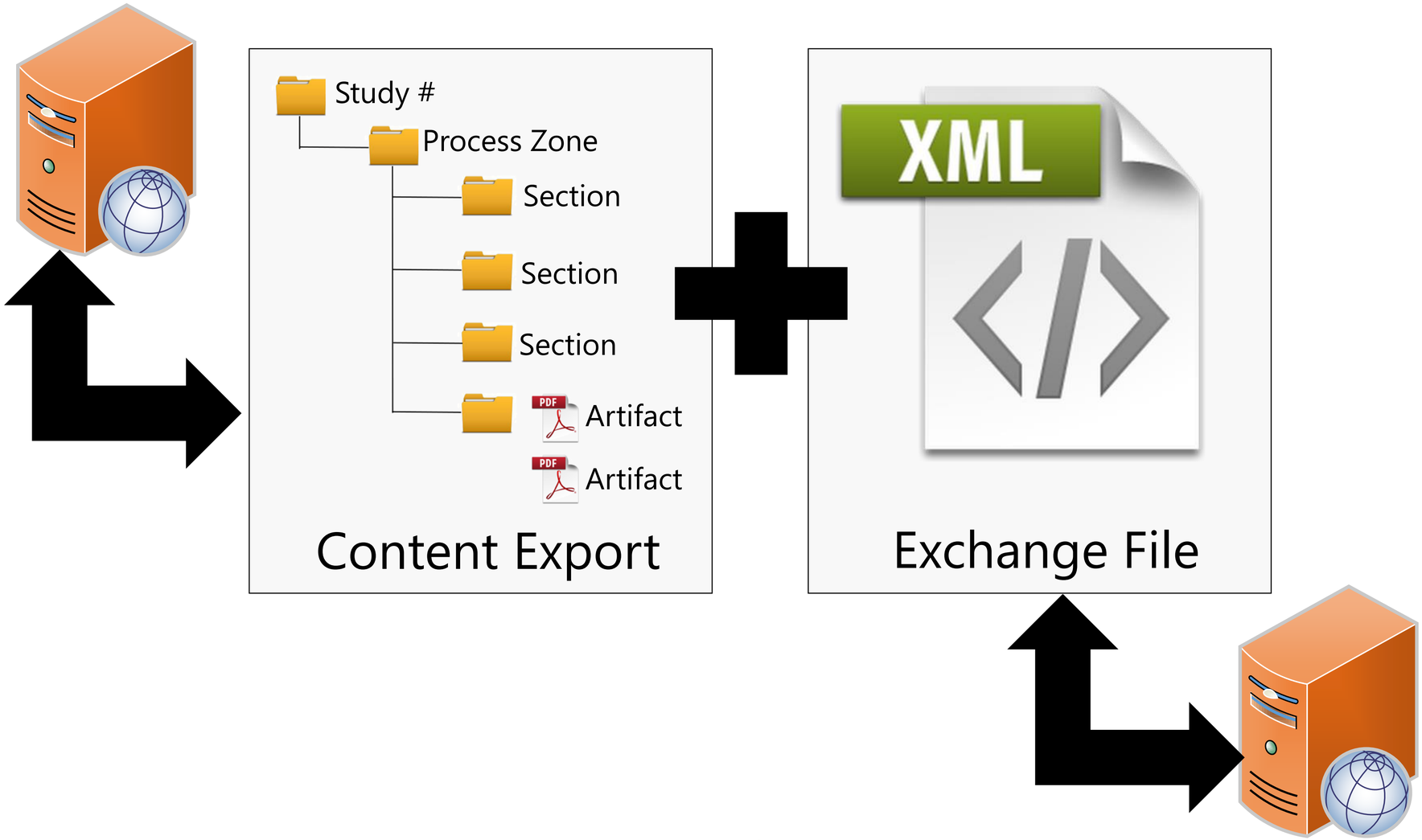
How it works – In simple terms…



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How the standard could help in inspection readiness

- Would allow the **exchange** of artifacts or information **between different systems** easily
- **Import** of this information could be **automated**
- Clearly indicates whether an artifact is a **copy or authoritative source**
- Can be used for **interim / ongoing** transfers
- Could significantly **reduce preparation time** for inspections while providing **one environment** for the inspection

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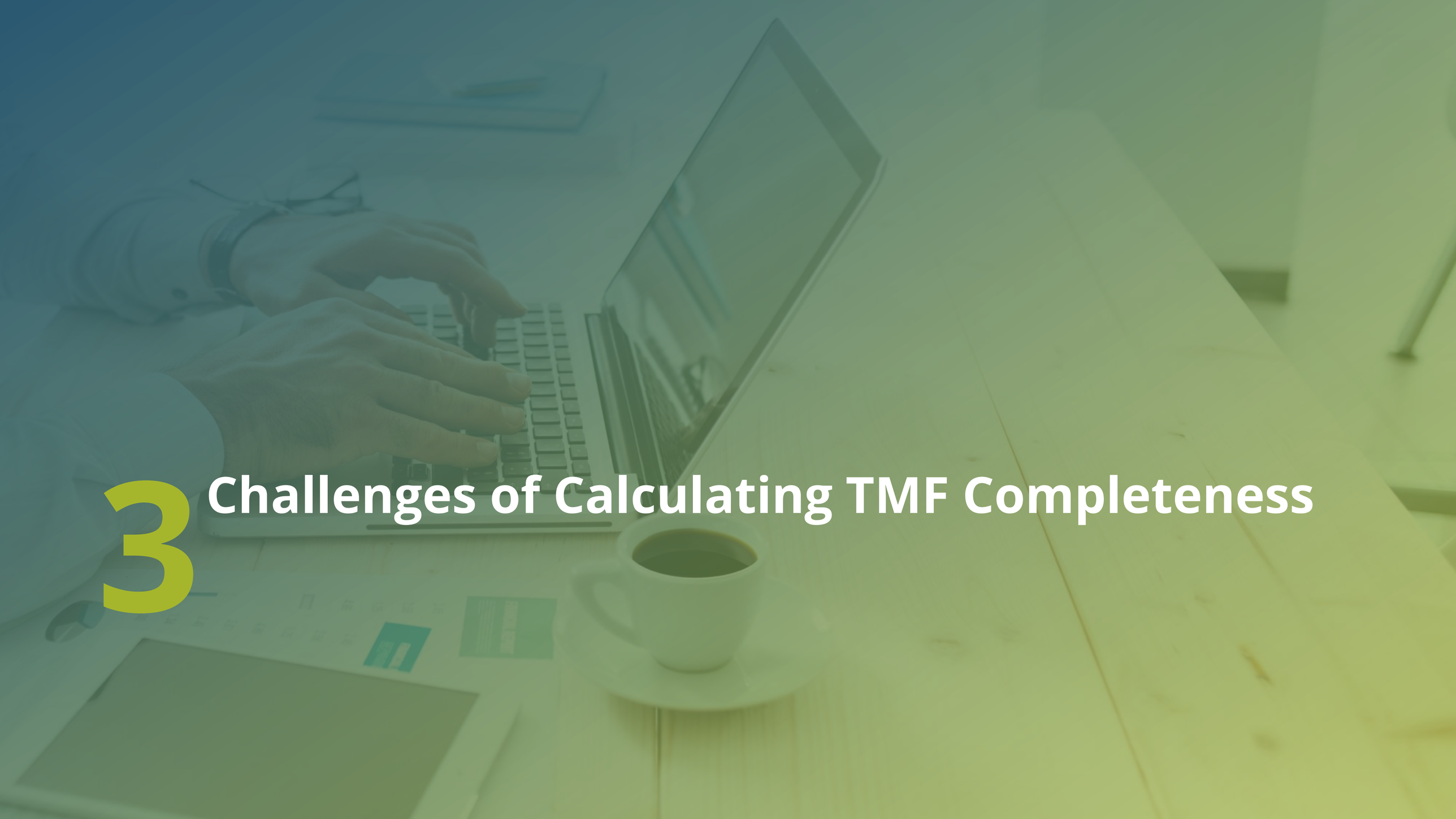

3 Challenges of Calculating TMF Completeness

eTMF Completeness is not an exact science….

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Challenges of eTMF Completeness Calculation

- **Accuracy** is a big issue
- Much content is unstructured i.e. **emails**
- Dependent on study **design**, **regional** requirements, study **events,** study **organization** and **milestones**

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Challenges of eTMF Completeness Calculation

- **Systems** need to be more **agile** in being able to calculate completeness **intelligently** based on these attributes
- **Connectivity** between systems and **sharing of information** is the **foundation** of being able to calculate **completeness accurately**
- The **TMF RM exchange standard** may be able to help with this in the future

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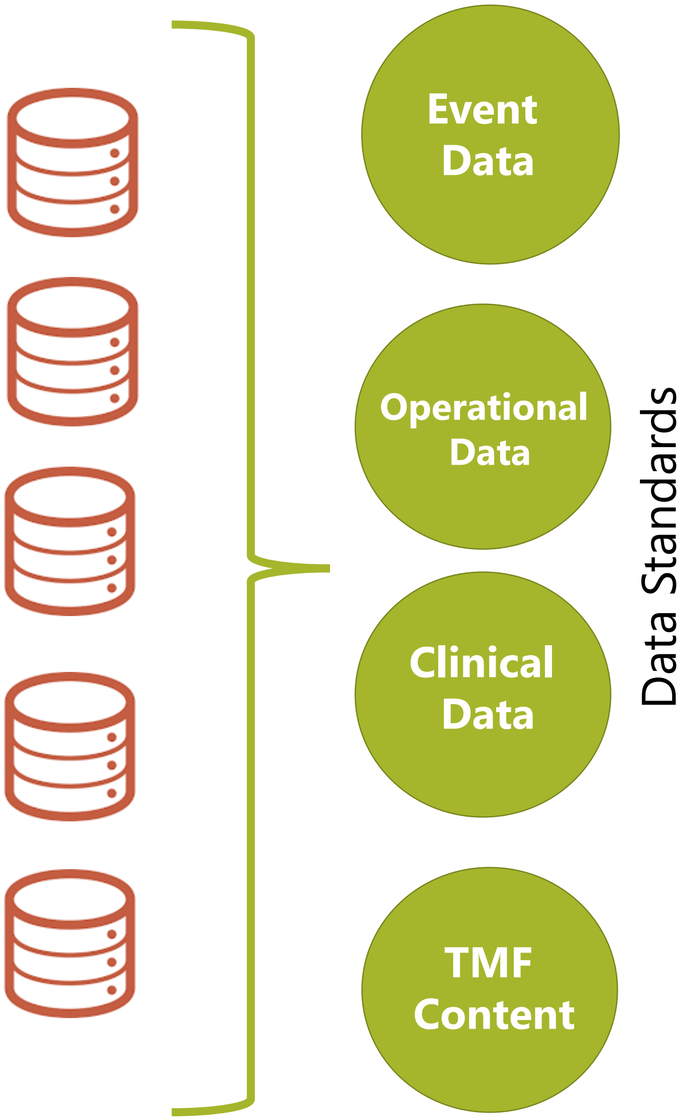
Future solutions for TMF Completeness



Event Data

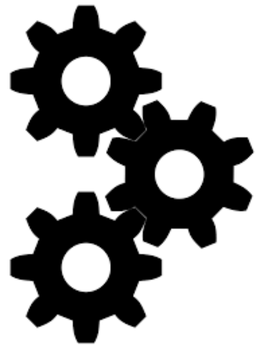
Operational Data

Clinical Data

TMF Content

Data Standards

Data Warehouse



Intelligent Algorithms

Study Team

Visualization

Inspector

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POLL

Q: How accurate do you think eTMF completeness calculation is in your organization?

A. 100% accurate
B. Very accurate
C. Somewhat accurate
D. Not very accurate
E. I don’t have an eTMF

Recommended approach

- Start with the **easiest** attribute – **milestones**
- Build eTMF **plans** based on **different** study designs
- Identify **study events** which would require **artifacts** i.e. protocol amendment, safety case
- Consider **systems integration** and/or **data warehouse** to improve accuracy of event data
- Evaluate **data needs** to identify and calculate completeness of artifacts contained outside of the primary system
- Implement a **eTMF completeness program** to build up capabilities over time
- Leverage **historical data** and **predictive algorithms** to **improve accuracy**

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4 Features your eTMF Needs to Facilitate Inspections

Key System Features Required

- Ability to filter content to show only **relevant content** which is **final**

- Ability to **easily provide access** with minimal training or self-training

- Ability for inspector to leave **placeholders, sticky notes and questions**

- Ability to **track** what the inspector has actually looked at

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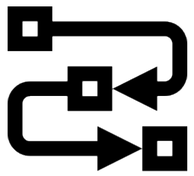
Key System Features Required

- Ability to mark attributes as **complete and inspection ready**

- Ability for the inspector to use **filters** and **structured / unstructured search** capabilities to easily find content

- Ability to prepare **‘electronic binders’** of artifacts which can be provided to the inspector in the system following a request



- Ability for the inspector to **trace** through a particular **process, event or aspect of the study**

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Key System Features Required

- Ability for the inspector to understand what is **authoritative source** versus copies
- Ability for inspector to **click through** to another system holding artifacts (?)
- Ability for the inspector to **access the system remotely (?)**

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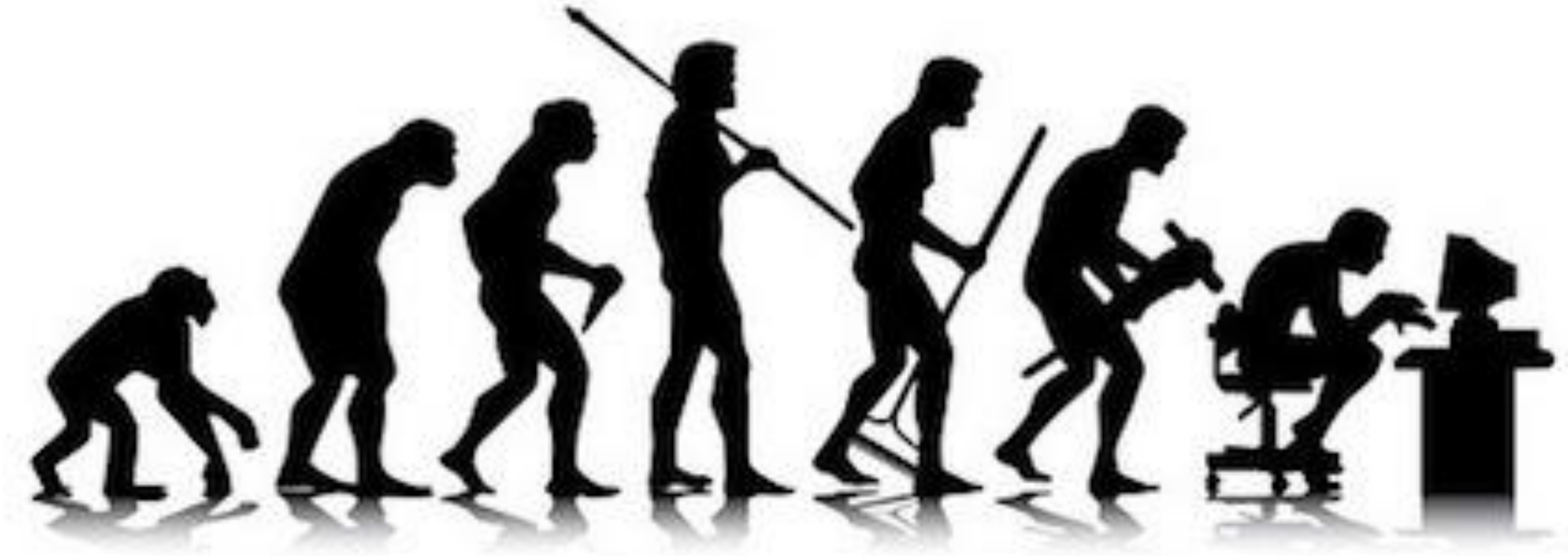
POLL

Q: Do you think that inspectors should be able to access the eTMF remotely?

A. Yes
B. No
C. Maybe….under certain conditions



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ANY QUESTIONS?

Ask your questions now!

Get in Touch

We're here to answer any questions

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