

A panoramic view of the Berlin skyline at sunset, featuring the TV Tower (Fernsehturm) and various city buildings.

2024 CDISC + TMF  
EUROPE INTERCHANGE

**BERLIN**

24-25 APRIL: CONFERENCE & EXPO | 22, 23, 26 APRIL: TRAININGS

**There is something rotten in the realm of the TMF  
Why the eTMF doesn't deliver to its promise**

Presented by Dr. Max Horneck, CEO, elderbrook solutions



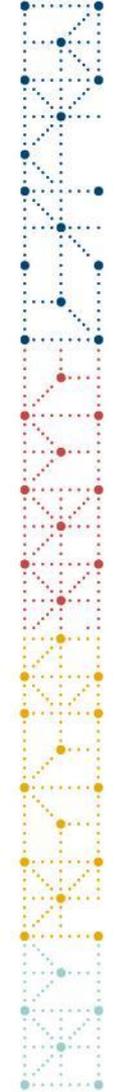
# Meet the Speaker

Dr. Max Horneck

**Title:** CEO

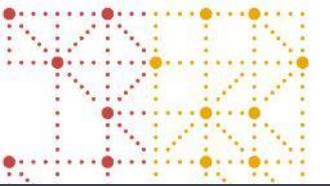
**Organization:** elderbrook solutions GmbH

- > 30 years in the biopharmaceutical industry
- Data and IT expert
- eTMF experience
  - Developing an eTMF System @maxclinical
  - Consulting eTMF vendors in the development of eTMF
  - Consulting CROs, Sponsors in eTMF selection and introduction
  - System owner of eTMF @medac



# Disclaimer and Disclosures

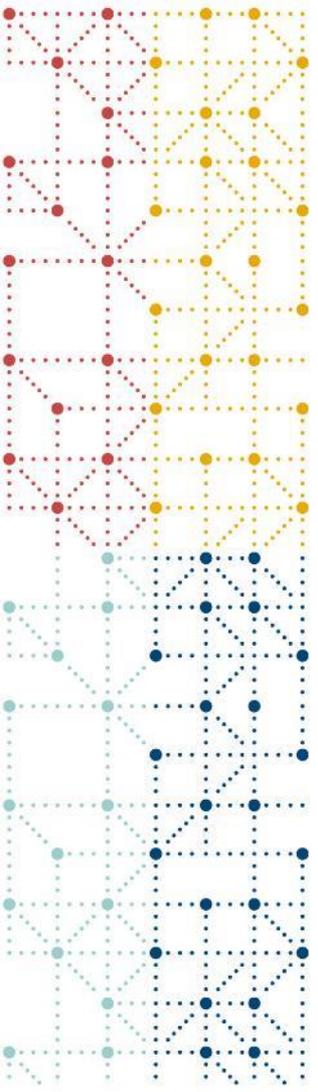
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- The author has no conflict of interest to report



**There is something rotten in the realm of the TMF  
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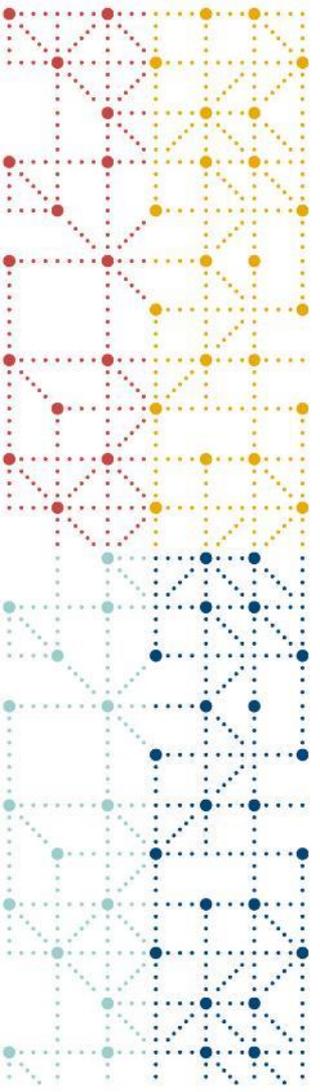
**A polemic**





## Agenda

1. The good old days that never were
2. Introducing the better solution - A new Sheriff in Town
3. So, where are we today
4. Some thoughts on root causes
5. Is there hope?



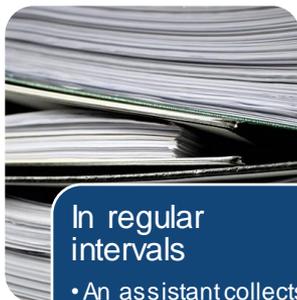
## The good old days that never were

Because what you have in black and white  
you can take home with confidence

# The benefits of the paper TMF

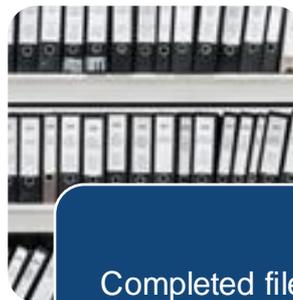


An author places a finished document in the storage basket



In regular intervals

- An assistant collects the documents
- Perforates them
- And staples them in the appropriate section of the file folder.



Completed file folders are moved to the TMF cabinet.



At the end of the trial all documents are properly filed in the TMF cabinet.

# Culture eats strategy for breakfast



- Paper handling is taught in schools
  - A paper process is easy to understand
  - Filing can be done by support staff
  - Document owners see their physical document moving
  - A paper can be modified, annotated
  - Storage is a physical process
- 
- Why did we make a change to something as simple as this?

# Let's talk money!



As a rule of thumb, managing the TMF of a very average to mid-sized Phase 3 trial in the

- 10-center, 100 patients
- 4-years overall duration,
- 3-4 countries range

would cost approximately 60 to 80 thousand Euros in CRO costs.

- Why did we change something that was so cheap to do?

## ... that never were

Why did we make a change to something as simple as this?

Why did we change something that was so cheap to do?

The dark sides of this simple process:

Documents were often kept in inboxes for extended periods, filed incorrectly, and sometimes went missing.

Changes were made to some documents without informing everyone involved.

Additionally, documents were collected in various locations, leading to inconsistencies and duplication.

Proving the completeness of the TMF during inspections was difficult.

Finalizing the TMF took a long time.



# Introducing the better Solution – a new Sheriff in Town

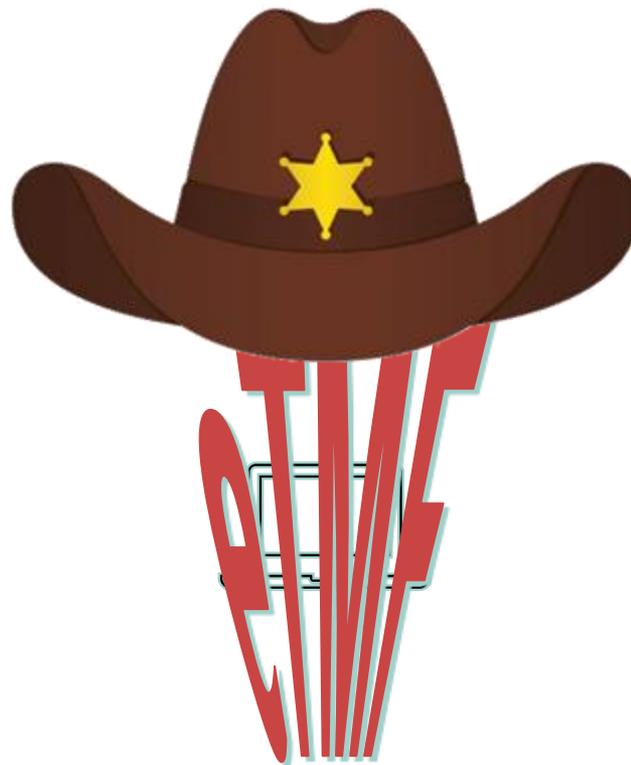
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# Introducing the better Solution – a new Sheriff in Town



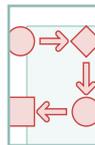
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Workflows for immediate filing and QC



Full audit trail and history on documents



Single digital storage location globally accessible



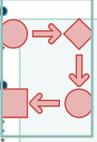
Completeness reports, extensive search functionality

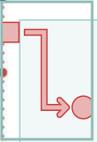


Event driven document requests

# All's well that ends well?



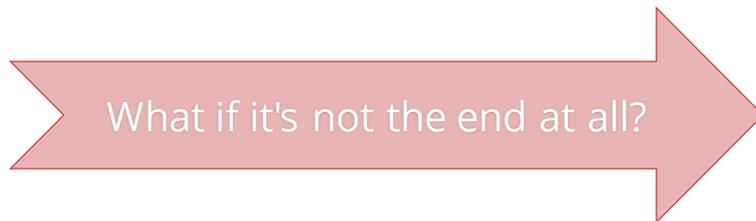
 Workflows for immediate filing and QC

 Full audit trail and history on documents

 Single digital storage location globally accessible

 Completeness reports , extensive search functionality

 Event driven document requests



# So, where are we today?

## Observations from Real Life:

Discussions about how to manage the TMF often get bogged down in unnecessary issues.

- System management roles and responsibilities
  - Deciding which system (sponsor or CRO) to use
  - Naming conventions
  - Filing responsibilities
- Significant delays in system availability (total or by trial)

# So where are we today?

## Observations from Real Life:

Discussions about how to manage the TMF often get bogged down in unnecessary issues.

It takes forever to get the eTMF in place.

- Historically grown processes are not agile
- Living documents are not understood as such
- High volatility at CRO staff results in repeated training
- Systems are duplicated

# So where are we today?

## Observations from Real Life:

Discussions about how to manage the TMF often get bogged down in unnecessary issues.

It takes forever to get the eTMF in place.

CRO staff are discouraged from using the sponsor's eTMF.

- When a CRO has implemented an eTMF, processes are tailored to the internal eTMF system.
- Interfaces with other systems (e.g. CTMS) are built.
- Employees with highly specialized roles are trained on the exact process supported by the CRO system.

# So where are we today?

## Observations from Real Life:

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CRO staff are discouraged from using the sponsor's eTMF.

Filing is a distributed process with a loss of document ownership.

- A poorly designed TMF process kills document ownership.
- Filing is disconnected from business.
- Filing specialists work mechanistically.
- A simple process becomes opaque.

# So where are we today?

## Observations from Real Life:

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Filing is a distributed process with a loss of document ownership.

Transferring a CRO eTMF to a sponsor is not a standardized process.

- Still waiting for a TMF exchange (data) standard.
- Adopting proprietary variations of the TMF reference model.
- Heavy reliance on naming conventions.
- Data transfer of large amounts of data not anticipated.

# So where are we today?

## Observations from Real Life:

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Transferring a CRO eTMF to a sponsor is not a standardized process.

An auditor or inspector immediately recognizes process violations and sloppiness.

- Inspectors and auditors expect access to the system.
- They can use reporting tools.
- Late efforts to “fix the TMF” are clearly visible in the audit trail.
- Missing and incomplete records are highlighted by the system.

# So where are we today?

## Observations from Real Life:

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Transferring a CRO eTMF to a sponsor is not a standardized process.

An auditor or inspector immediately recognizes process violations and sloppiness.

Costs have skyrocketed when using modern technology.

- Changing the configuration is both cumbersome and expensive.
- Organizations switch systems during clinical trials, causing significant negative impacts.
- **Managing an eTMF costs more than 10 times the amount of managing paper TMFs.**

## There is something rotten in the realm of the TMF

Documents were often kept in inboxes for extended periods, filed incorrectly, and sometimes went missing.

Changes were made to some documents without informing everyone involved.

Additionally, documents were collected in various locations, leading to inconsistencies and duplication.

Proving the completeness of the TMF during inspections was difficult.

Finalizing the TMF took a long time.

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## There is something rotten in the realm of the TMF

Documents were often kept in inbox folders for long periods, filed incorrectly, and some were missing.

Changes were made to the process without informing everyone involved.

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Proving the completeness of the TMF for inspections was difficult.

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Discussions about how to manage the TMF often got bogged down in unnecessary issues.

It took a long time to get the eTMF in place.

Staff are discouraged from using the sponsor's TMF.

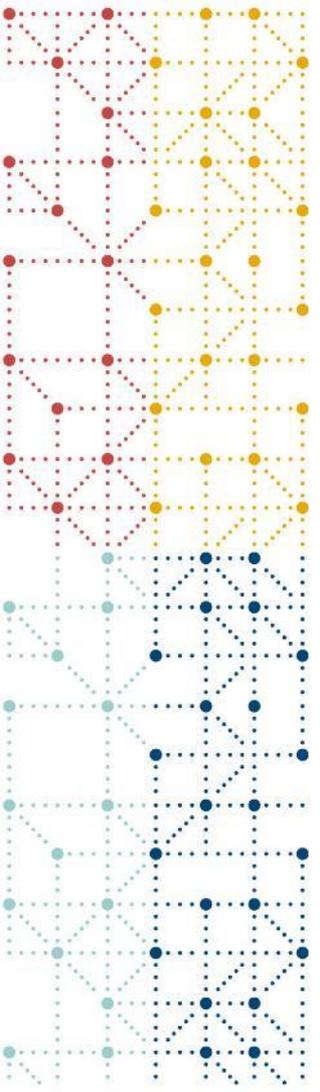
The TMF process is inefficient with a loss of productivity.

Getting the TMF to a sponsor is not a simple task.

The sponsor immediately recognizes the issues and sloppiness.

Staff are frustrated when using modern TMF systems.

Are we worse off than before?



# Thoughts on Root Causes

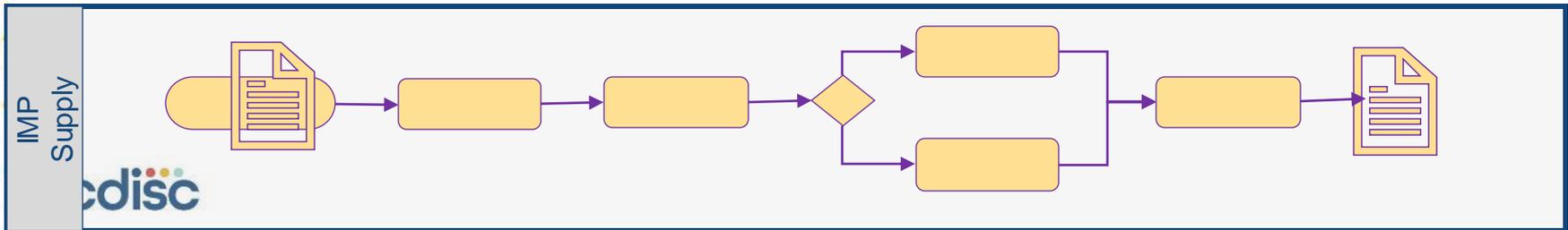
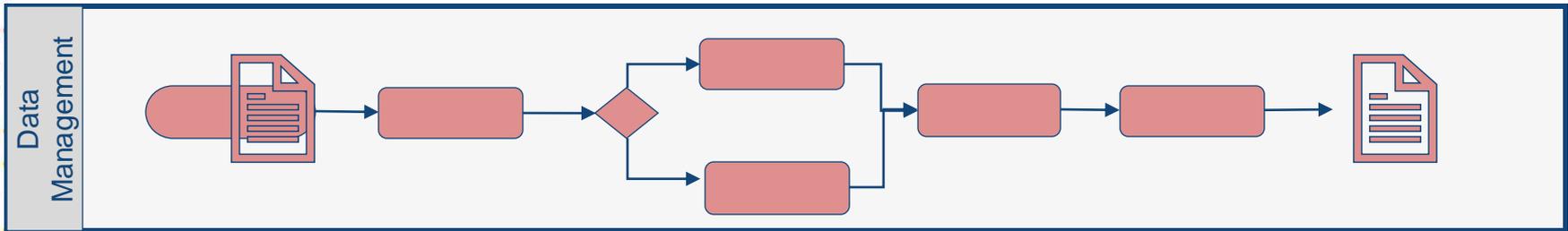
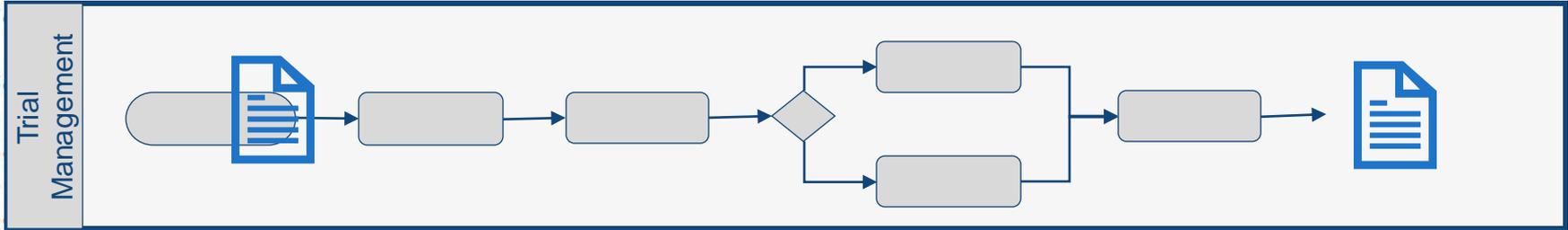


# The Bad and the Ugly... Potential Candidates for Failure

- The independent TMF process
  - Good Idea, Bad Result?
  - Crossing the Swimming Lanes
  - The Chinese Room Argument

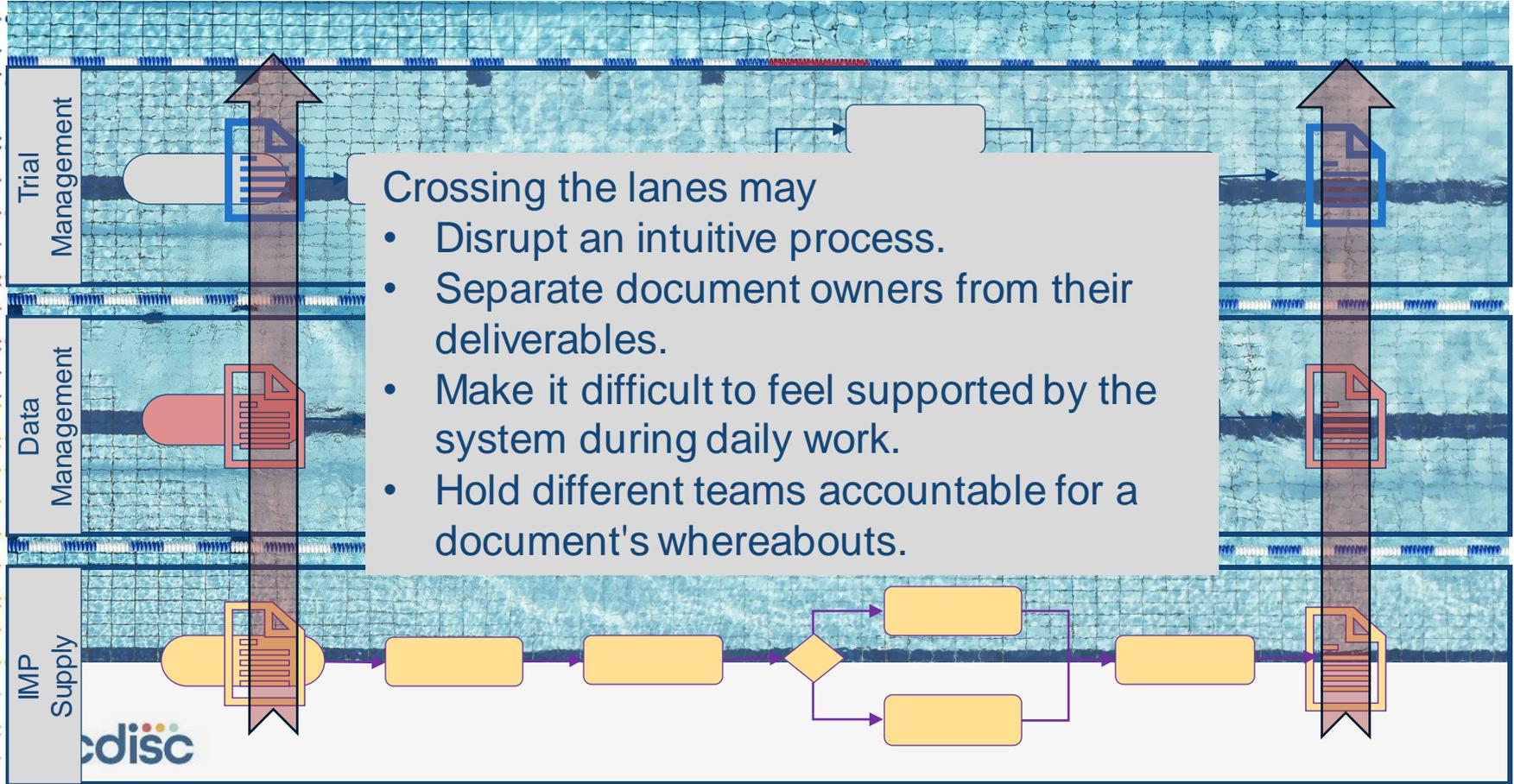
**I HAD A  
GOOD IDEA.  
ONCE.**

# What could be wrong with an independent TMF process?





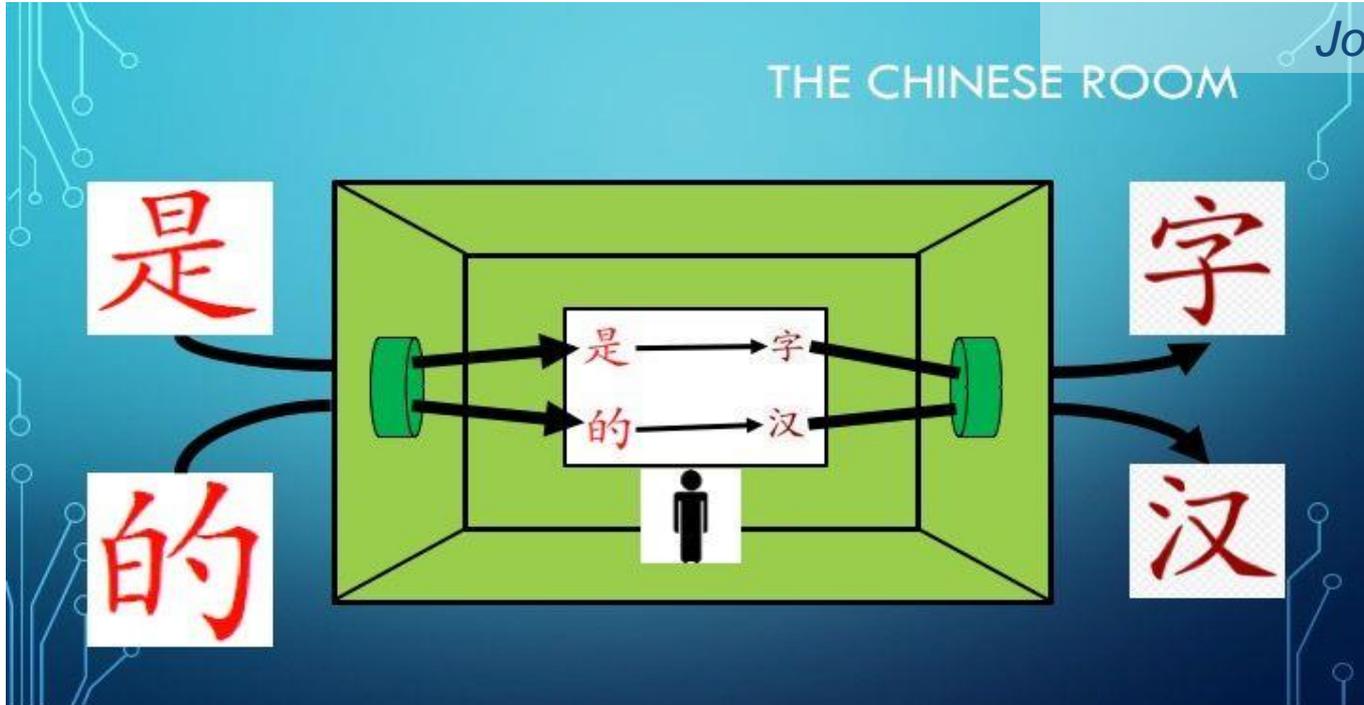
# Crossing the Swimming Lanes



# The Chinese Room Argument

*A person or computer following purely syntactic arguments (formal rules) may appear to understand language but does not produce real understanding.*

John Searle

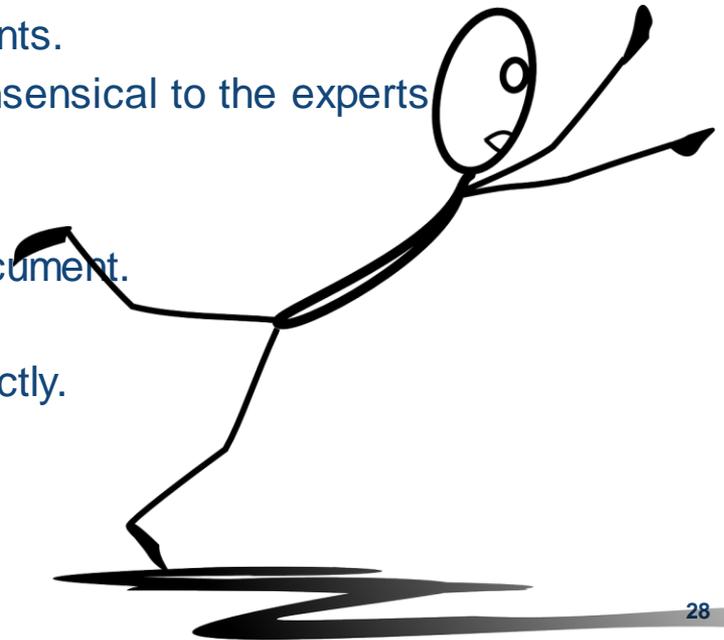


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- The teams that submit TMF documents
  - Are not specialists in the content of the documents.
  - Ask questions that are incomprehensible or nonsensical to the experts
  - Focus primarily on formal criteria.
  - Overemphasize details such as file names.
  - Do not always understand the meaning of a document.
  - Often work on many different projects.
  - May mix up projects and file documents incorrectly.



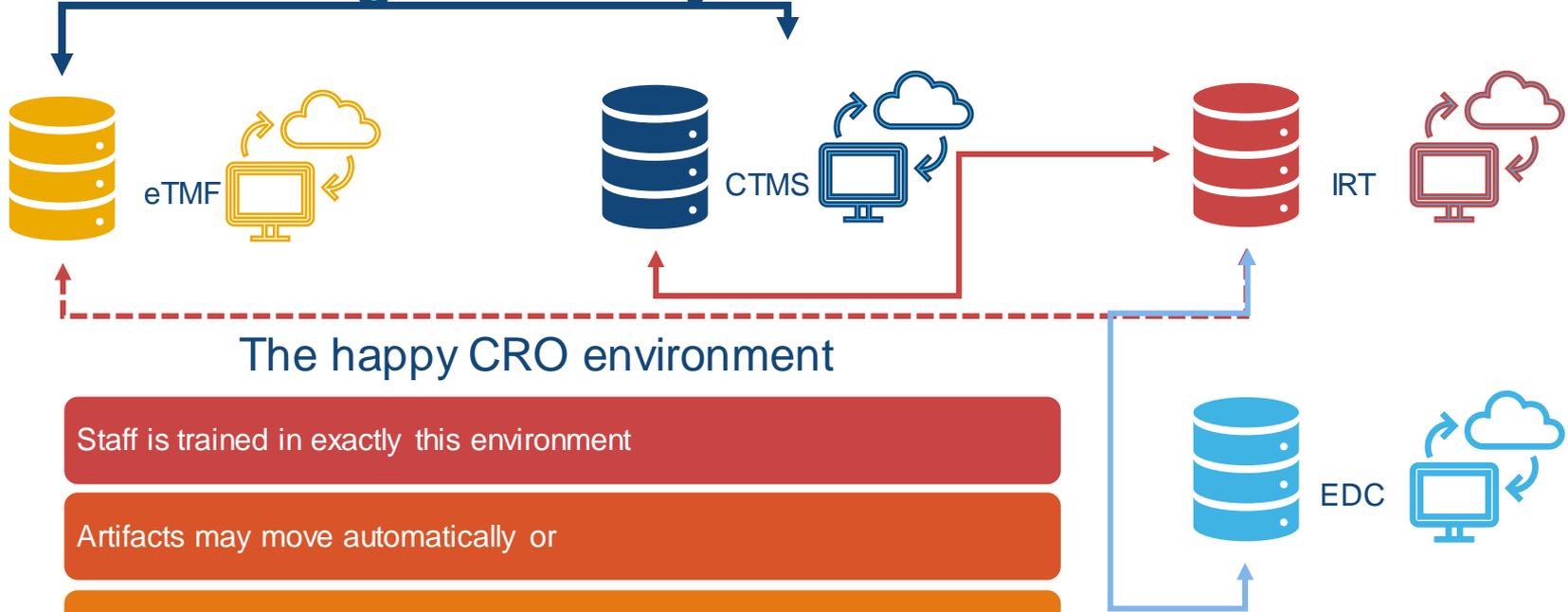
# The Bad and the Ugly...

## Potential Candidates for Failure

- **The independent TMF process**
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- **The systems trap**
  - Systems integration at CRO/sponsor
  - Staff training on very specific setting
  - Incompatible processes
  - Mixed setup (more than one eTMF)  
Transfer of TMF from CRO to sponsor
  - Final storage of eTMF



# What could possibly go wrong with the integration of systems?



## The happy CRO environment

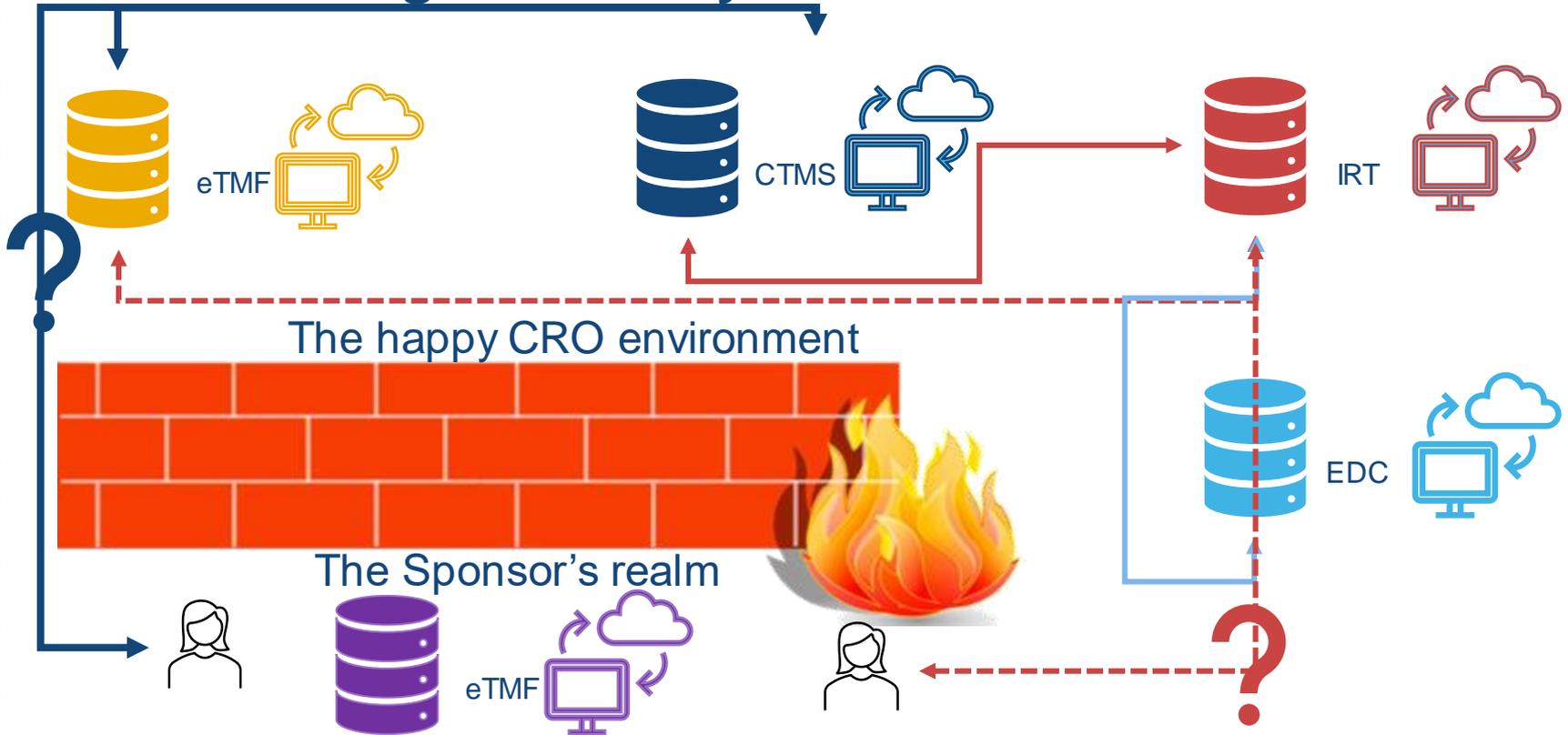
Staff is trained in exactly this environment

Artifacts may move automatically or

Transfer is a well established process

CRO feels free to change enhance or alter this complete setting or components

# What could possibly go wrong with the integration of systems?



# What could possibly go wrong with the integration of systems?

Keep CRO eTMF and copy to sponsor

Keep some documents here others there

Keep CRO eTMF transfer to sponsor

Work on sponsor TMF and change CRO internal process

## Duplication of systems

- Leads to the bad of two worlds.
- Leads to complex TMF maps.
- Leads to non-transparent status of the eTMF.
- Leads users to mix rules and conventions.
- Leaves end of study and post-study status in limbo.



eTMF



# The end is near!

## Where does the eTMF go?

- Keep it in the eTMF in an archived state?
- Transfer it to a document / records management system at the sponsor?
- Export it to permanent media (WORM) and file physically?



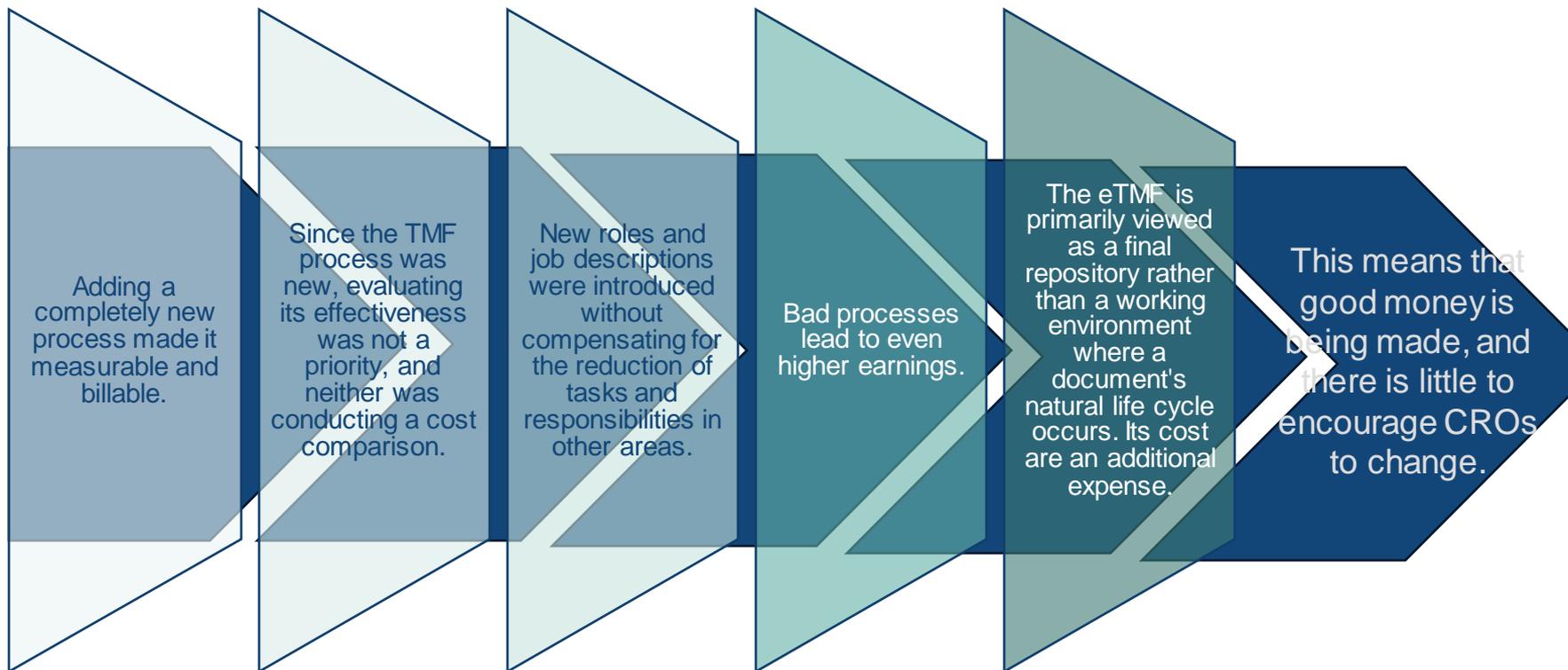
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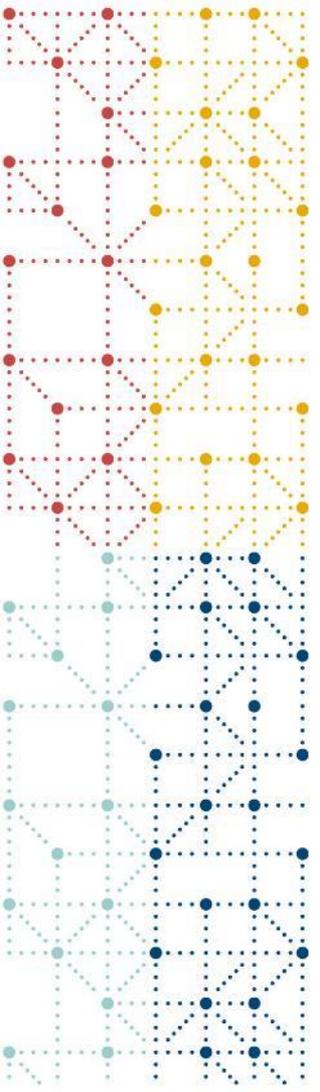
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Transfer of TMF from CRO to sponsor
  - Final storage of eTMF
- **The cash cow that wasn't there before**
  - New service
  - Agile required but not adopted
  - No incentive for vendors to change



# Vendors added eTMF management to the budgets





**Is there hope?**

Ideas for improvement...



**CONTINUOUS  
IMPROVEMENT**

## 2 paths to the goal

- Using established technology in the best way
  - Let the machines do the work
  - Let the machine learn
  - Use automation where possible
- Plan what can be planned
- Plan when it can be planned
- Be smart
- Learn during each single trial
- Continuously Improve your predictions
- Metrics are not an end in themselves, use them



## 2 paths to the goal



- Change processes in a way that
  - Chooses the right focus:  
The TMF is the place where a study should be traceable, however the TMF is not the purpose of the study.
  - Implements an agile planning process for the eTMF.
  - The eTMF is part of the natural document lifecycle.
  - The ownership of a document does not change throughout a document's lifecycle.
  - The eTMF is part of the natural document lifecycle.
  - The leading principle is good documentation practice, not just the mechanistic completion of process steps.

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- Using established technology in the best way

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- The ownership of a document does not change throughout a document's lifecycle.
- The eTMF is part of the natural document lifecycle.
  
- The leading principle is good documentation practice, not just the mechanistic completion of process steps.

# Don't forget the people!

Educating people instead of conditioning them to act like robots.

Train them in good documentation practice.

Ensure TMF experts are knowledgeable about trial processes.

Train the usage of metadata and document descriptions.

Empower TMF specialist staff to make sensible changes within limits.

Allow for sensible agility in trial processes.

Not all plans may be finalized prior to TMF start.

Adjust expectations and variables during the conduct of a trial.

Ensure, documentation is understood as part of process and not just an unpleasant annex.

Empower document owners to file

And ideally the final storage location should be the natural home within the eTMF.

During review and approval all required information for correct filing should be available.

Implement automated filing as part of the document life cycle.

## The rest is silence?



In many cases, the use of eTMF is unsatisfactory.



The costs of eTMF have reached unacceptable levels.



Technological evolution has not yet resulted in efficiency gains.

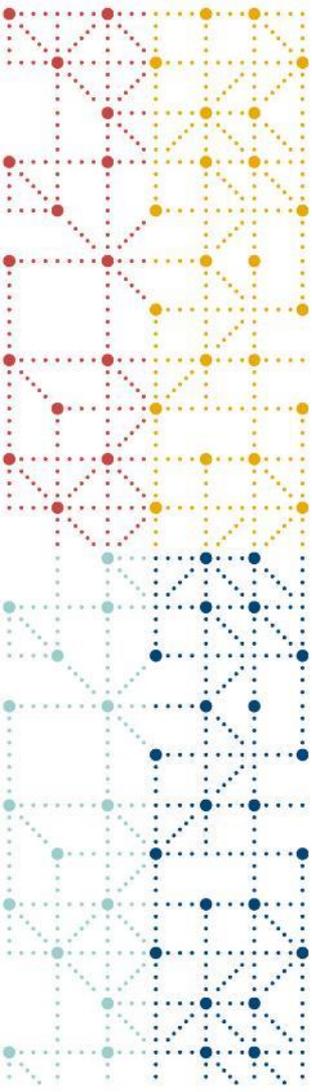


Proper use of existing tools could solve some issues.



To realize the promise of eTMF, a change in processes and culture still is required.





# Thank You!

There is something rotten in the realm of the TMF.  
Why the eTMF doesn't deliver to its promise

Dr. Max Horneck

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