Release Notes v3.3

Release Date 31-MAR-2023

Identification

Authors

Name	Organization
Kelley Robinson (Former CCB Lead)	Sention Therapeutics

Contributing Change Control Board Members

Allison Grosik	Arcus Biosciences
Emma Zuccaro	Sarepta Therapeutics
Gift-Tafadzwa Chareka	UZ-UCSF-Collaborative Research
Joanne Bilmazes	Device SME
Kate Santoro	Intellia Therapeutics (CCB Co-Lead)
Kim Songco	Pfizer
Kristen Bretzius	Pharvaris
Leila Ponce	Seagen (CCB Lead)
Mary-Ann Brooks	Baxter Healthcare Corporation
Noreen Bouchard	Astellas Pharma US
Soraya Nossoughi	Regeneron Pharmaceuticals

Version History

Version	Steering Committee Approval Date	Changes
1.0	31-MAR-2023	N/A

Table of Contents

1 Introduction

These Release Notes relate to TMF Reference Model v3.3.0, the third minor update to TMF Reference Model v3.0, Version 3.2.1 was released in March 2021.

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 addition to minor updates to existing artifacts, the 3.3.0 version of the TMF Reference Model includes the addition of the ISO 14155 reference column (column K), additional sub-artifacts and updates to definitions for device studies.

3 Changes to Artifact Definitions

Artifact 01.01.03 Quality Plan

Previous text	New text
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.	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, serious breach assessments; 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..
Reason for change: To clarify where serious breach assessments should be filed in the TMF	

Artifact 05.02.10: Financial Disclosure Form

Previous text	New text
To document financial disclosures, certification documentation and conflicts of interest, which include but are not limited to: completed disclosure forms of financial interests and arrangements of clinical investigators (e.g. FDA Form 3455/3454, NIH COI, clinical investigator financial certification (Canada))	To document financial disclosures, certification documentation and conflicts of interest, which include but are not limited to: completed disclosure forms of financial interests and arrangements of clinical investigators ~~(e.g. FDA Form 3455/3454, NIH COI, clinical investigator financial certification (Canada))~~
Reason for change: To align definitions	

Artifact 02.01.05 Financial Disclosure Summary

Previous text	New text
Summary documentation of compliance with financial disclosure reporting requirements, per company and/or local government policies. May include summaries, lists, other reports. Not specifically intended for program level records such as Forms FDA 3455 or 3454.	Summary documentation of compliance with financial disclosure reporting requirements, per company and/or local government policies. May include summaries, lists, other reports. ~~Not specifically intended for program level records such as Forms FDA 3455 or 3454.~~
Reason for change: To align definitions	

Artifact 04.03.01 Notification to IRB or IEC of Safety Information

Previous text	New text
To assure the IRB/IEC are promptly notified of all findings (new, important information on serious adverse events and or safety concerns) that could adversely affect the safety of subjects, impact the conduct of the trial or alter the IRB/IEC's approval/favorable opinion to continue the trial. Notifications/Communication may include but are not limited to - periodic safety line listings, USADEs, SUSARs, CIOMS, MedWatch, Analysis of Similar Events, cover letters and/or IRB/IEC-specific reporting forms. The records referenced in these notifications may be filed as appropriate in Zone 07.	To assure the IRB/IEC are promptly notified of all findings (new, important information on serious adverse events and or safety concerns) that could adversely affect the safety of subjects, impact the conduct of the trial or alter the IRB/IEC's approval/favorable opinion to continue the trial. Notifications/Communication may include but are not limited to - periodic safety line listings, USADEs, SUSARs, CIOMS, MedWatch, Analysis of Similar Events, cover letters and/or IRB/IEC-specific reporting forms. The records referenced in these notifications may be filed as appropriate in Zone 07. May include IRB/IEC Acknowledgement of Receipt.
Reason for change: Clarification	

Artifact 05.04.01 Subject Log

Previous text	**New text**
To anonymously list all subjects including screened, screen failures and enrolled for the sponsor. Not anonymous at the Investigator site	To anonymously list all subjects including screened, screen failures and enrolled for the sponsor. ~~Not anonymous at the Investigator site~~
Reason for change: Remove duplication with 05.04.10	

Artifact 05.03.02 Site Training Material

Previous text	**New text**
Training materials used to train the sites. Materials may be related to Electronic Data Capture (EDC), Interactive Response Technology (IRT), Rater training. (Also includes training done after site initiation)	Training materials used to train the sites. Materials may be related to, but not limited to, Electronic Data Capture (EDC), Interactive Response Technology (IRT), Rater training. (Also includes training done after site initiation)
Reason for change: Clarification	

Artifact 05.04.05 Additional Monitoring Activity

Previous text	**New text**
To document additional monitoring activity such as co-visits and sponsor-specific monitoring activities.	~~To document additional monitoring activity such as co-visits and sponsor-specific monitoring activities.~~ To document additional sponsor and/or study-specific monitoring activities
Reason for change: Clarification (Co-Visits are filed in 05.04.03)	

Glossary: Core

Previous text	**New text**
If created or collected, the artifact must be in the TMF as dictated by either the ICH Guidelines, regulations, or by consensus of the TMF Reference Model group.	If created or collected, the artifact must be in the TMF and/or ISF as dictated by either the ICH Guidelines, regulations, or by consensus of the TMF Reference Model group.
Reason for change: Clarification	

4 Changes to Document Level

Artifact 05.01.01 Site Contact Details

Previous Level(s)	**New Level(s)**
Site	Trial, Country & Site
Reason for change: To accommodate scenarios where site contact details come in the form of a report at study or country levels rather than one per individual site	

Artifact 05.02.13 Indemnity

Previous Level(s)	**New Level(s)**
Site	Country & Site
Reason for change: To accommodate for country level filing	

Artifact 10.05.02 Tracking Information

Previous Level(s)	**New Level(s)**
Trial & Site	Trial, Country & Site
Reason for change: To correct an error	

5 New Sub-artifacts

New Sub-artifacts identified in red.

Artifact #	Artifact name	Recommended Sub-artifacts - Documents/documentation recommended to be filed to the artifact.	Reason for Change
02.01.03	Protocol Synopsis	Protocol Summary Protocol Synopsis	Sub-artifact added to accommodate country regulations.
02.03.01	Clinical Study Report	Clinical Investigation Report Clinical Study Report Clinical Study Report Synopsis Integrated Clinical and Statistical Report Interim Clinical Study Report Interim Clinical Study Report Synopsis Form FDA 3654 (devices)	Sub-artifacts added for device studies.
04.03.01	Notification to IRB or IEC of Safety Information	Acknowledgement of Receipt of Safety Information Evidence of Distribution of Safety Information Notification to IRB or IEC of Safety Information	Sub-artifact added to clarify where acknowledgements should be filed.
05.03.02	Site Training Material	Site Training Material Quick Reference Guide	Sub-artifact added for device studies.
05.04.02	Source Data Verification	Source Data Specification and Agreement Source Data Verification Device Extracts Source Document Maps	Sub-artifacts added for device studies.
05.04.03	Monitoring Visit Report	~~Co-Monitoring Visit Report~~ Monitoring Visit Confirmation Letter Monitoring Visit Follow Up Letter Monitoring Visit Report Monitoring Visit Waiver	Co-Visits are filed in 05.04.05
05.04.05	Additional Monitoring Activity	Additional Monitoring Activity Co-Monitoring Visit Report Non-Routine Visit Report Non-Routine Visit Report Confirmation Letter Non-Routine Visit Report Follow Up Letter Oversight Monitoring Visit Report Oversight Monitoring Visit Report Confirmation Letter	To clarify where co-visits are filed and align with this artifact definition

Artifact #	Artifact name	Recommended Sub-artifacts - Documents/documentation recommended to be filed to the artifact.	Reason for Change
		Oversight Monitoring Visit Report Follow Up Letter Site Improvement Plan	
06.01.09	IP Quality Complaint Form	IP Quality Complaint Form Device Deficiency Report	Sub-artifact added for device studies.
06.02.03	IP Verification Statements	Controlled IP Storage DEA 223 GMP Certificate GMP Manufacturer's License GMP Statement IP Verification Statements Manufacturing Authorization Manufacturer's Certificate of Compliance TSE Certificate	Sub-artifacts added for device studies.
06.02.04	Certificate of Analysis	Batch Records Certificate of Analysis Certificate of Conformance Device Quality Certification	Sub-artifact added for device studies.