ORACLE
Health Sciences

PHLEXGLOBAL

The Clinical Trial Technology Space

9th October 2019

Introductions

Jim Streeter

- Based in Burlington, Mass (Home Based in CT)
- Global VP Life Sciences Product Strategy
- 21 Years Life Science experience (Pharma, CRO, Software)
- Move the industry to event based data collection
- Patients are waiting

Karen Roy

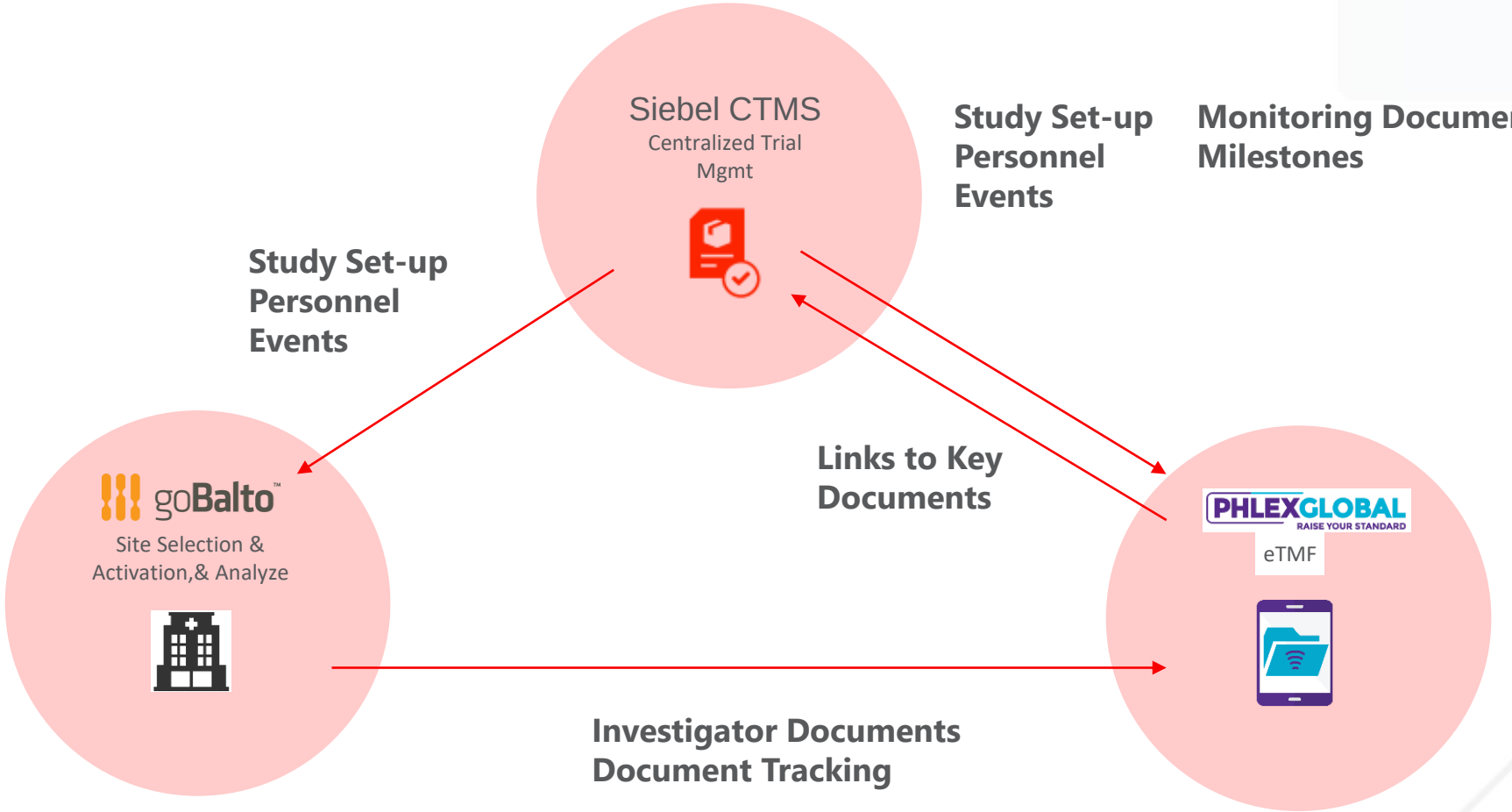
- Based in Amersham, United Kingdom (from Johannesburg, South Africa)
- Chief Strategy Officer at Phlexglobal Ltd
- 25 years Life Sciences experience (CRO and eTMF Vendor)
- Started the TMF Reference Model in 2009 - Chairman of the Steering Committee
- TMF = Too Much Fun, love good food…and wine too!

Oracle – Phlexglobal Partnership

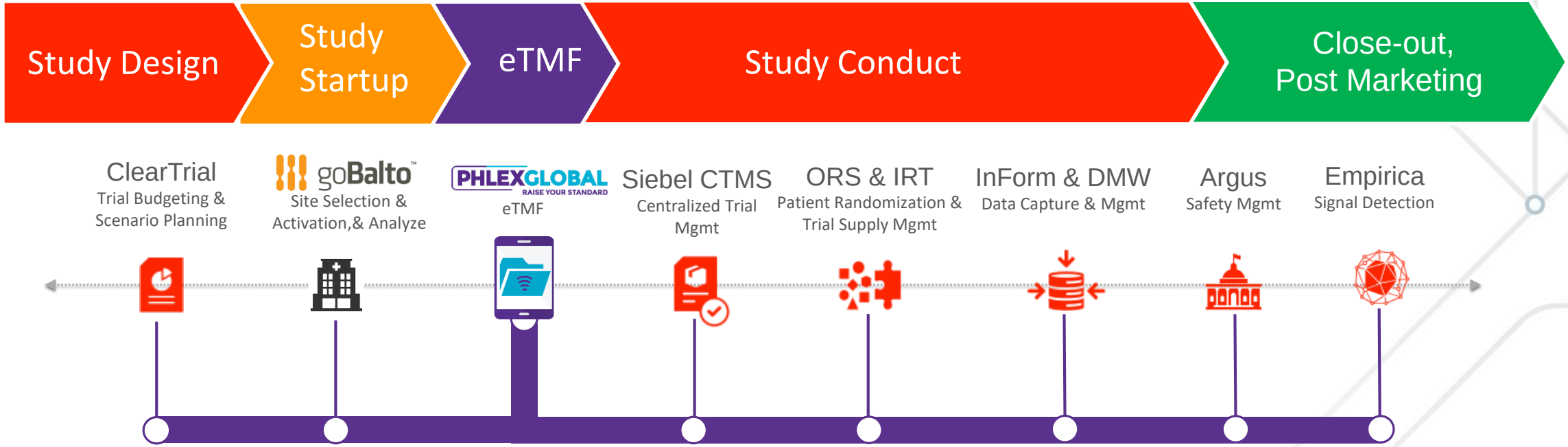
Why PhlexGlobal and Oracle

- Phlexglobal provides the best in class TMF with PhlexEview
  - Fit for Purpose – just like goBalto SSU product and Oracles CTMS
  - Comprehensive solution from Phlexglobal
- Phlexglobal's experience with TMF
- Phlexglobal's people and vision
- Creates a seamless Ecosystem
  - Together is better for our customer and their clinical trials
- Integrations with PhlexEview will not just be sharing data but allow both companies to enhance the end to end process
  - Next level workflow to enhance the complete clinical process

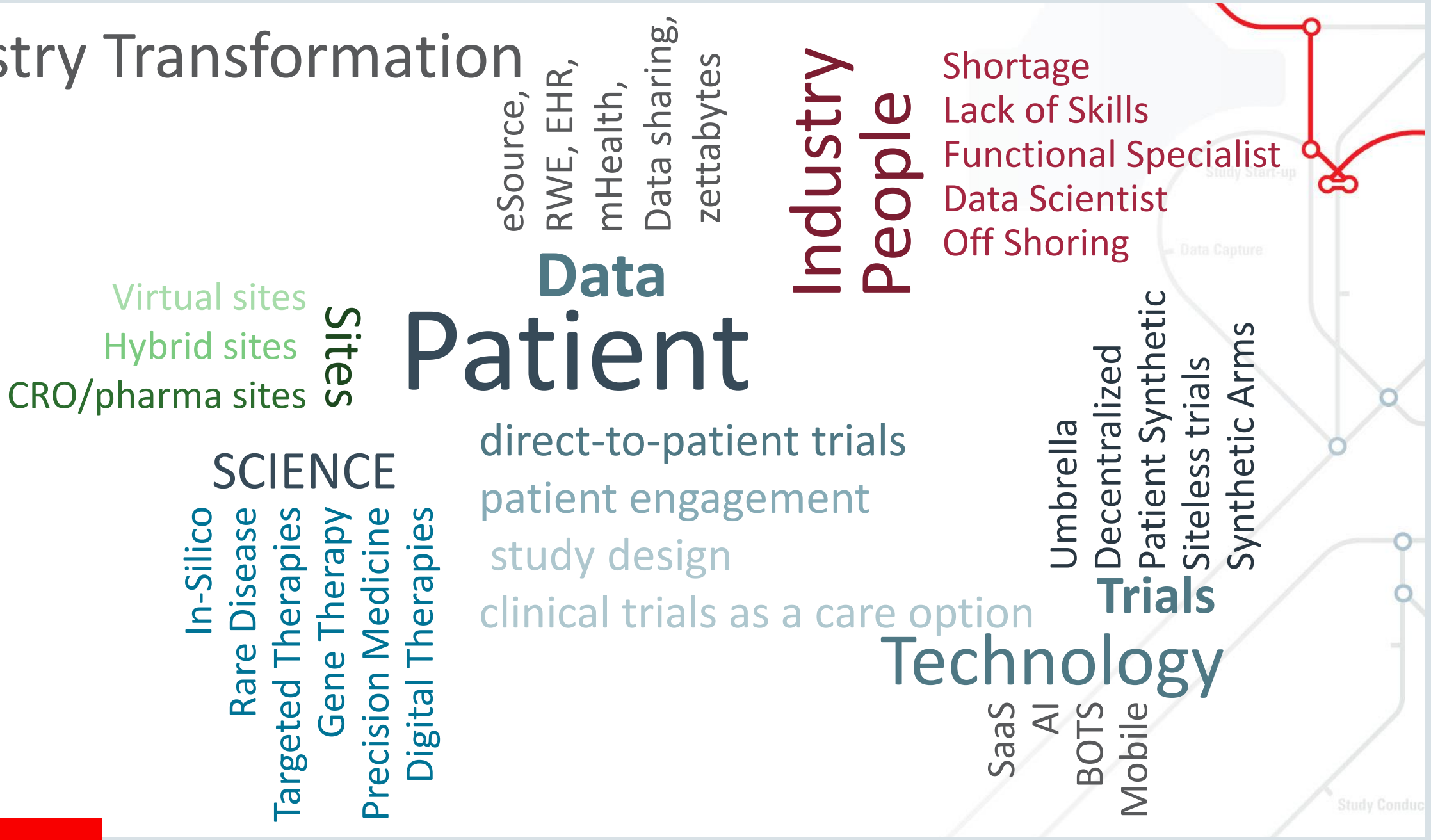
Initial Oracle and Phlexglobal Integration



A Best-of-Breed Solution from Oracle and Phlexglobal

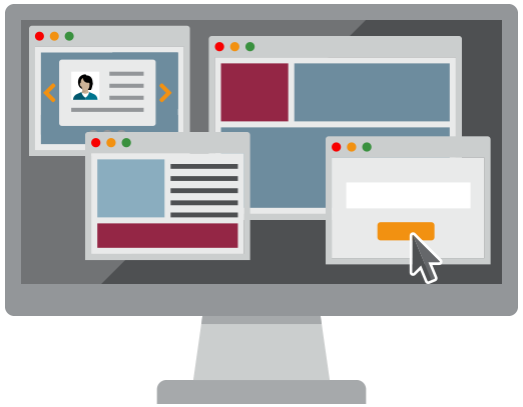


Industry Transformation



The path to ***the present***… *how did we get here??*

First, there was
paper…



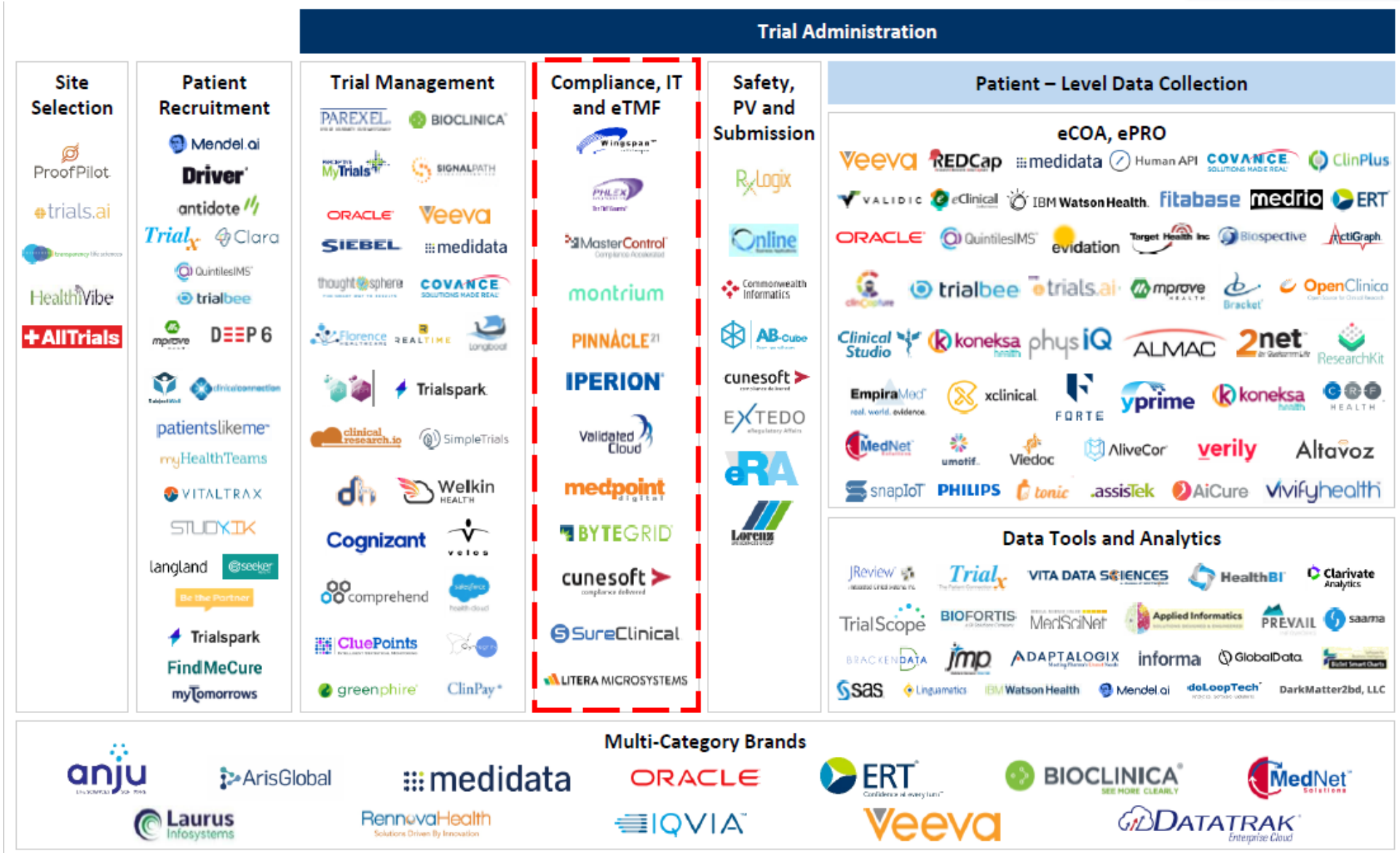
Then, there were
point solutions…

Now, there's
a mess…

Issues with the present…

COST	Overall impact of eClinical can increase clinical trial costs by **$2.5M***
DELAY	Potential revenue loss due to data quality issues can be **$180M****
RISK	**Data issues** resulting in regulatory rejection of drug approval
THREAT	**Inability to keep pace** with technology, clinical trials and competition
VUNERABILITY	**Inability to handle the data** collections methods needed for patient centric trials

** Average Phase III clinical trial costs **$30K/day**; average set-up & integration time with multiple systems is **12 weeks***
*** by not getting an approved drug in market = **$1M/day**; average approval delay due to data quality issues is **six months***



Market Trends & Drivers

TRENDS	DRIVERS
1) Increasing regulatory scrutiny	• Increased cost for compliance • Cost is not the key driver
2) Increasingly complicated trial design and process	• Increased need to specialize
3) Focus on R&D productivity	• Integration of systems • Risk based approach for quality control
4) Outsourcing market share 50% and increasing	• We have two masters – Pharma and CROs • Outsourcing models demand flexibility

"The provision of the TMF is your way to demonstrate compliance. Failure to provide the TMF in an appropriate way for MHRA domestic inspections will result in critical findings and potential further inspection days. For EMA inspections, if inspectors cannot assess compliance, this may mean the application for a MA is rejected."

MHRA

Essential Ways eClinical Must Change

Remove Barriers

Traditional applications silos become shared and business specific capabilities

Collaborative Platform

Clinical Team members have true collaborative access to trials.

Single Source of Truth

Eliminate redundant sources and entry of data and move towards interoperability

One Login

Single User ID, single URL access to all trials (across sponsor tenants for all site users)

User centric experience

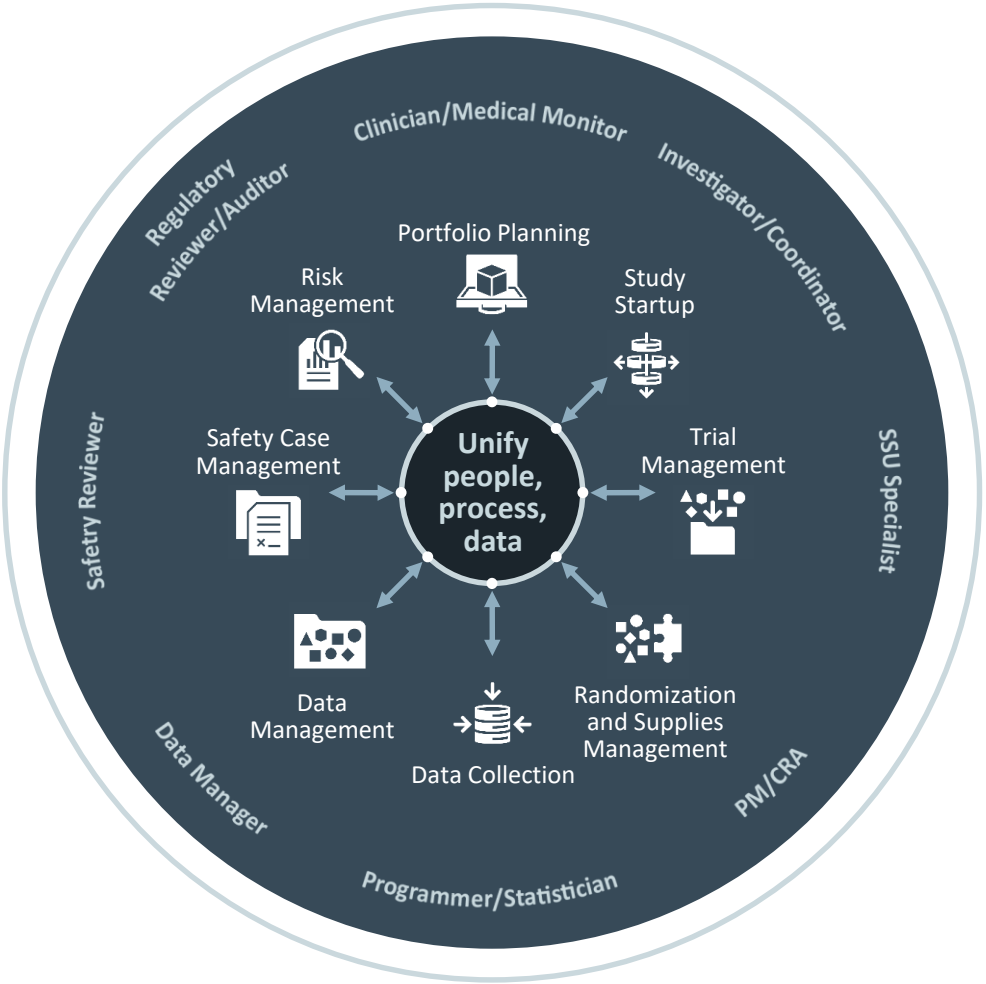
Personalized, Dynamic experience for advanced and casual users

Optimize Value Based Upon Use

Flexibility to provide support for predictable and for metered usage models

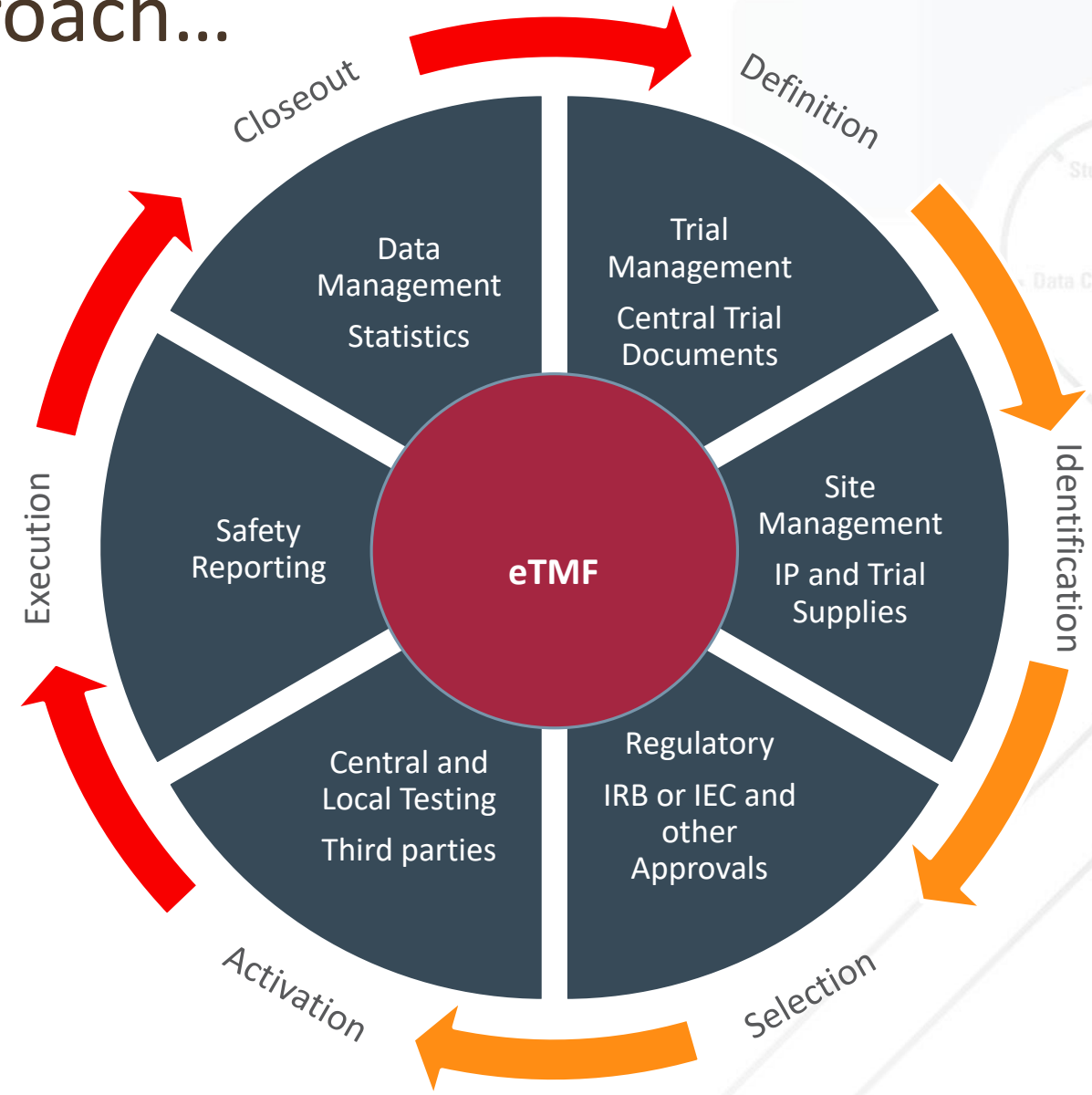
Modern requirements for success

Unified platform



A Comprehensive Approach…

- Joining the Transactional with the Study Content for regulatory review
- An eTMF represent all study content[1]



1 – Zones. Trial Master File Reference Model. September, 2018. https://tmfrefmodel.com/resources/

Objectives

- Reduce manual processing of source documents
  - Continuous year over year increases in data volume are unsustainable for BioPharma organizations to address by hiring more people
- Improve quality by decreasing manual data entry errors and through enhanced duplicate detection that reduces new case errors
- Improve regulatory reporting compliance requirements by increasing meeting targeted reporting windows
- Expand supported data structures

Artificial Intelligence in Safety*

Applications in Both Major Areas of Multivigilance

Safety Case Management

Intake

- NLP/ML extraction of data elements
- Triage

Processing

- Duplicate / initial / follow-up detection
- Coding
- End-to-end workflow automation

Assessments

- Seriousness
- Severity
- Expectedness
- Causality
- Follow-up significance

Safety Signal Management

AE Extraction from Varied Data Sources

- Scientific literature
- Healthcare records
- Product labeling
- Social media

Signal Detection

- Multiple data source combinations
- AE prediction
- Severity progression
- AE proxies

Signal Validation / Assessment

- Real-world evidence
- Pharmacokinetics / pharmacodynamics / pharmacogenomics

* Planned product direction

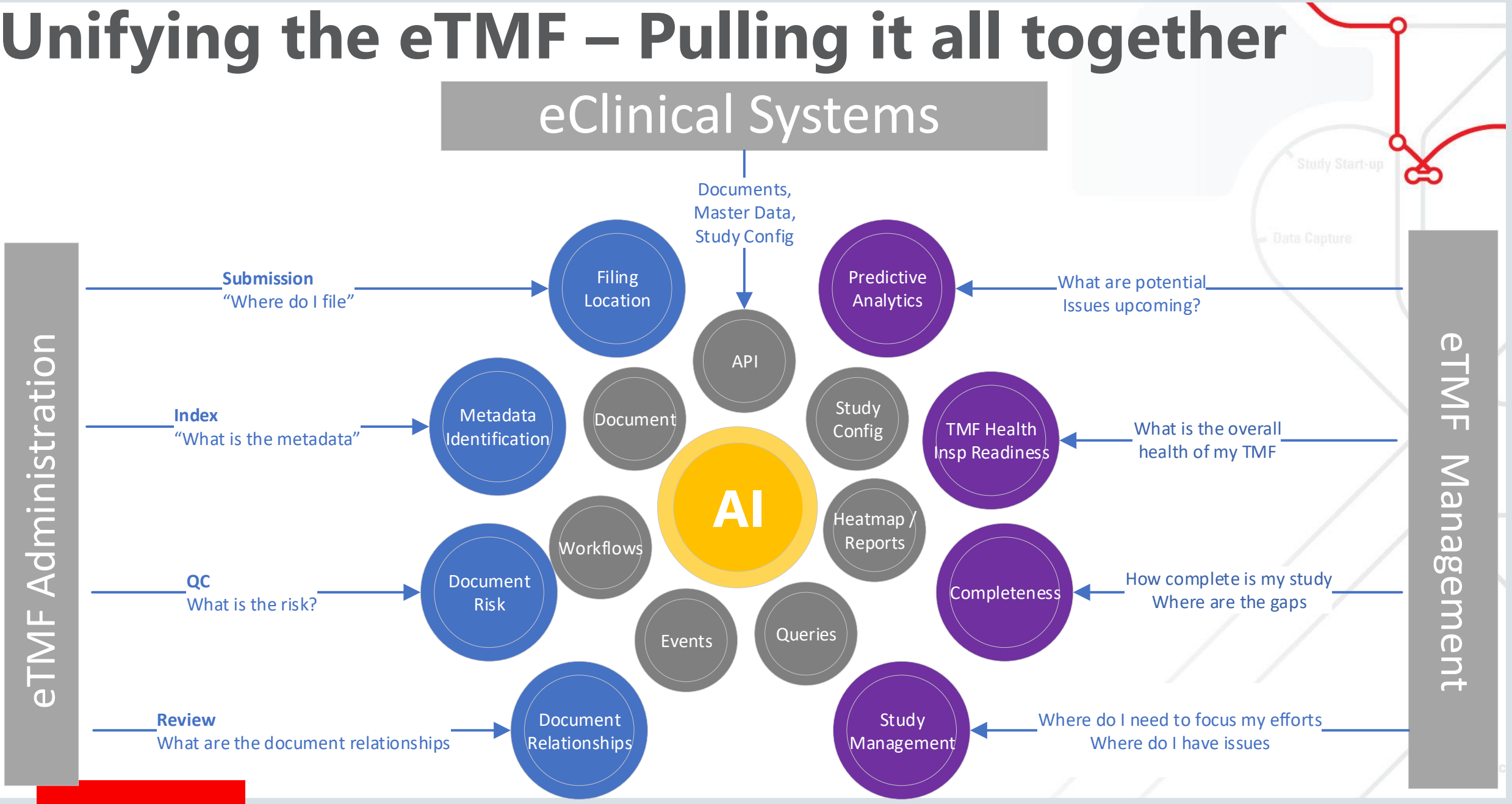
Predictive Business Cases

- What countries should I conduct this trial in?
- What sites are best suited for this study?
- How many sites do I need to activate to hit my enrollment requirements?
- How long will it take to achieve database lock so I can budget and resource accordingly?

SSU predictive analytics plan

predictive analytics (site activation cycle times)	predictive analytics (site selection)	predictive analytics (enrollment cycle times)	smart study design
1. essential docs distributed to site contracted 2. essential docs distributed to site IP Released	1. Automated site identification 2. Patient enrollment projections	1. database open to first patient in 2. first patient in to last patient in 3. last patient visit to database lock	1. Number sites required for study 2. Country recommendation list 3. Site recommendation list
data sources (Activate)	**data sources (Select)**	**data sources (CTMS / Data Warehouse)**	**data sources (Study Protocol)**
• Therapeutic Area • Phase • PI study experience • Start month • IRB Type • Country • Region • # of study countries • Institution	• Therapeutic area • Specialty • Indication • Phase • PI study experience • Country • Region • Site survey responses • Site enrollment performance	• Subjects enrolled • Subjects screened • Subjects failed • Subjects randomized • First patient in • Last patient in • database open • database lock	• Number of patients required • Indication • Inclusion/exclusion criteria • Phase

Unifying the eTMF – Pulling it all together



Lets talk Quality

How can we reduce QC effort?

- The required human effort @ 100% QC can quickly add up

Average Phase 3 trial

40,000 pages @ trial

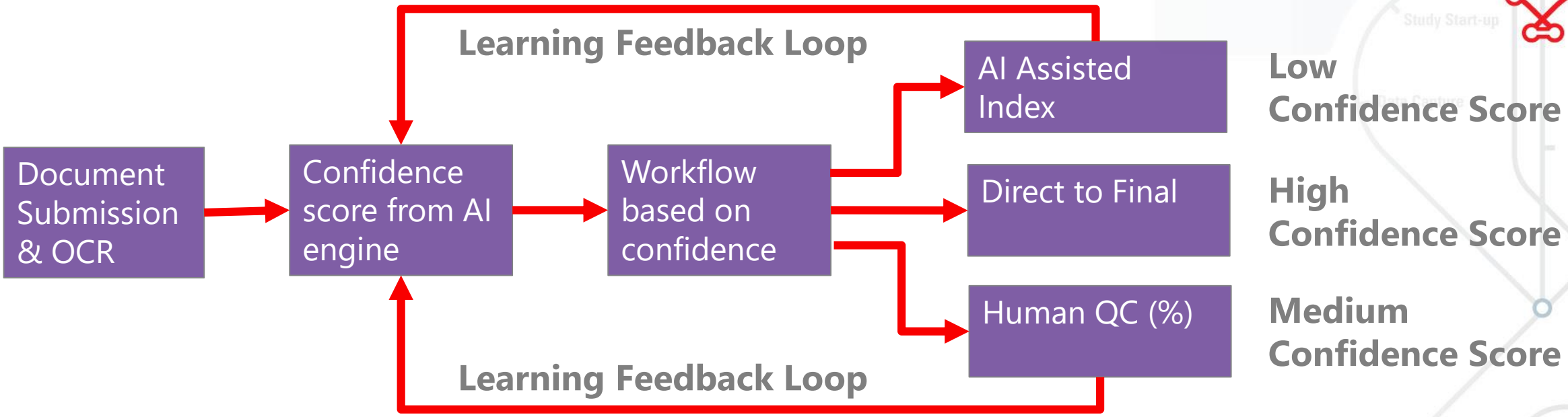
1500 pages @ country x 10

750 pages @ site x 200

= 205,000 pages

Can ML reduce QC effort?

Increased automation confidence will allow fully automated submissions



Artifacts with **high confidence** once proven can be fully **AI indexed**
Artifacts with **medium confidence** can be AI indexed with **human QC**
Artifacts with **low confidence** can be indexed manually with **AI Assistance**

Quality Example

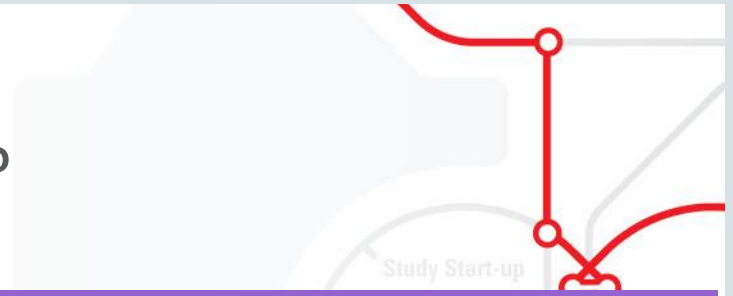
- Communications typically contain duplicate threads with attachments

- 50 "correspondence" emails submitted all having the same attachment - an IB that is already in the system
- AI identifies and removes duplicate email chains
- AI extracts subject for Descriptor and the orginating Date
- System links email documents to existing IB
- System fulfils relevant placeholders for the IB "event"

Lets talk Timeliness

Timeliness

- How do you meet the requirement to be Contemporaneous?



WHY?

Your TMF should be used real time for decisions; how can they be made if the documents are not present?

WHAT?

Measure the difference between document date and date submitted

Understand what is missing based on milestones

Measure the time to resolve queries

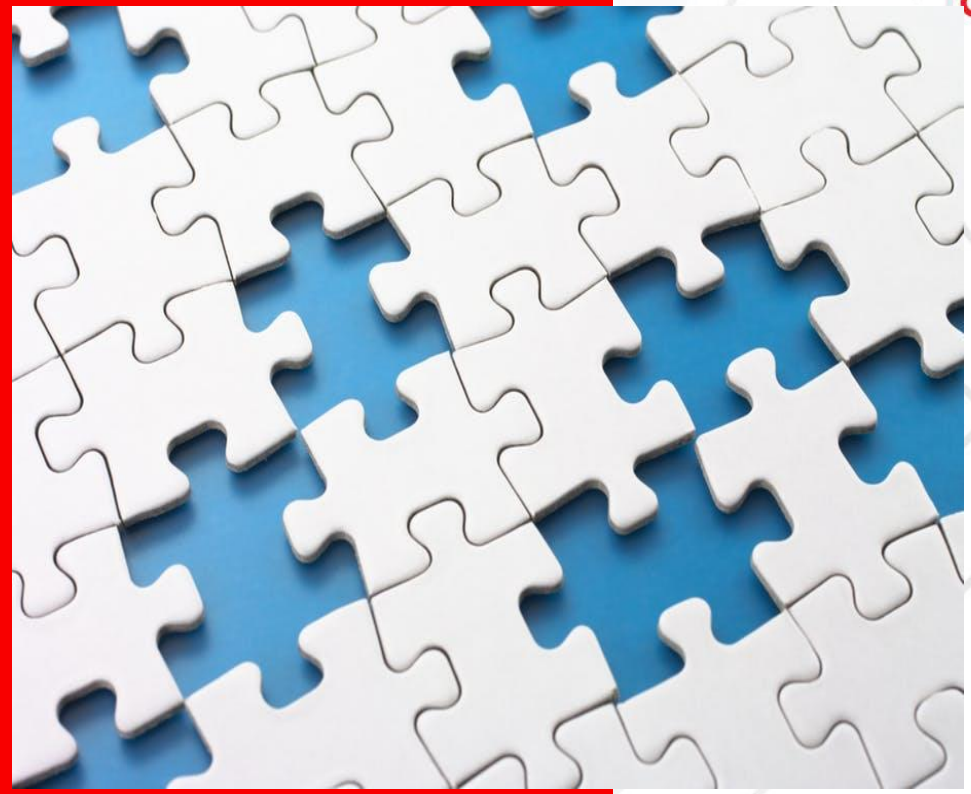
Measure the time to close the TMF

Timeliness Example

- AI supported scanning expedites document submission direct from site

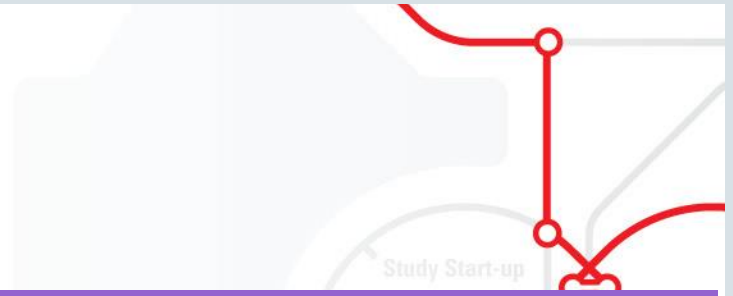
- 1572 Document scanned at site using mobile app
- AI suggests the filing location
- AI Extracts the site personnel list
- System identifies a missing person is not registered
- System generates a CV and Medical Licence placeholder
- AI notes the site has a trend for missing signature
- AI pro-actively reminds the site submitter and flags for 100% human QC check when it arrives

Lets talk Completeness



Completeness

- Is this the hardest aspect to get right?



How do you ascertain what is missing?

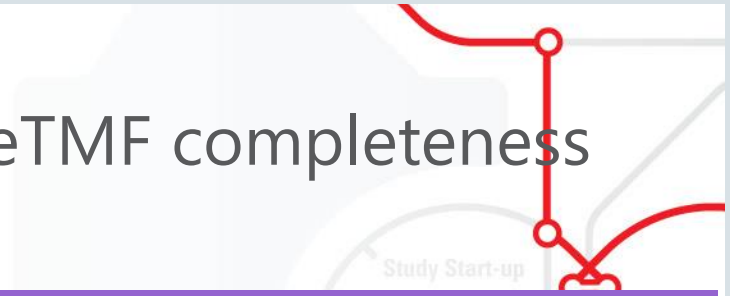
- Study set-up driving placeholders or expected documents
- Milestones linked to subartifacts to understand when due
- Events driving placeholders or updating expected documents

The Answer?

- Automating Accurate Time-based Completeness Assessments through placeholders and integrations

Completeness Example

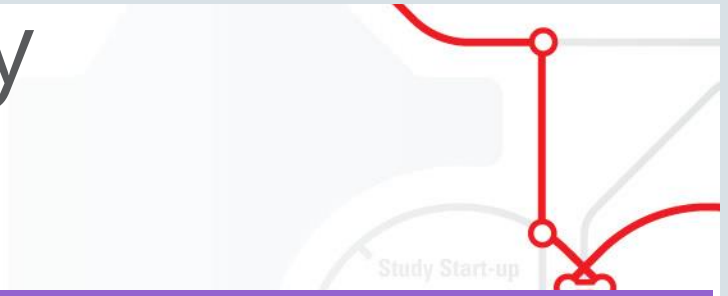
- Systems integration through open standards facilitates eTMF completeness



- New protocol amendment sent from integrated CTMS
- System verifies integrity of document chain of custody
- System generates requirement for signature pages
- AI notifies two sites with predicted timeliness issues
- AI requests translation of non-English documentation
- System creates a note in the TMF story to explain the temporary reduced completeness avoiding red flag

Best of breed eTMF is evolving rapidly

- eTMF vendor offered solutions will:



- Move away from representations of paper documents
- Be data and predictive/prescriptive driven
- Offer open integration for systems interoperability
- Support extended chains of document custody
- Handle *all* data representations as searchable data sets
- Be "AI first" with fully automated processes running document filing, QC workflows, and TMF oversight