TRIAL MASTER FILE
TMF
REFERENCE MODEL

Release Notes v3.1.0

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Identification

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Version History

Version	Steering Committee Approval Date	Changes
1.0	29-Aug-2018	N/A

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1 Introduction

These Release Notes relate to TMF Reference Model v3.1.0, a minor update to TMF Reference Model v3.0.

A minor update is defined as a substantial change to the content of the Reference Model, but the changes are unlikely to cause incompatibility issues with the previous version of the Reference Model and/or no significant technical changes to implement the update for electronic TMF solutions.

Examples of changes that would require a minor release include:

- Inclusion of an additional optional element to the Model
- Changes to the alignment of artifacts with filing level (study, country and site)
- Attribute updates or attribute additions
- Attribute deletions that are unlikely to cause incompatibility issues

This minor release also includes maintenance changes, defined as no significant impact on adoption or implementation of the Model. Examples of changes that would require a maintenance release include:

- Changes to the definition/purpose text that do not substantially modify the meaning e.g. additional text for clarification
- Inclusion or deletion of example sub-artifacts
- Addition or modification of regulatory guidance references
- Correction of typographical errors

2 General Changes

In some regions, there is a difference in the meaning of ‘trial’ and ‘study’, based on specific definitions from regulatory authorities. ‘Trial’ is sometimes a more restrictive term and may exclude observational and other non-interventional clinical studies. The ICH term ‘trial’ is used throughout the reference model. The reference model does not exclude studies that do not need to comply with ICH GCP e.g. non-interventional studies. Therefore, throughout the model, the word ‘trial’ can be also read as ‘study’. The term ‘study’ has been retained in artifact definitions and milestones/events.

The artifact dating conventions that were released as a TMF Reference Model Project deliverable on 15 February 2017 have been included in the core Reference Model (see column AA). There is a guidance document on the TMF Reference Model website which explains how this optional data should be interpreted and used.

The recommended milestones/events to be associated with each artifact, published 10-May-2017 and revised 16-Jan-2018, have been included in the model as three additional columns (column V for study-level milestones/events, column X for country-level milestones/events and column Z for site-level milestones/events).

Computer System Validation: An assessment has been completed and these artifacts will be maintained outside of the official TMF Reference Model and not incorporated as a new Zone 12. They will remain as a separate tab for reference.

3 Changes to Artifact Name

Artifact 03.01.02 Regulatory Approval Notification

Previous text	**New text**
Regulatory Approval Notification	Regulatory Authority Decision
Reason for change: The trial master file must contain a record of the decision from the Regulatory Authority, irrespective of whether the decision is approval, conditional approval, suspension, withdrawal or rejection. The previous artifact name implied that only approval notifications need be included.	

Artifact 03.02.02 Import or Export License

Previous text	**New text**
Import or Export License	Import or Export Documentation
Reason for change: The record confirming all compliance with all requirements for import/export is not always an import license or export license. The requirement may be satisfied with other documentation, such as an import or export letter of approval.	

Artifact 03.03.01 Notification to Regulatory Authority of Safety or Trial Information

Previous text	**New text**
Notification to Regulatory Authority of Safety or Trial Information	Notification of Safety or Trial Information
Reason for change: The length of the artifact name was too long for some eTMF systems, being greater than 64 characters. The words “to Regulatory Authority” have been removed as being unnecessary as the artifact is found in the Regulatory zone. In addition, “Trial” is changed to “Study” (see General Changes).	

Artifact 10.03.10 Data QC or QA Plan and Results

Previous text	**New text**
Data QC or QA Plan and Results	Data Review Documentation
Reason for change: The artifact name was unclear and implied it was restricted to a limited number of specific document types (Data QC/QA Plan and Data QC/QA Results).	

4 Changes to Artifact Definition / Purpose

Artifact 01.05.04 Filenote

Previous text	New text
To document any decision or to clarify any information relating to this zone. Filenotes referencing general topics and/or topics across multiple zones may be files within this zone.	To document any decision or to clarify any information relating to this zone. Filenotes referencing general topics and/or topics across multiple zones may be filed within this zone.
Reason for change: To correct a typographic error.	

Artifact 02.01.01 Investigator's Brochure

Previous text	New text
To provide relevant and current clinical and non-clinical data on the investigational product(s) that is related to the study of the product(s) in human subjects.	To provide relevant and current clinical and non-clinical data on the investigational product(s) that is related to the study of the product(s) in human subjects. The Investigational Medicinal Product Brochure (IMPD) can additionally be filed here if held in the TMF.
Reason for change: IMPD has been removed as a regulatory submission component in artifact 03.01.01. This is a more suitable filing location for those wishing to file the IMPD in a trial master file.	

Artifact 03.01.01 Regulatory Submission

Previous text	New text
A set of documents, along with required associated regulatory forms and correspondence, submitted to one or more regulatory agencies requesting approval to conduct the study or for the purpose of notification, or requesting approval of changes to the study documents or of any study events that could adversely affect the safety of subjects, impact the conduct of the study or alter the regulatory authority's approval/favorable opinion to continue the study. Example Investigational New Drug Application (IND), Clinical Trial Application (CTA), Investigational Medicinal Product Dossier (IMPD), Investigational Device Exemption (IDE).	A set of documents, along with required associated regulatory forms and correspondence, submitted to one or more regulatory agencies requesting approval to conduct the study or for the purpose of notification, or requesting approval of changes to the study documents or of any study events that could adversely affect the safety of subjects, impact the conduct of the study or alter the regulatory authority's approval/favorable opinion to continue the study. Example Investigational New Drug Application (IND), Clinical Trial Application (CTA), ~~Investigational Medicinal Product Dossier (IMPD)~~, Investigational Device Exemption (IDE).
Reason for change: No rationale for specifically identifying one component of a regulatory submission. See also 02.01.01 for related change.	

Artifact 03.03.01 Notification of Safety or Study Information

Previous text	New text
Notification to Regulatory Authorities of any study events that could alter the regulatory authority's approval/favorable opinion to continue the study. Notifications may include, but are not limited to: Quarterly line listings, suspected unexpected serious adverse reactions (SUSARs), Unexpected Serious Adverse Device Events (USADE), Council for International Organizations of Medical Sciences (CIOMS), xEVMPD, MedWatch, Analysis of Similar Events, Serious Breaches, cover letters and/or country-specific reporting forms.	Notification to Regulatory Authorities of any study events that could alter the regulatory authority's approval/favorable opinion to continue the study. Notifications may include, but are not limited to: Quarterly line listings, suspected unexpected serious adverse reactions (SUSARs), Unexpected Serious Adverse Device Events (USADE), Council for International Organizations of Medical Sciences (CIOMS), ~~xEVMPD,~~ MedWatch, Analysis of Similar Events, Serious Breaches, cover letters and/or country-specific reporting forms.
Reason for change: Submissions to xEVMPD are not trial-specific and are not part of the trial master file. They are product-level submissions for the EudraVigilance Medicinal Product Dictionary.	

Artifact 06.01.06 IP Transfer Documentation

Previous text	**New text**
To document the transfer of IP between depots and sites (within or across protocols). Examples include sponsor approval for transfer and evidence of consultation with Qualified Person (QP).	To document the process and approval for the transfer of IP from one depot to another depot and/or from one site to another site (within or across protocols). Examples include sponsor approval for transfer and evidence of consultation with Qualified Person (QP)
Reason for change: To provide clarification that the artifact included inter-depot and inter-site transfers, and also includes any associated approvals.	

Artifact 08.02.05 Record of Retained Samples

Previous text	**New text**
To document location and identification of body fluid or tissue samples being held for possible future (re)testing; to include destruction records, when and if this occurs.	To document location and identification of body fluid, tissue samples or genetic samples being held for possible future (re)testing; to include destruction records, when and if this occurs
Reason for change: To clarify that “retained samples” can include genetic samples.	

Artifact 11.03.02 Analysis QC Documentation

Previous text	**New text**
To confirm the QC procedures planned for the analysis programs as well as the actual output of the QC steps.	To confirm the QC procedures for analysis programs and validation of analysis QC programs, as well as the actual output of the QC steps.
Reason for change: Definition required extending to cover validation activities for statistical analysis, e.g. validation plan, validation report.	

Artifact 11.03.09 Final Analysis Datasets

Previous text	**New text**
The datasets used for the final analysis.	The datasets used for the final analysis/case report tabulation (CRT) package. If required, study-level submission datasets can be filed here.
Reason for change: To clarify that datasets such as SDTM datasets; ADaM datasets; define.xml file may be filed as this artifact.	

5 Additional Sub-Artifacts

Artifact 10.03.09 Dictionary Coding

New Sub-Artifacts: Coding Approval Document; Coding Listing Form; Coding Consistency Report; Final Coding Listing

Artifact 10.03.10 Data QC or QA Plan and Results

New Sub-Artifacts: Data Review Quality Plan; Data Review Quality Report; Error Rate Report

Artifact 02.03.01 Clinical Study Report

New Sub-Artifacts: Clinical Study Report Synopsis

6 Changes to ICH Code

Artifact 02.01.02 Protocol

Previous code	**New code**
1.4.4	1.44
Reason for change: To correct an error	

Artifact 02.01.04 Protocol Amendment

Previous code	**New code**
1.4.5	1.45
Reason for change: To correct an error	

7 Changes to Filing Level

Artifact 03.01.01 Regulatory Submission

Previous level(s)	**New level(s)**
Country	Study, Country
Reason for change: Depending on the study design, regulatory submissions may be at study level.	

Artifact 03.01.02 Regulatory Approval Notification

Previous level(s)	**New level(s)**
Country	Study, Country
Reason for change: Depending on the study design, regulatory approval notifications may be at study level.	

Artifact 06.03.02 IP Unblinding Plan

Previous level(s)	**New level(s)**
Study	Study, Site
Reason for change: Although the unblinding plan is most commonly a study-level document, there are occasions when a site-specific unblinding plan is required. For example, a local IRB/IEC may request a change that is only agreed for specific sites.	

8 Changes to Alternate Name

Artifact 03.01.02 Regulatory Authority Decision

Previous Alternate Name(s)	New Alternate Name(s)
	Regulatory Approval Regulatory Approval Withdrawal Regulatory Application Rejection Regulatory Approval Suspension

Artifact 03.02.02 Import or Export Documentation

Previous Alternate Name(s)	New Alternate Name(s)
	Import License Export License Import/Export Letter of Approval