Quality Subgroup Output

07 November 2016

Overview

- Objective: Define minimum requirements for quality control of TMF content
- Goals: Produce a document that can be used throughout the industry to define TMF Quality
- Timeline Q3/Q4 2016

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TMF
REFERENCE MODEL

Overview

- As a group, we agreed:
  - To use the term “TMF review” in order to distinguish the two part process for TMF QC which are:
    - document QC
    - TMF QC
  - Completeness definition: All TMF documents that enable the reconstruct of the study are available in the TMF contemporaneously of milestones and events.

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Version History

Version	Steering Committee Approval Date	Changes
1.0	11 October 2016	New definition and approach

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OVERVIEW

In order to be considered "TMF Ready" a document should meet the following criteria:

Retrievable – documents have appropriate metadata and appropriately filed as per TMF Reference Model or company's filing structure

Unique – no duplicates exist

Translations – all appropriate translation documentation is available as per country regulatory requirements and company policy/procedures

Original – unaltered wet ink signature required when applicable as per regulatory agencies and/or company's policy

Legible – Readable, clean and stamps/signatures identifiable

Applicable – document that supports the story of a clinical trial and is required as per TMF Reference Model and/or company's policy

R.U.T.O.L.A.

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OVERVIEW

In order to be considered "**Inspection Ready**" the TMF (in it's entirety) should meet the following criteria:

To assess TMF completeness it imperative to know what is expected to be in the TMF and when (e.g. milestones). Completeness can be assessed against TMF specifications and also against regulatory requirements, company Standard Operating Procedures (SOPs) and business processes (e.g., business process requirements will help to determine number of versions or instances expected for a given artifact/document type).

Considerations

Quality Considerations	Document QC	TMF QC	Comments
Functional Line Engagement	Functional Lines are the Document Owners and should ensure TMF readiness prior to filing the document into the TMF	Functional Lines should ensure that all expected documents (i.e. versions) are present in the TMF.	Education and engagement at the beginning of the study and on an ongoing basis.
Timeline	Upon receipt of document	Considerations should be given to study milestones/events (TMF content should be contemporaneous of the latest milestone and event) ensuring that the TMF is inspection ready at all times. Frequency should not exceed more than six months.	

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Considerations

Quality Considerations	Document QC	TMF QC	Comments
Scope	100% of documents should be reviewed prior to filing into the TMF.	Risk based or full QC may be performed.	Scope of document QC could be risk based or required for specific document types. The tab specifying the document QC does not fit this sheet document QC description. It is not possible to do a 100% QC of the documents as described in the 'Document QC' tab (RUTOLA) prior filing in the TMF. I suggest that a document QC is a document 'content' QC to ensure this is the required and expected document and that it is complete. Furthermore to check for T, O and L (in RUTOLA) . This must be done by the document owner upon receipt of the document. This is only part of the RUTOLA. I suggest that the TMF QC can be a two step activity. One for the single TMF where there is a check for completeness and no duplicates (U and A in RUTOLA), and one for TMF across trials where there is a risk based approach checking R (in RUTOLA) and filing timeliness.

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Considerations

Quality Considerations	Document QC	TMF QC	Comments
Oversight QC		Sponsor oversight of the CRO/vendors Written proof of QC from the CRO (in the contract)	
List of TMF Repositories	Document (i.e. artifact) location of each document type (may be an appendix to the TMF Plan). Document (i.e. artifact) owner (may be an appendix to the TMF Plan)		All of the TMF documents may not reside in the same location. Important to understand document location and how this impacts the TMF quality.

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Tools

TMF Review Tools	Comments
TMF Reference Model	Maybe a modified version customized based on individual needs.
TMF Management Plan	May include TMF Master List (i.e. TMF Specifications) or TMF Table of Contents (TOC). Specifically define which functional line is responsible for which sections of the TMF. This plan may also include the frequency of the TMF review. TMF Master List may also include a link or reference to the Standard Operating Procedures where each TMF document is described. The TMF Master List may also include an indication of when each document is expected during trial conduct i.e. prior first site initiation, FPFV, LPFV, DBL, study report or other relevant milestones as relevant per company.
Corrective Action Plan	If discrepancies are identified, there should be a documented way to correct the discrepancies (including timeline, method (i.e. documentation) and responsible party).

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