Lessons Learnt from Implementing an eTMF

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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.
Process Overview

- Initial Phase - Set-up / Planning
- eTMF Configuration/ Mapping
- eTMF Implementation
- eTMF Ongoing Maintenance, Evaluation And Improvement
Initial Phase - Set-up / Planning
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.
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
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
# DIA reference model

## TMF Reference Model

**Version 3.1.0**

<table>
<thead>
<tr>
<th>Zone</th>
<th>Section</th>
<th>Artifact Name</th>
<th>Alternate names (artifact also commonly known as)</th>
<th>Definition / Purpose</th>
<th>Sub-artifacts (each type or document refers to different artifact)</th>
<th>Core or Recommended for inclusion</th>
<th>ICN Code</th>
<th>Artifact name in v1.1 (TMF Reference Model)</th>
<th>Unique ID Number</th>
<th>Sponsor Document</th>
<th>Investigator Document</th>
<th>Scopes Document</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>01</td>
<td>Trial Management</td>
<td>01.01.01</td>
<td>Trial Master File Plan Records Management Plan</td>
<td>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. It may include TMF filing structure to be used. May include TMF content list. Filing structure and how to store records.</td>
<td>Core Document List</td>
<td>1.1.7</td>
<td>Core Document List</td>
<td>011</td>
<td>X</td>
<td>NO</td>
<td>X</td>
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<tr>
<td>10</td>
<td>01</td>
<td>Trial Management</td>
<td>01.01.02</td>
<td>Trial Management Plan Project Management Plan</td>
<td>To describe overall strategy for timelines, management and conduct of the trial and typically includes references to other artifacts. Artifact can include details concerning project teams for site start-up planning.</td>
<td>Site Selection Strategy</td>
<td>2.2</td>
<td>Site Selection Strategy</td>
<td>022</td>
<td>X</td>
<td>NO</td>
<td>X</td>
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<tr>
<td>10</td>
<td>01</td>
<td>Trial Management</td>
<td>01.01.03</td>
<td>Quality Plan Clinical Development Plan</td>
<td>To describe the specific techniques and activities undertaken within the quality management system to verify that the requirements for quality of the trial-related activities have been met. Relevant parts may include, but are not limited to, audit plans for internal quality management, an audit plan, quality review, and data verification procedures. Includes information on the extent to which QA issues have been identified and corrective and preventive actions determined. Artifact can include any evidence of plan execution including, but not limited to, plans, reports, checks, etc.</td>
<td>Quality Report</td>
<td>2.1</td>
<td>Quality Report</td>
<td>032</td>
<td>X</td>
<td>NO</td>
<td>X</td>
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<td>10</td>
<td>01</td>
<td>Trial Management</td>
<td>01.01.04</td>
<td>Lot of SOPs Current During Trial</td>
<td>To document which standard operating procedures (SOPs) and which version were in effect for the duration of the trial and trial-specific procedures created for the trial. Subsets of SOPs may be included in order to avoid list of SOPs. This artifact does not include the SOPs themselves. May include SOP workflow and document description specific deviations from a named SOP or supporting procedure and the rationale for the deviation, when applicable.</td>
<td>SOP Deviation SOP Wander</td>
<td>3.1.1</td>
<td>SOP Deviation SOP Wander</td>
<td>043</td>
<td>X</td>
<td>NO</td>
<td>X</td>
</tr>
<tr>
<td>10</td>
<td>01</td>
<td>Trial Management</td>
<td>01.01.05</td>
<td>Operational Procedure Manual Study Reference Manual Work Instruction Manual of Procedures</td>
<td>To describe the detailed processes not covered by formal standard operating procedures. Includes manuals that include SOPs and vendor-specific manuals as well as study-related tools provided to investigators sites not subject to IRB/CRA approval. Artifact can include any evidence of plan execution including, but not limited to, plans, reports, checks, etc.</td>
<td>Recommended</td>
<td>3.1.1</td>
<td>Recommended</td>
<td>056</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>01</td>
<td>Trial Management</td>
<td>01.01.06</td>
<td>Recruitment Plan</td>
<td>To describe the planned subject enrollment goals during the trial, including adverse events planning. Artifact can include any evidence of plan execution including, but not limited to, plans, reports, checks, etc.</td>
<td>Recommended</td>
<td>3.0</td>
<td>Recommended</td>
<td>056</td>
<td>X</td>
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<td>X</td>
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<td>01</td>
<td>Trial Management</td>
<td>01.01.07</td>
<td>Communication Plan</td>
<td>To describe communication strategy and plans between sites during the trial, including adverse events planning. Artifact can include any evidence of plan execution including, but not limited to, plans, reports, checks, etc.</td>
<td>Recommended</td>
<td>3.0</td>
<td>Recommended</td>
<td>057</td>
<td>X</td>
<td>NO</td>
<td>X</td>
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<td>01</td>
<td>Trial Management</td>
<td>01.01.08</td>
<td>Monitoring Plan</td>
<td>To describe how monitoring will be performed during the trial, including strategy for data verification. Artifact can include any evidence of plan execution including, but not limited to, plans, reports, checks, etc.</td>
<td>Core</td>
<td>3.10.3</td>
<td>Core</td>
<td>056</td>
<td>X</td>
<td>NO</td>
<td>X</td>
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</tbody>
</table>

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**Theradex Oncology**

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*There may be some targeted exceptions (i.e. countries).*
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
eTMF Implementation
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
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
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
eTMF Ongoing maintenance
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
DIA reference tools

- [https://tmfrefmodel.com/resources](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
Conclusions
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.