Lessons Learnt from Implementing an eTMF

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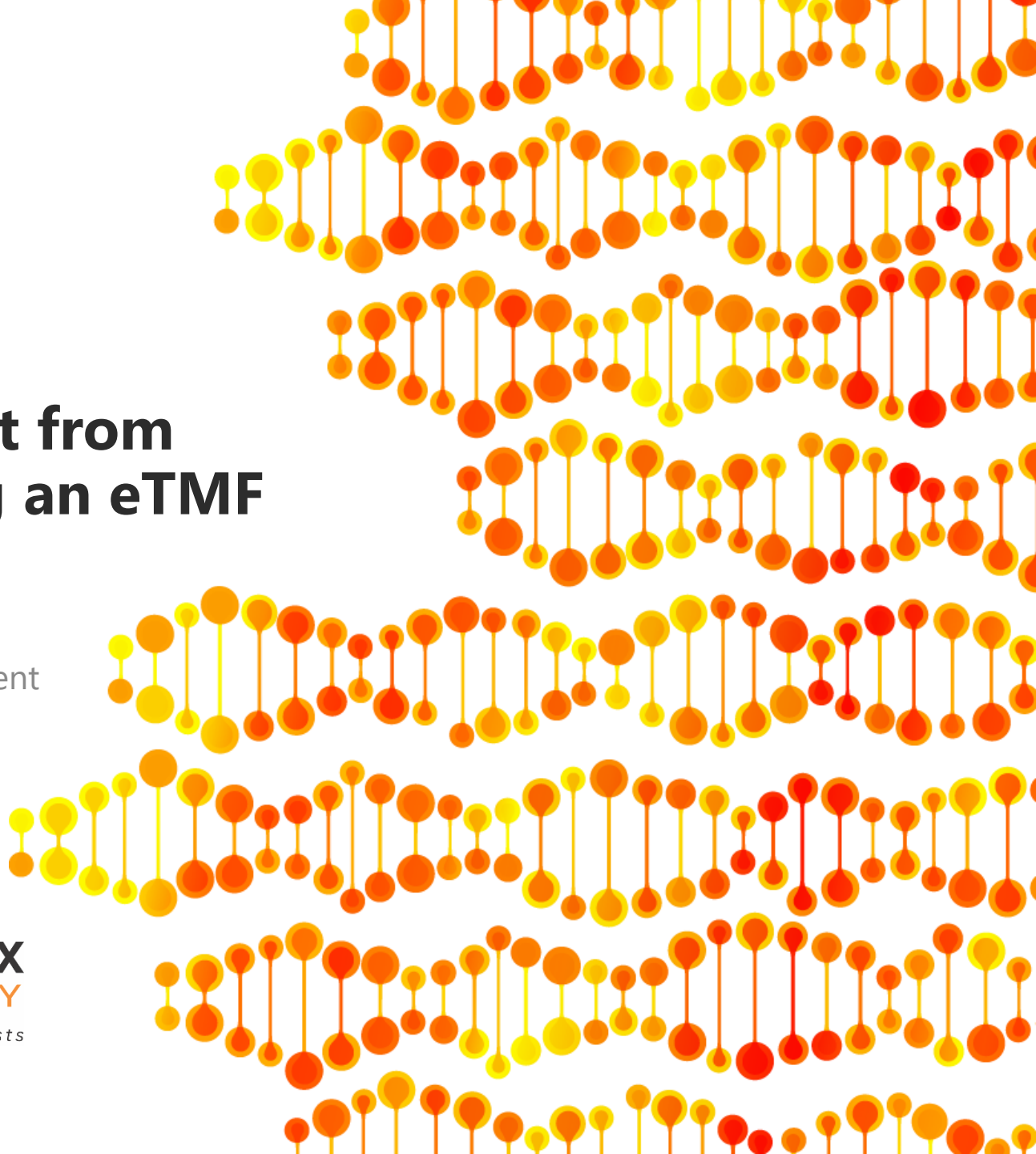

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The early phase specialists

Theradex

- Theradex Oncology
  - Full-service CRO, conducting early-phase oncology trials in the United States, Europe,
  - Working in phase I, II and III trials.
- Responsible for TMFs/ large parts of TMF on behalf of Sponsors
- eTMF project (configuration/ eTMF Mapping) started one year ago
- Implemented eTMF and Study Start-Up (SSU) component simultaneously.

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Process Overview

- Initial Phase - Set-up / Planning
- eTMF Configuration/ Mapping
- eTMF Implementation
- eTMF Ongoing Maintenance, Evaluation And Improvement

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Initial Phase - Set-up / Planning

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Initial Phase - Set-up / Planning

- Designate a Project Manager who will lead the project delivery
  - Designate a Technical Lead to work alongside the PM
  - Ensure sufficient time and resource allocated at all stages
- Establish expectations with Vendor.
  - Timelines for configuration and implementation.
  - Timelines for the administration team training program.
  - Time requirement for internal team members and over what period.
  - Timelines for effective functioning/ working of the system.
  - The level of the support Vendor will offer during configuration and maintenance.

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Initial Phase - Set-up / Planning

- Establish a global internal implementation team with representatives from all departments within organisation
  - Keep QA at center of discussions
  - Create a team that supports change
- Set timelines for delivery
  - Phased delivery of implementation
    - Internal TMF/ Sponsor use/ Site use
- Change management
  - Be prepared for resistance

eTMF Configuration / Mapping

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eTMF Configuration / Mapping

- Aim - set-up the eTMF configuration/mapping to follow company processes and SOPs.
- Mapping meetings
  - Global implementation team in the same location for dedicated period of time (multiple meetings)
  - Teams could address their own areas of responsibility and ensure consistency at interfaces and areas of overlap.
    - Quick agreement between departments
  - Obtain experienced facilitator(s) from vendor who can highlight unintended consequences or suggest solutions
  - Keep QA involved to ensure ICH-GCP perspective maintained
  - Do not deviate from DIA model without a strong rationale.
    - Fully understand the impact of configuration changes

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DIA reference model

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
1		**TMF Reference Model**					TMF RM Website	**Version 3.1.0**	**10-Sep-18**							X: applicable; NO* : Not appl *There may be some targeted exceptions (i.e. countries)
2																
3	Zone #	Zone Name	Section #	Section Name	Artifact #	Artifact name	Alternate names (artifact also commonly known as)	Definition / Purpose	Sub-artifacts (examples of document types different from the artifact provided, overwrite with your company-specific records)	Core or Recommended for inclusion	ICH Code	Artifact name in v1.3 EDM Reference Model	Unique ID Number	TMF Artifacts (Non-device) Sponsor Document	TMF Artifacts (Non-device) Investigator Document	TMF Sponsor Document
4	01	Trial Management	01.01	Trial Oversight	01.01.01	Trial Master File Plan	Records Management Plan Central File Maintenance Plan Filing instructions Filing and archive plan	To describe how records for the trial will be managed and stored during and after the trial, including study-specific processes and documentation for archiving and destruction. To include TMF filing structure to be used. May include TMF content list, filing structure and chain of custody records. Artifact can include any evidence of plan execution including, but not limited to: plan, reports, checklists, etc.	Core Document List TMF Report TMF Transmittal Form TMF Setup Request	Recommended	5.5.7		001	X	NO	X
5	01	Trial Management	01.01	Trial Oversight	01.01.02	Trial Management Plan	Project Management Plan Clinical Development Plan	To describe overall strategy for timelines, management and conduct of the trial and typically makes reference to other artifacts. Artifact can include details on contingency plan covering details for site start up planning.	Site Selection Strategy	Recommended	2.2		002	X	NO	X
6	01	Trial Management	01.01	Trial Oversight	01.01.03	Quality Plan		To describe the operational techniques and activities undertaken within the quality management system to verify that the requirements for quality of the trial-related activities have been fulfilled. Relevant parts may include, but not be limited to, a plan written for internal oversight of study quality management, an audit plan, data verification steps; also includes escalation in the event of a quality issue being identified and all corrective and preventative actions determined. Artifact can include any evidence of plan execution including, but not limited to: plan, reports, checklists, etc.	Quality Report	Recommended	5.1		003	X	NO	X
7	01	Trial Management	01.01	Trial Oversight	01.01.04	List of SOPs Current During Trial		To document which standard operating procedures (SOPs) and which versions were in effect for the duration of the trial and trial-specific procedures created for the trial. To include sponsor and third party SOPs. This artifact does not include the SOPs themselves. May include SOP waivers to document and describe study-specific deviation from a named SOP or working procedure and the rationale for the deviation, when applicable.	SOP Deviations SOP Waivers	Core	5.1.1		004	X	NO	X
8	01	Trial Management	01.01	Trial Oversight	01.01.05	Operational Procedure Manual	Study Reference Manual Work Instruction Manual of Procedures	To describe trial-related processes not covered by formal standard operating procedures. Includes manuals given to sites for ISFs and vendor study-specific manuals as well as any study related tools provided to investigator sites not subject to IRB/IEC approval. Artifact can include any evidence of plan execution including, but not limited to: plan, reports, checklists.		Recommended	5.1.1		005	X	X	X
9	01	Trial Management	01.01	Trial Oversight	01.01.06	Recruitment Plan		To describe the planned subject enrolment/recruitment goals during the trial, including contingency plans. Artifact can include any evidence of plan execution including, but not limited to: plan, reports, checklists, etc.		Recommended	5.6		006	X	NO	X
10	01	Trial Management	01.01	Trial Oversight	01.01.07	Communication Plan		To describe communication strategy and plans between trial stakeholders, including communication escalation procedures/steps. Artifact can include any evidence of plan execution including, but not limited to: plan, reports, checklists, etc.		Recommended			007	X	NO	X
	01	Trial Management	01.01	Trial Oversight	01.01.08	Monitoring Plan		To describe how monitoring will be implemented during the trial, including strategy for source data verification. Artifact can include any evidence of plan execution including, but not limited to: plan, reports, checklists, etc.		Core	5.18.3		008	X	NO	X

eTMF Configuration / Mapping

- Metadata / Artifact
  - Define Ownership/Department
  - Hide rows/columns not applicable, you may choose to unhide at later date- following subsequent review
  - Try to keep artifact name per DIA model
- Sandbox for configuration and testing
- Be open to changing process / SOPs
  - Global implementation team to review SOPs
  - Avoid copying your paper process into the electronic system
  - The process does not need to mirror paper process/ process may not work in eTMF
  - Develop separate eTMF SOPs where appropriate

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eTMF Implementation

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eTMF Implementation

- Launch within Company
  - Generate interest and excitement with big launch
  - Explain rationale / advantages of system
  - Announced by CEO etc
- Training – offer high level of support
  - Make sure all users are well trained on the software
    - Hands on - Sandbox used as training environment, for people to gain confidence in system – with practical exercises
    - Record training sessions for reference
  - Expect some resistance
- Target study teams with early adopters who can champion the system,
  - Use to demonstrate that use of system achievable, efficient and build momentum in the company

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eTMF Implementation

- Migrations of ongoing studies
  - Ensure all content ready for migration
  - Establish a QC controlled process and tracking – with small dedicated team
  - Keep migration plan as a live document.
  - Takes longer than planned
- Implementation of new studies
  - Encourage teams to start as early as possible
  - Minimise options for filing elsewhere.
- System design to be inspection ready
  - QC personnel allocated on study basis (ownership)
  - Review QC feedback regularly and feedback to the team

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eTMF Implementation

- eTMF Working Group
  - The group will allow for new ideas from each department with the aim of improving companywide processes
  - Addresses processes that are study-specific and those that are company process
  - Alignment of new eTMF processes globally
  - Larger brainstorming team to solve issues and questions in Veeva
  - Provide feedback structure, so people know who to contact
  - Acts as champions for eTMF in the company

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eTMF Ongoing maintenance

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eTMF Ongoing maintenance, evaluation and improvement

- Configuration in house – less reliant on vendor for support
  - Additional training for administrators
  - Use vendor for support / in depth technical knowledge.
  - Identify knowledgeable vendor support person to guard against unintended consequences
- Use system reports for ongoing evaluation of metrics & quality
  - Provide regular feedback to users
  - Adapt or modify processes as required
  - Frequent updates / clarifications to eTMF index
- Continue ongoing evaluation of system
  - As teams become aware of capabilities of system, leads to revaluation of processes/SOPs
  - Opportunity to implement more efficient processes

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DIA reference tools

- https://tmfrefmodel.com/resources
- Includes
  - TMF Reference Model v3.1.0
  - Presentation / User Guide /Model Process Maps:
  - eTMF Exchange Mechanism Standard (eTMF-EMS):
  - TMF Reference Model User Guide
  - TMF Reference Model Implementation Guidance
  - TMF Plan Template

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Conclusions

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Conclusions

- One year in
  - Allow enough time and resource for eTMF Configuration / Mapping
  - Ensure understand fully implications of changing the DIA TMF reference model
  - Maintaining and developing the system is an ongoing project
  - Overall benefits for projects are very worthwhile.

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