DAIDS TMF Index Guiding Principles

The purpose of this document is to provide a high-level overview of the DAIDS TMF Index in terms of structure and content, as well as provide guidelines and best practices as it relates to the TMF Index review process.

During the development, review, and update of each protocol specific TMF Index, DAIDS Primary Contacts (PCs) and Authoritative Sources (AS) will follow the guiding principles outlined below to ensure accuracy and consistency, where appropriate.

Changes to the TMF Reference Model

The DAIDS TMF Index is a living, protocol specific document generated for each study TMF per DAIDS-OPC-A15-WI-00004. The TMF Index is based on the TMF Reference Model, version 3.1, effective as of 10-Sep-2018, and has been adapted to align with DAIDS processes and industry standards.

For example, the following were added:
- Columns:
  - Status
  - Authoritative Source (AS)
  - DAIDS Primary Contact (PC)
  - Milestones for artifact filing (e.g., Study Start, Conduct, Close)
- Zone 12 – Electronic Systems

High Level Outline of TMF Index

Artifact Status Definitions

The status column is included in each protocol specific TMF Index to identify if a given artifact is required.

There are three accepted values for status, defined as follows:

1. **Required** (Core or Recommend Artifacts): The artifact is/will be generated and collected during the course of a study.
2. **Not Generated** (Core Artifacts Only): The artifact is/will not be generated or collected, but may still be required based on applicable regulations.
   a. Identifies gaps in the DAIDS processes to be identified and addressed and/or remediated.
3. **Not Required** (Core and Recommended Artifacts): The artifact is not applicable per the protocol.

Note: Artifacts that are identified as "Recommended" by the TMF Reference Model and have a status of "Not Required" will be removed prior to finalization of the protocol specific TMF Index. Artifacts identified as Core regardless of status will remain in the final version of the protocol specific TMF Index. There is no need to differentiate these items via shading or other methods. These items serve a purpose to highlight those items that are listed as Core to indicate that they are not being collected due to gaps vs. not being applicable; therefore, they need to remain in the TMF Index.

Identification of Source Locations and Listing of Sub-Artifacts

Source Location

DAIDS is utilizing a decentralized approach for TMFs. All electronic systems approved to store TMF documents are listed in that protocol's Electronic System Mapping (ESM) document. Only systems which have been qualified and approved by DAIDS and included in the ESM will be identified in the protocol specific TMF Index, as the source location for artifacts.

Sub-Artifacts

Within the TMF Index, each artifact (and associated sub-artifacts) is listed within their own rows, along with the AS identified for filing the document(s), and the applicable source location. For an artifact, if the associated sub-artifacts are being filed by multiple Authoritative Sources and/or mapped to multiple Source Locations, each location and AS combination will be listed in separate rows, for clarity. Additional rows to capture new electronic systems, Authoritative Sources, and sub-artifacts can be added as needed. See the examples in Appendix A.

> ***Note***: Currently there is an exception made for separating each sub-artifact, AS, and electronic system into its own line item when the intention is to cover a variety of groups and electronic systems (e.g., Relevant Communications artifacts in each zone, system specific plan documents). In these cases, one line will capture all systems listed in the Source Location and a general title grouping the AS may be used, such as "System Owners."

Examples of Sub-Artifacts

Trial Master File Plans

The Trial Master File Plan (TMF Plan) is a document developed for each protocol to outline the processes and procedures that DAIDS, as the Sponsor, will utilize to ensure a high-quality TMF. The TMF Plan will be classified into artifact 01.01.01.

Other Electronic Systems Owners will have specific documents outlining to TMF related activities within their systems. These documents will also be classified into artifact 01.01.01 but will be distinguished from the DAIDS TMF Plan that cover processes across the entire decentralized Sponsor TMF. Electronic System Owner-Specific System Plans or "TMF Plans" will be filed into the corresponding vendor system for the plan and DAIDS TMF Team will work with the System Owners to ensure these processes are consistent with the DAIDS TMF Plan.

Protocol Trial Team

The protocol trial team will be defined as the Trial Team listed in the Protocol Roster when listed within the DAIDS TMF Index. Staff from DAIDS, vendors, and other involved parties working on the protocol, but not identified within the Protocol Roster, are not considered the protocol trial team when referenced within the TMF Index and for the purposes of filing associated artifacts.

Any personnel qualification documents and training for persons not on the protocol trial team can be filed into internal QMS or other management databases to be referenced as needed. If an Electronic System Owner is using their eTMF system for both internal document management and DAIDS protocol eTMF activities, documents for non-protocol trial team members will be classified in the artifacts under Zone 9 – Third Parties.

Referencing Other Artifacts (located elsewhere within the TMF)

There are instances when a given document (e.g., IP Handling) is found within another related artifact (e.g., Protocol Document) filed elsewhere within the TMF. For these situations, the line item that lists said document (e.g., IP Handling) within the TMF Index will reference the artifact number for the related artifact (e.g., Protocol Document 02.01.01). In addition, the line item will also include the DAIDS AS/PC and Source Location listed for the referenced artifact (e.g., Protocol Document).

See the examples in Appendix A with excerpts from Zone 1 – Trial Management, Zone 2 – Central Trial Documents, and Zone 6 – IP and Trial Supplies to illustrate how these artifacts will point towards the information in each TMF Index.

Standardized Components of the TMF Index

What items can be modified within the TMF Index?

When the TMF Index is under review, the following should **not be** modified or removed:

The following columns are per the TMF Reference Model:

- Zone, Section, and Artifact (Number and Names)
- Definition/Purpose of artifacts (including sub-artifact names)
    - If additional details are needed, a "DAIDS Specific Definition:" will also be included in order to clarify.

Exception: Alternate Names and Sub-Artifact/Examples can be modified and added as needed to correlate to specific document types and content.

Standardized Entities

The following columns have been standardized, as much as possible:

- Authoritative Source
- DAIDS PC
- Source Location
- System Owner

Entities identified in these columns will be abbreviated when applicable and defined on the Definitions and Abbreviations tab of the document.

> **Note**: Any changes to existing names or new titles provided in these columns will be reviewed by the DAIDS TMF Team and then updated to maintain a master list. The values of these columns may be locked to editing during document review and comment, in which case updates can be indicated using the comment feature in order to maintain consistency through revisions.

Providing TMF Index Feedback

The DAIDS TMF Index will be distributed as an Excel document to collect feedback during the creation of version 1.0 and subsequent major updates. All AS, DAIDS PCs, and other stakeholders (as necessary) will be given a chance to review and verify the protocol specific information for zones they support. TMF Index review discussions will be conducted as needed to review comments collected across groups simultaneously and facilitate the correct identification of responsible entities and locations.

Any feedback and updates identified between these reviews will be collected and tracked to be included in the next major TMF Index version update. AS and DAIDS PCs can send comments to the DAIDS TMF Team and RSC TMF Team to be included in future updates and any issues may be resolved in advance of implementing the next version update.

> **Note**: Only finalized TMF Index versions will be used for ongoing TMF document submissions; comments provided for future TMF Index updates will not be effective until included in a subsequent final version. Each finalized TMF Index version will be distributed to all protocol stakeholders per DAIDS approved processes.

Zone Specific Templates

The nature of certain zone contents will not be as variable from protocol to protocol as other zones. In instances where a group will expect similar details across all DAIDS protocol TMFs, a request to the DAIDS TMF Team can be made in order to create a zone specific template. These zones will have a standardized template to be used as a starting point for TMF Index creation and new reviews. Groups who have convened with the DAIDS TMF Team to standardize their applicable zone in the TMF Index will still be required to review and confirm protocol specific documents for any exceptions.

Appendix A: Sub-Artifact Reference Examples

Core or Recommended per DIA	Status	Authoritative Source	DAIDS Primary Contact	Zone #	Zone Name	Artifact #	Artifact Name	Sub-Artifact / Examples	Source Location (System)
Recommended	Required	Network LOC	Network PO	01	Trial Management	01.01.05	Operational Procedure Manual	Operational Procedure Manual	Transperfect Trial Interactive eTMF
Core	Required	RSC	DAIDS SPT	02	Central Trial Documents	02.01.01	Investigator's Brochure	IBs & Addendums, Summary of Changes (SOC)	TRI - Veeva Vault
Core	Required	Network LOC	DAIDS MO	02	Central Trial Documents	02.01.02	Protocol	Protocol, MRPG Review and Approvals	Transperfect Trial Interactive eTMF
Core	Required	Network LOC (protocol, MOP, SSP)	Relevant DAIDS Programs & Offices and Staff	06	IP and Trial Supplies	06.01.02	IP Instructions for Handling	IP Instructions for Handling, Protocol, MOP, SSP	Transperfect eTMF (included in the MOP in artifact number 01.01.05, Protocol in artifact number 02.01.02, and SSP)
Core	Required	RSC	DAIDS SPT	06	IP and Trial Supplies	06.01.02	IP Instructions for Handling	IP Instructions for Handling, IB/Package Insert	TRI - Veeva Vault (included in the IB in artifact number 02.01.01)

Selected excerpt of artifacts 01.01.05, 02.01.01, 02.01.02, and 06.01.02 from protocol IMPAACT 2023 TMF Index to illustrate reference format for the source location of documents.