Inspection Readiness Guidance for Global Trial Coordination

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Follow this step-by-step guidance for keeping your study inspection ready!

In this guidance you will find an overview of some important activities related to inspection readiness. In addition, we have included helpful reports and great tools that can boost your trial's inspection readiness.

*Note: this is a living document and sections will be periodically added/updated and is specific for GTC roles. This is a J&J Innovative Medicine internal document and not to be shared with third parties.

Contents

Version History

Version	Changes
4.0	• Updated new terms and acronyms (e.g. IWRS to RTSM, CAT to EAT report • Included guidance for IDM studies • Changed chapter 4 from COVID-19 specific to general global/regional crisis guidance • Included new Trial Contact List version and process • Expanded vendor oversight chapter • Updated paragraph on ICF review & approval and reconsenting • Added guidance on filing of financial information • Added Essential Document Tracker example • Added medidata RAVE EDC form activation process • Added Financial Disclosure VIPER report • Updated links and examples Updated language and corrected small errors
3.1	• Removed references to QRM3 and included ATLAS • Added link to Start-up Portal • Added a section on Signature History and Compliance Dashboard • Added GCO Table of Contents • Added a section on Curation Activity Review • Updated links to iGuide with links to Blackbird Updated VIPER links
3.0	• Updated links in the document • Updated language throughout the document • Added guidance on electronic signatures • Updated processes that changed since version 2.1 (e.g., timely filing, AQR) • Updated resources embedded in document, like Word or PPT files Updated inspection readiness checklist in appendix based on user feedback and added an Excel tracker
2.1	• Added a Version History • Updated links in the document

	Statement added on the first page that this is a J&J Innovative Medicine internal document
2.0	• Improved consistency across the document regarding abbreviations/references • IDM involvement • Removal copy/paste wording from instructions/ guidance captured in previous versions of the SOPs/FRMs/WI • Reworded/improved guidance on the different topics • COVID-19 references APPENDIX: IR tool / checklist
1.0	Initial version

Introduction

J&J Innovative Medicine has an obligation to ensure that all studies are conducted using the highest quality standards. Inspection readiness is a quality objective that helps to ensure that we are prepared for Regulatory Authority inspections.

Inspection Readiness means:

- All clinical data, documentation, and records have been subject to appropriate quality control (QC) checks, are therefore accurate, up to date and correctly filed.
- Information is readily accessible, and if applicable filed in an official repository, when questions are received from Regulatory Authorities.

This guidance document created for the GTC community aims to provide you with information and activities that you can/should perform throughout your study to ensure it is always inspection ready.

If it is not documented, it never happened. Documentation is KEY (**V-TMF maintenance is CRITICAL**), and we need to ensure all documentation is in line with our procedures and guidelines. In addition, Regulatory Authorities can and will access our V-TMF during inspections and can search the spectrum of trial-specific folders. Therefore, V-TMF maintenance per our guidelines is essential.

This guidance is aimed to support CTM, IDMM, GCTA and UGCTA roles.

Before anything else, preparation is the key to success!

- Alexander Graham Bell

List of Abbreviations

- ADIR – Actions, Decisions, Issues and Risks
- AE – Adverse Event
- AQR – Annual Quality Review
- ARBM – Analytical Risk Based Monitoring
- CAPA – Corrective and Preventive Action
- CAR – Curation Activity Review
- CFTT – Cross Functional Trial Team
- CRM – Clinical Risk Management/Manager
- CRO – Clinical Research Organization
- CTL&D – Clinical Trial Learning and Development
- CTM – Clinical Trial Manager
- CTMS/mCTMS/OneCTMS – Clinical Trial Management System/Medidata CTMS
- CV – Curriculum Vitae
- DL – Delegation Log
- EAT – EDL Assessment Tool
- EDC – Electronic Data Capture
- EDL – Expected Document List
- EMA – European Medicines Agency
- ESP – External Service Provider
- FAP/eFAP – Filling and Archiving Plan/Electronic FAP
- FDA – Food and Drug Administration
- FQR – Final Quality Review
- FUL – Follow-up Letter
- GCO – Global Clinical Operations
- GCP – Good Clinical Practice
- GCTA/CTA/UGCTA – Global Clinical Trial Associate/ Unblinded GCTA
- GD – Global Development
- GLP – Good Laboratory Practice
- GMP – Good Manufacturing Practice
- GPL – Global Program Lead
- GPTP – Global Protocol Training Plan
- GTC – Global Trial Coordination
- GTL – Global Trial Leader
- IB – Investigator's Brochure
- ICF/eICF – Informed Consent Form/Electronic ICF
- ICSR – Individual Case Safety Report
- IDAR – Integrated Data Analytics and Reporting
- IDM – Independent Drug Monitor
- IDMM – Independent Drug Monitoring Manager
- IDMT – Independent Drug Management Team
- IEC – Independent Ethics Committee
- IMP – Investigational Medicinal Product
- IN – Inspection Narrative
- IP – Investigational Product
- IPPI – Investigational Product Preparation Instructions

- IRB – Institutional Review Board
- ISF – Investigator Site File
- LMS – Learning Management System
- LTM – Local Trial Manager
- MG – Monitoring Guidelines
- MV – Monitoring Visit
- MVR – Monitoring Visit Report
- PD – Protocol Deviation
- PI – Principal Investigator
- PMDA – Pharmaceuticals and Medical Devices Agency
- POL – Policy
- QC – Quality Control
- QR – Quality Review
- QRCF – Quality Review Confirmation Form
- RA – Regulatory Authority
- RCT - Role Clarity Tool
- R&D – Research & Development
- RTSM – Randomization & Trial Supply Management
- SAE – Serious Adverse Event
- SDV – Source Data Verification
- SII – Self-Identified Issue
- SIPPM – Site Investigational Product Preparation Manual
- SIV – Site Initiation Visit
- SM – Site Manager
- SME – Subject Matter Expert
- SMT – Study Management Team
- SOP – Standard Operating Procedure
- SRP – Study Responsible Physician
- SRS – Study Responsible Scientist
- SUSAR – Suspected Unexpected Serious Adverse Reaction
- TCF – Trial Central File
- TCL – Trial Contact List
- TL – Training Log
- TMF – Trial Master File
- TOC – Table of Contents
- TW – TrackWise
- V-TMF – Veeva Vault Trial Master File
- WI – Work Instruction

CHAPTER 1: Some useful information before you start

1.1 What steps can I take to ensure I am Inspection Ready?

Be prepared for an inspection – EVERY DAY

- Know your job/role and be knowledgeable about the roles and responsibilities, per your job description and as outlined in the Role Clarity Tool (RCT) for your study. Role Clarity Tools can be found on The JJCO Study Management Playbook. For the IDMM role, the RCT is available on the IDMM knowledge hub, only accessible for IDMM and UGCTA. Note: the RCT is sometimes named the Task Assignment List (TAL).
  Specifically:
  - Be able to explain responsibilities, hand-over documentation should be in place, decision making process.
  - Have evidence of actions you are responsible for.
- Have your CV/job description updated and available in My Training Plan.
- Document your training, ensure your training file is up to date and that you complete the assigned training prior to the due date.
- If you joined the team while the study was ongoing, ensure hand-over documentation is appropriately completed, signed and filed.
- Ensure the Trial Contact List for your assigned studies is up to date for your role.

Know and follow your procedural documents, Job Aids, and study-specific plans and guidelines.

In order to develop our job properly, we need to know and follow the Global and Local procedures within the company. The Table of Contents (ToC) of procedural documents can be accessed from the R&D SharePoint in the Quality Management section under Procedural Documents section: https://jnj.sharepoint.com/sites/PHM-GCSP-RND/GCO/Pages/default.aspx

Two folders are available in this SharePoint:

- Global Table of Contents (ToC) of Procedural Documents.
- Local Table of Contents of Procedural Documents. Local procedures are country specific and are intended for local specific practice exclusively.

The Global ToC provides an overview of procedural documents supported by R&D Quality Process & Data Management (Policies, SOPs, Work Instructions, Manuals, Forms, Guidelines). The purpose is to define when new SOPs are implemented at Global level and became effective, if they are applicable and to summarize major changes.

With the Global ToC you are always able to access the current effective version of a procedural document, particularly if a new version becomes effective between issuance of the next version of the ToC and you are aware of related procedural documents, including deviations (if applicable), implementation instructions, as well as any other supporting documents, such as implementation memoranda.

Resources

- Procedural Documents
- Tru'Vault Viewer to consult the procedural documents once identified in the Global ToC. (procedural documents can also be found through Blackbird)
- In case of questions direct your message to the Learning @ Pharma R&D Admins mailbox (RA-JACNL-lprdadmins@its.jnj.com)
- My Training Plan

1.2 What resources/tools are available?

There are several resources/tools available that help to understand the inspection process and support inspection readiness activities. These are summarized in this chapter under:

- 1.2.1 R&D Quality - Quality Assurance – Inspection Management - Toolkit
- 1.2.2 V-TMF Resources (V-TMF Portal Inspection Support Documents)
- 1.2.3 FDA and EMA guides

1.2.1 R&D Quality – Quality Assurance- Inspection Management Toolkit

The R&D Quality - Quality Assurance – Inspection Management - Toolkit is the central portal for GCP, GLP, GMP, Pharmacovigilance, and MedTech inspection-related information. It provides the following:

- Resources for boosting inspection awareness
- Tools, checklists, and training materials for ensuring inspection readiness and preparation for inspections (mock-/sponsor-)
- Access to R&D Quality inspection data and metrics
- Site Master File quality review check list
- Links to global Regulatory Authorities
- Links to documents frequently requested during Regulatory Authority inspections specifically for FDA, EMA, and PMDA (i.e., Japanese Pharmaceuticals and Medical Devices Agency)
- Links to informational slides/trainings, for example:
    - Lessons Learned presentations
- Inspection Readiness Assessment Interview Questions:
    - Inspection Readiness Assessment
        - This assessment is a list of questions related to all Functional Areas of a trial to support preparation for an inspection

1.2.2 V-TMF Resources

V-TMF related procedural documents and Jobaids are available on Blackbird.

Other useful information can be found on the V-TMF portal

The portal includes different sections with additional resources such as guidance materials like Quick Reference Cards (QRCs) and instruction videos (e.g., quality review and the Filing and Archiving Plan), and inspection support documents (e.g., Inspector V-TMF Access Form and Inspection Checklist).

Contact the TMF CoE Inspection Mailbox once you have been made aware of an announced Regulatory Authority Inspection: *RA-RNDUS-TMF-CoE-Ins@ITS.JNJ.com*

V-TMF Inspection Toolkit

This section of the V-TMF portal includes several resources and training materials that can assist you in preparing for any upcoming inspection/audit around the Trial Master File (TMF).

V-TMF Inspection Access Form

This Access Form is used to request and track the creation of V-TMF accounts which have limited V-TMF access for documents in final state (Approved, Superseded, and Expired Documents Only) for the following roles:

- Study Team Driver: J&J personnel (or designee) navigating V-TMF during inspections. Anyone navigating V-TMF during the inspection will need this access type. The Driver account is a new account that is created in addition to the existing standard user account. Access to the standard user account will be maintained. Driver account must be used during inspection while interacting with the Inspector.
- Inspector: Direct access into V-TMF system for External Inspector/Internal Auditors. For internal auditors, inspector direct access is recommended, however it is not required. Typically, direct access is requested when access to restricted (unblinded) content is required to be reviewed during an audit.

V-TMF Inspection Checklist

The V-TMF inspection Checklist was put together to encompass the inspection activities related to V-TMF from beginning to end. For example, you will find information on how to request Inspector/Driver access to the V-TMF system prior to the inspection and how to revoke access once the inspection has ended. It also includes key areas to focus on during your inspection readiness activities and key responsible Points of Contacts for each item listed.

For IDM studies, unblinded auditor/inspector Access to systems might be required. If unblinded access is required, the IDM is to coordinate for the access arrangement. For instance, for access to restricted V-TMF access, refer to the V-TMF Inspection Tool Kit. For access to unblinded eCRF, refer to TV-MAN-00258: Study, Site, and User Account Management for All RAVE URLs. If needed, the UGCTA is able to provide support.

Trial Master File Documents often requested during inspections

The documents in the table below are often requested during Regulatory Authority (RA) inspections. These can be sampled for completeness and content quality. Note that RAs can request direct access to our V-TMF; thus, content (quality) checks are critical.

STUDY level	COUNTRY level	SITE level
• Trial Master File Plan & TOC • List of SOPs Current During Trial (to be filed by Study Closure) • Monitoring Plan • Medical Monitoring Plan • Vendor Management Plan (ESP Oversight Plan) • Independent Data Monitoring Committee Charter • Independent Data Monitoring Committee Correspondence • Investigators Meeting Material – Training records • Protocol & Protocol Amendment • Insurance Update Assessment • Sample Case Report Form • Subject Diary • Master ICF Review and Approval Form • Master Clinical ICF and Amendments and ICF Tracker • Public Registration evidence • Investigational Material Packaging Agreement (IMPA) • Investigational Medicinal Product Dossier (IMPD) • IP Supply Plan • Safety Management Plan • Data Management Plan • Database Release Plan • Annotated CRF (Case Report Form) • Statistical Analysis Plan • Clinical Study Report • List of Major Protocol Deviations and Site Issues • IB • Central Lab Documentation (certification, Normal Ranges…) • Key vendors (imaging) charters • IMP CoA (Certificate of Analysis & key related reconciliation records • Master Randomization List if applicable • Audit Certificates • List of Vendors/External Partners • List of staff involved, by functions • All key study manuals (RTSM, Covance, ERT, etc.) • RTSM reports	• Clinical Trial Application Cover Letter (initial & Amendments) • Clinical Trial Application Form & Submission package (initial & Amendments) *Note: above also includes IB and ICSRs, and related approvals* • Country Confirmation for Additional Labeling • National Insurance • Import license • Insurance certificates • Local ICF & approval documentation • Sponsor documentation related to significant issues or Serious Breaches, incl. RA reporting as applicable	• IRB/IEC Submission Letter & Submission package (initial & Amendments) • IRB/IEC Approval (initial & Amendments) • IRB/IEC Composition • IRB/IEC Annual Report if applicable • Financial Disclosure Form • CV PI • Clinical Trial Agreement • Protocol Signature Page • Normal ranges local lab • IMP Accountability records • IP Site Release Documentation • IMP CoA (Certificate of Analysis) • Site Staff Delegation and Training Log • Site Signature Sheet • Initiation Monitoring Report • Monitoring Visit Follow-up Letter • Monitoring Visit Report • Final trial close-out monitoring report • SUSAR • Completed SAE forms • ICF templates used by site • Site Insurance (if any) • Completed CRF / DCF (Data Clarification/Correction Form) • Record of retained body fluids/ tissue samples (if any) • Drug Accountability reports

1.2.3 FDA & EMA Guidelines

- FDA Compliance Program Bioresearch Monitoring document
    - The purpose of this compliance program is to provide uniform guidance and specific instructions to FDA's Office of Regulatory Affairs and center personnel for conducting inspections of clinical investigators- and sponsor-inspections and for gathering and preparing the evidence to support recommendations as part of the regulatory decision-making process.
        - BIMO (Bioresearch Monitoring) Guide for Clinical Investigators
        - BIMO Guide for Sponsor Inspections

- EMA Good Clinical Practice (GCP) Inspection Procedures webpage
    - GCP Inspectors Working Group has developed procedures for the coordination, preparation, conduct and reporting of GCP inspections requested by the EMA's Committee for Medicinal Products for Human Use (CHMP) in the context of the centralized procedure. The webpage includes references/links to procedural documents for general inspections and remote inspections during a global/regional crisis.
        - EMA Guidance for the Conduct of GCP Inspections – Investigator site
        - EMA Guidance for the Conduct of GCP Inspections - Sponsor and CRO

1.2.4 Useful Links

Website	Address	Comments
Global Development (GD) Links	https://jnj.sharepoint.com/teams/GLOBALDEVELOPMENT/SitePages/Hot-links.aspx	Contains a comprehensive list of all platforms used within GD e.g., ATLAS, VIPER, V-TMF, Blackbird
Global Clinical Operations (GCO) Links	https://jnj.sharepoint.com/teams/GlobalDevelopment-GlobalClinicalOperations/SitePages/GCO---LINKS.aspx	Contains a comprehensive list of all platforms used within GCO e.g., DrugDev, Over-C, CTMS Portal, ARBM Portal.

CHAPTER 2: Good Documentation Practices: key documents, forms, and quality processes

Everything is connected! The Expected Document List (EDL) provides guidance on what document types are expected to be filed in V-TMF and who is responsible to manage the TMF content filed in V-TMF (i.e., 'Managed By' column). This feeds into several reports, like the electronic Filing & Archiving plan (eFAP) and the VIPER EDL Assessment Tool (EAT) report. The V-TMF Content Map (TV-FRM-06254) shows where all study documents should be filed. The Annual Quality Review requirement provides confirmation that each Functional Area, study team, and local team has filed the expected documents per EDL in V-TMF using the Quality Review Confirmation Form in conjunction with the evidence of review.

For a list of documents/forms that should be created at study start, please refer to the Start-up Trials Actions Resource Tool on SharePoint. There you will find a useful roadmap to each step in the process with the needed links to SOPs/Job Aids and Forms.
Role specific study start-Up Checklists for In-house trials are also a great resource during study start, containing key tasks that the specific role is responsible for during Study start-up. The checklist can be found in the JJCO Playbook>Study Start-Up>Role Specific Checklists. The IDMM study start-up checklist is available on the IDMM Knowledge Hub.

2.1 Expected Document List (EDL)

The EDL is a functionality within V-TMF that provides Functional Areas and local teams the ability to indicate and identify which document types will be collected and which Functional Area is responsible to manage this content (i.e., 'Managed By' column) in V-TMF during the trial at study-, country-, and site level.

The EDL feeds among others into the eFAP, which will be discussed further on in this guidance in **Section 2.3: Filing & Archiving Plan (FAP).** The VIPER EAT report also uses EDL data which is discussed further in **Section 3.2.1: EDL Assessment Tool (EAT) Report**.

The EDL:

- Allows study teams to define which Classifications are "Required, Not Required, Pending Decision" and which Functional Area is responsible to manage this content in V-TMF.
- Gives the ability to identify missing documents and documents that were unexpectedly filed.
- Shows Document Types not applicable to the trial

Each Functional Area is responsible for configuring their own EDL settings as well as filing their required documents in V-TMF in a timely manner. Similarly, the local teams are required to configure the EDL settings for their countries and sites.

Important to know:

- EDL settings are to be reviewed and updated within 30 days of the first site opened actual date. Best practice is to start on time as some team members might not be so experienced with V-TMF. Having the EDL in place within the recommended timeframe will provide a good overview of the documents pending.
- EDL needs to be reviewed prior to the creation of the eFAP (if applicable for study).
- The EDL must be reviewed as part of the Annual/Final Quality Review by all Functional Areas and local teams or as needed with study changes.

The GTL is responsible for overseeing the process of setting the EDL on study level, and the CTM-LTM oversees this on country/site level.

The Functional Areas may not be as familiar with the EDL settings as the GTL/CTM/IDMM/(U)GCTA are. Therefore, Functional Area/country/site member may be trained during the CFTT meeting for the Functional Areas and during the SMT meeting and IDMT meeting for the countries and sites. Make sure this activity is started well in advance of the deadline, as the process of setting the EDL can take time.

Resources

- V-TMF EDL Training
- EDL Quick Reference Cards
- EDL Training Recording and Slides
- Let's Talk EDL Training
- TV-eFRM-07104: EDL Governance Document

2.2 TMF Content Map

The V-TMF Content Map can be downloaded from TruVault as TV-FRM-06254. It contains a Listing of all potential J&J Innovative Medicine TMF content.

One can also access a visualization of the V-TMF Content Map from the VIPER homepage: https://jnj.sharepoint.com/teams/Operational_Insights/SitePages/Viper.aspx . The dashboard allows for more detailed information for all versions of the TMF Content Map and a Change Log history.

- The TMF Content Map contains:
    - Instructions on where to file documents in V-TMF

- All TMF classifications
- TruVault document numbers
- Includes content location, authoritative source, and Functional Area content owner/managing information for each identified document type.
- At which milestones documents should be filed
- Recommended filing level (study-, country- or site level)
- Provides description for each document using the standard description convention used in pharma as noted in V-TMF. V-TMF description reminders:
  - When uploading a document ALWAYS REMEMBER TO INCLUDE A DESCRIPTION of the document. However, when documents are integrated from an external system, attribute/ metadata incl. description fields should not be edited, as this may break the integration.
  - Avoid repeating in the Description field, if possible.
  - The description and guidance for description columns are included in the Viper TCM Visualization Tool, and not in the Truvault TCM version.

- The TMF Content Map is to be used as a reference tool when managing TMF content in alignment with TV-SOP-12844: Management of the Trial Master File.

2.3 Filing & Archiving Plan (FAP)

The (electronic) Filing & Archiving Plan (eFAP) is a roadmap used to determine the following for a specific study:

- What TMF content is being managed?
- Who is managing the content?
- Where the content is being maintained in collaboration with the TMF Content Map (TV-FRM-06254)

Most studies will use the electronic FAP, called eFAP, which is a VIPER report that pulls information from the EDL and V-TMF in general [including whether documents are filed and referrals to Non-V-TMF external locations]. The eFAP is created in the VIPER V-TMF Quality & Metrics Dashboard.

For some studies, the eFAP is not in scope. Instead, a Word format of the FAP is used called the FAP Form (TV-FRM-10860). This Inspection Readiness Guidance will only focus on the eFAP. Check the FAP Job Aid to see what type of FAP is in scope for your study and for Guidance on how to use the FAP Form (TV-FRM-10860).

Important to know:

- The EDL must be reviewed by all participating Functional Area and updated prior to finalizing the initial (e)FAP version.

- EDL needs to be reviewed prior creation of eFAP.
- eFAP instruction videos can be found here.
- Once the initial (e)FAP is created, it needs to be approved by the CTMS/ TMF CoE. This is done through the submission of a SAM ticket (via the SAM Form: 'Filing and Archiving Plan FAP: request for TMF CoE review'), that requests the TMF CoE to review and approve the eFAP.
- Once approved the (e)FAP needs to be uploaded to V-TMF and routed for signatures from the GTL and TMF CoE representative.
- Approval and Upload in V-TMF should occur within 90 days of the first site open actual date to ensure timely filing compliance.
- Although updates to the eFAP throughout the study are not required (as this is a living system document), the eFAP should be refreshed or updated for audits/inspections and study close.
    - It is recommended to review EDL updates periodically throughout the year, especially during the Annual Quality Review. If any updates to the eFAP arise, it is your prerogative to create a new eFAP in VIPER and file it in V-TMF with GTL approval; additional TMF COE approval is not necessary for subsequent versions.
    - For Study close, the Filing and Archiving Plan should be reviewed and should reflect the current status of the EDL. Updated FAPs should be uploaded into V-TMF prior to Study Lock. eFAPs can be uploaded directly to V-TMF with GTL approval; additional TMF COE approval is not necessary for final eFAP.

Resources

List of training documentation:

- e-/FAP Training Materials (Training videos, Job Aid)
- TV-SOP-12844: Management of the Trail Master File
- e-FAP Quick Reference Cards (QRC) [[under Topic: Viper V-TMF Quality and Metrics Dashboard]]
- EDL Quick Reference Cards
- Instructional Video on the Filing and Archiving Plan (FAP)

2.4 GCO V-TMF Annual Quality Review (AQR)

Quality review of the TMF is an ongoing process overseen by the 'Managed By' Owner(s) for all studies in scope of TV-SOP-12844: Management of the Trial Master File. TMF quality review consists of conducting quality checks (QCs), cross-checks, co-dependency checks, unauthorized and unexpected activity checks, and identifying missing documents within a defined review cycle (annually at a minimum) for the entirety of the study for the full TMF, both paper and electronic filing.

The GCO Quality Review Job Aid provides GCO Specific Guidance on how to utilize the GCO Quality Review Guidance Documents in conjunction with the Conduct Quality Review Feature in V-TMF and the GCO Quality Review Evidence Reports during Quality Reviews.

The first V-TMF Annual Quality Review should be completed within the 12 Month Annual interval after the Study Start Date (First Site Open Actual FSOA) of the study. Subsequent reviews should be completed annually as per AQR Due date. The AQR can be completed at any time within the annual review time frame. One does not have to wait until the annual date of the last AQR – there is a perception that QR is completed on the same date each year, but there is flexibility to conduct at any time during the 12-month window.

Final Quality review (FQR) of TMF content must be performed by each functional area when all expected TMF content have been filed, and study is completed or as per departmental process if timelines differ for FQR . Ensure TMF is complete, and all outstanding issues are addressed. The FQR process is described in the FQR section in the GCO QR Job Aid. Each Functional Area (FA) is required to perform the review for documents within their Functional Area. Local teams review the documents for each country and each site. For IDM trials, IDM is to review site level documents, while the IDMM reviews country and study level documents.

The review is only considered 'complete' when there is an approved Quality Review Confirmation Form (TV-eFRM-02260) and Quality Review Evidence for each Functional Area, study-, country-, and site level filed separately in V-TMF.

In this section you can find mandatory instructions on how to perform the Annual Quality Review for GCO. These instructions aimed towards CTMs, IDMMs, and (U)GCTAs, but it can be used by other roles as well. In that case there is usually just one reviewer. It is however recommended to having a second pair of eyes involved in the review to catch anything that may have been missed.

REMINDER: All Functional Areas are required to perform their own quality review/checks, and the Quality Review Confirmation Form and evidence of the review is required to be filed for all functional departments as outlined in the eFAP/FAP. The GCTA may send reminders to all functional departments in advance of the due date. Best practice is for each functional area to use the VIPER AQR Compliance report to proactively manage upcoming AQR due dates for each of their trials and not rely on GCTA reminders. Please ensure the following things are in place before the AQR:

- ✓ Due date of the Annual Quality Review, which is FSOA (First Site Open Actual) + 1 year, 2 years, 3 years etc. The due date for each review interval can be found in the in VIPER AQR Compliance Report.
- ✓ Access to V-TMF for applicable team members.
- ✓ All documents have a standard description in V-TMF. See Viper Vizualisation Tool for Description and Guidance for Description especially around integrated documents.
- ✓ Access to VIPER.
- ✓ Download latest version of the Quality Review Confirmation Form (TV-eFRM-02260) from TruVault.

2.4.1 Performing the AQR Review with the GCO Quality Review Evidence Report:

The GCO Quality Review process is mandatory for GCO Functional Area. Throughout this section you will be able to find links to various resources.

The roles and responsibilities for the AQR should be agreed upon within the study team. The team may decide other roles tasked to perform each step. For IDM functional area documents, IDMM and UGCTA are involved in this process. Consider that the first review of V-TMF usually takes more time and requires more in-depth review than subsequent AQRs. As per TV-SOP-12844, and Job Aid GCO Quality Review, the following steps are mandatory and should be followed in order for performing the V-TMF Annual Quality Review:

1. Verify EDL Settings (both Requiredness and Managed By)
2. Use the Conduct QR Feature on a minimum of 10% of documents uploaded since completion date of previous AQR. (Remember- this can be applied throughout the year, not just at the time the review is due)
3. Run and export the GCO Quality Review Evidence Report ((U)GCTA may provide support)
4. Review all documents uploaded since last review period and enter discrepancies in the provided columns of the report.
5. Send the Evidence Report with discrepancies to the CTM/IDMM [(U)GCTA]
6. Review the work and any discrepancies the (U)GCTA noted [CTM/IDMM]
7. Follow-up on any findings [(U)GCTA, and/or CTM/IDMM]
8. Sign and file the Quality Review Confirmation Form and as well separately file the GCO Quality Review Evidence Report in V-TMF as evidence of review [(U)GCTA or CTM/IDMM].

Step 1: Verify EDL Settings

Refer to **Section 2.1** for details on how to review and revise EDL settings. It is important to perform this step first as GCO QR evidence reports uses “Managed By” field to pull information into the report.

Step 2: Use of Conduct QR Review Feature

The Conduct QR Feature is a feature in V-TMF. Its purpose is to facilitate quality checks and visual inspections of specific documents at various levels.

Refer to the Job Aid: Conduct Quality Review Feature in V-TMF for detailed information on how to use this feature:

Access the Job Aid: GCO Quality Review to watch an instructional video on “How to Use the Conduct Quality Review Feature in V-TMF".

Use of the Conduct QR Feature needs to be completed prior to running the GCO Quality Review Evidence Report(s) as the Conduct QR Feature results will populate automatically into the GCO Quality Review Evidence Report.

In GCO, the Conduct QR Feature in V-TMF should be applied at a minimum to 10% of documents uploaded from last review cycle, or if completed during first QR, a minimum of 10% of documents uploaded in the past year. If significant issues are noted, the scope of the review should be extended beyond 10% until the reviewer can confirm completeness and accuracy of the documents filed.

For guidance on which documents to apply the QR Feature, please consider the "Documents Frequently Requested by Health Authorities" located in the Regulatory & Compliance Inspection Toolkit (see links below) as well as the Role Based Guidance documents and your general knowledge of the study.

- EMA GCP Inspection Readiness Documents-Anticipated Docs
- FDA Sponsor Inspections Commonly Requested Docs
- PMDA GCP Inspection Documents

Step 3: Run and export the GCO Quality Review Evidence report [(U)GCTA]

Use the V-TMF Reports tab to run the GCO Quality Review Evidence report.

For this report to work properly, the EDL setting for documents Managed by GCO should be correct. This report will pull in only documents where the EDL setting lists GCO or IDM and Various within the Managed by field. For details on how to access, run and export the GCO Quality Review Evidence report, please review the Job Aid: GCO Quality Review.

Step 4: Review the documents applicable to your scope and enter comments in the GCO Quality Review Evidence report [(U)GCTA]

Please note this step may be performed by (U)GCTA and/or CTM/IDMM. Review the documents and add comments/findings in the Reviewed by (Date) column. In addition, always add who has reviewed it and when it was reviewed.

What should you look at?

- Are the documents complete?
- Are all documents filed?
- Are they filed in the correct place (e.g. Classification, Level)?
- Are they duplicate?
- Are they "draft"? If so, can you find out why?
- Are track-changes included and if so, why?
- Are all signatures present?
- Are all versions present?

- Is the document description complete and standard description applied?
- Patient Identifiers and financial information should be redacted.
- Is the document date and document version (if applicable) correct?

It is easy to sort/filter on document type or document description, so the same documents are grouped together in the sheet.

Review the Document Status Dashboard in V-TMF. This tool will help identify documents that require some actions, such as blank description, draft status, paper TMF reconciliation. The QRF: V-TMF Document Status Dashboards: Study, Country, Site, shows the steps to run and navigate the V-TMF document status dashboard.

Filing Level	Doc Type	Doc Sub Type	Doc Class
Study	Central Trial Documents	Subject Documents	Master Clinical ICF
Study	Central Trial Documents	Subject Documents	Master Clinical ICF
Study	Central Trial Documents	Subject Documents	Master Clinical ICF
Study	Central Trial Documents	Subject Documents	Master Clinical ICF
Study	Central Trial Documents	Subject Documents	Master Clinical ICF

In the process of performing the Annual Quality Review please also make sure to review the VIPER EAT report, along with other tools (refer to section above on V-TMF Resources) and solve any errors indicated in the report. What do the EDL errors in the first column mean (in our own words)?

- Available – Outlier = Document is required [EDL], but misfiled
- Error = Document is not required [EDL], but a document is filed
- Error – Outlier = Document is not required [EDL], but a document is filed and misfiled
- Missing – Outlier = Document is required [EDL] but at wrong level. No document yet.
- Missing – Pending Decision = EDL setting is pending. No document filed yet.
- Missing – Required = Document is required [EDL], but no document is filed.
- Missing Final – Pending Decision = EDL setting is pending. Document uploaded is draft.
- Missing Final – Required = Document is required [EDL], but document uploaded is draft.
- Timepoint not reached = Document is required [EDL], but milestone has not passed.
- Unexpected = EDL setting is pending. Document uploaded.
- Unexpected – Outlier = EDL setting is pending. Document misfiled.

Step 5: Send the GCO Quality Review Evidence report with comments to the CTM/IDMM [(U)GCTA]

After the GCTA has finished the review, send the sheet to the CTM for review. The UGCTA will support the IDMM.

Step 6: Review the work and comments of the (U)GCTA [CTM/IDMM)]

The CTM should review the work and comments of the GCTA. If desired, the document categories can be divided, or a meeting can be organized to discuss.

Make sure the CTM shares the comments with the GCTA again. This recommendation also applies to the IDMM and the UGCTA

Step 7: Follow-up on any findings [(U)GCTA, CTM/IDMM]

Track down any missing documents, remove duplicates, correct document descriptions, etc. Any role can be involved here: (U)GCTA and CTM/IDMM. Keep track of the findings and resolutions in the GCO Quality Evidence Report.

If by the time of the QR deadline it was not possible to resolve all the open issues, please indicate such in the Quality Review Confirmation Form, noting issues are still open along with corresponding evidence and file QRCF and QR evidence in V-TMF prior to AQR due date. You will have 30 days from the completed AQR date, or as soon as feasibly possible, to resolve the open issues. For details, please refer to the GCO Quality Review Job Aid.

Step 8: Sign and file the Quality Review Confirmation Form & file GCO Quality Review Evidence Report in V-TMF as evidence of review [(U)GCTA/CTM/IDMM]

The GCO Quality Review Evidence Report is a report that can be built upon throughout the course of your study. This build will ensure that all the supporting evidence is in one location for ease of reference. For more details and an instructional video, please refer to the GCO Quality Review Job Aid.

The QR evidence report does not need to be e-signed in V-TMF, even at the final timepoint. The Quality Review Confirmation Form, indicated as " Final" for the timepoint, must be e-signed in V-TMF once uploaded.

This completes the Annual Quality Review. Ensure all discrepancies are resolved before signing and filing the document. QRC forms must be filed by AQR due date with no exceptions. Please refer to GCO QR Job Aid for more details in an event all discrepancies are not resolved by AQR due date and the steps to take over the next 30 days to address them. Please see the Quality Review Confirmation Form template for signing and filing instructions. The template can be found in TruVault: TV-eFRM-02260.

Resources

Refer to Job Aids, VIPER, and the V-TMF Portal for additional Quality Review references to utilize when conducting Quality Review.

- TV-SOP-12844 Management of the Trial Master File (TMF)
    - Job Aid: Quality Review (Main QR Job Aid that applies to all Functional Areas)
    - Job Aid: GCO Quality Review
    - Job Aid: Scan and Upload Documents to V-TMF
    - Job Aid: Conduct Quality Review (QR) Feature in V-TMF
- VIPER
- V-TMF Portal: Process Resources; Quality Review
- Error definitions: EAT Definition File.
- Video: How to use/interpret the AQR Compliance report in VIPER- last and passed views https://web.microsoftstream.com/video/e4afb6fe-2c85-4283-bea1-b5dc4b52dea4
- Video: How to use/interpret the AQR Compliance report in VIPER - future views https://web.microsoftstream.com/video/c250252a-b34c-4914-92fb-62cedaf7f4f6
- Also, review the Document Status Dashboard in V-TMF. This tool will help identify documents that require some actions, such as blank description, draft status, paper TMF reconciliation. Here's a quick video on how to use it. https://web.microsoftstream.com/video/c271382b-debf-43df-8e56-0535c44dc493?list=studio

2.4.2 Performing the Curation Activity Review

In response to a Regulatory Authority inspection observation, a Curation Activity Review has been added to the Quality Review process as a 'GTL or delegate (G-CTA)' responsibility for studies with a Final or Annual Quality Review beginning on or following 01-Nov-2022. Due to how our V-TMF system is set up, there is potential for users to alter the TMF content for a trial they are not involved with, resulting in unauthorized and/or unexpected changes.

The unauthorized or unexpected activity check will confirm that no unexpected changes or unauthorized alterations of V-TMF content occurred for the study. It will be completed and documented using TV-eFRM-15411: Curation Activity Review (CAR) Form following the same schedule interval as the first and subsequent Quality Reviews. The Curation Activity Review Form will be filed in V-TMF no later than the corresponding Annual Quality Review due date.

The Curation Activity Review Report was not purposely designed to include restricted Content. It was found out later that this is included. After reviewing within our Team, we confirmed that the information in the report for the restricted content poses no risk for unintentional unblinding and

will be kept as is. The person reviewing the report should be able to assess if the soft deletion was carried out by a member of the trial team.

Steps to take for the Curation Activity Review:

1) Visit the TMF Portal Process Resources - Quality Review and search for the latest "Curation Activity Review report" under the curation activity review section to review all documents that have been soft-deleted for your study.
2) Review the **Trial Contact List (TV-FRM-09596)** to confirm that activity was conducted by authorized members of your study team. Update the Trial Contact List if necessary.
3) If evidence of unauthorized or unexpected activity is observed, it must be escalated to the study Global Trial Leader and/or 'Managed By' Owner for investigation and resolution.
4) File the TV-eFRM-15411: Curation Activity Review Form in V-TMF at the same location as your annual quality review (Trial Management - Trial Oversight - Quality Review Documentation).

Important to know:

- The CAR does **NOT** replace the requirements for annual and final Quality Review or filing of the Quality Review Confirmation Form (TV-eFRM-02260) and supporting evidence.
- **DO** conduct your V-TMF soft deletion activity checks following the same schedule interval as your annual and final quality reviews. Study Start (FSOA: First global Site Opened Actual Date) + 12 months, + 24 months, +36 months…
- **DO** update the Trial Contact List (TV-FRM-09596) to ensure it is accurate and current.
- **ESCALATE** to your study **Global Trial Leader** and/or **"Managed By" Owner** (formerly known as the TMF CoE) if you find evidence of unauthorized or unexpected activity.
- The unauthorized and unexpected activity checks do NOT apply to a Paper TMF and other approved TMF Filing Locations, but other aspects of annual and final Quality Reviews do apply.

Resources

- TV-eFRM-15411: Curation Activity Review Form (CAR)
- Process Resources- Quality Review

2.5 Trial Contact List (TCL)

The TCL is a document that contains the contact details of all persons working on the study, including:

- Central team members (e.g., GPL, GTL, CTM, GCTA, physician, scientist, Cross Functional Area study team members).
- Unblinded team members (e.g., UGCTA, IDM, IDMM)
- Local team members (e.g., LTM, SM, local CTA, CRM)
- Supplier/vendor project managers (e.g., Central Laboratories, RTSM Vendor manager, CRO staff)
- Site staff*

**If site staff are also present in OneCTMS, there is no need to copy it into V-TMF. Instead, add a sentence stating that site contact details can be found in OneCTMS. Reports can be pulled from VIPER PANORAMA with Site (staff) contacts or MaSCoT (Master Site Contact Tool) is used to share them with vendors.*

The TCL is not only important for the study team & study conduct, but inspectors will also ask for the TCL and the dates of when people started/ended their involvement on the study. As the eFAP no longer includes a location for where paper TMF content is maintained, the TCL now includes this information (not applicable for Sites and Suppliers tabs). Please refer to the TCL column labeled "Paper TMF Content Location (complete for responsible person only)". It is very critical that this field is accurately populated. This could be questioned during an inspection as it is Noted in the eFAP whether original paper is being maintained.

The TCL is kept in V-TMF on the study level. It should be filed in the following classification: 'Trial Management > Trial Team > Trial Team Details'. It is best practice to make updates directly in V-TMF and not to have a draft version in a different location.

The TCL is also used to assign study specific training to study team members. A "Role Curriculum Map" has been created and it serves to connect applicable roles in the study (as listed in the TCL) to the appropriate protocol-specific curriculum that will be assigned in SUMMIT.

Best practices:

- It is the GTL responsibility to initiate the TCL.
- GCTA should start updating the TCL as soon as people are assigned to the study during start-up.
- The GCTA should update the TCL asap in case of study team changes to ensure accuracy at all times. GCTA will upload it to the Clinical Study Specific Training Portal after updating.
- IDM, IDMM and UGCTA roles on the Unblinded tab is managed by the UGCTA.
- Enter as much contact information as you can in the TCL, so it is as complete as possible. Use Johnson & Johnson Enterprise Directory (JJEDS) to find it or ask the person for their contact information.

Resources

- Trial Contact List: TV-FRM-09596
- TV-SOP-12920: Study Plans and Systems During the Study Set Up and Conduct
- JJEDS: Browse JJEDS
- Clinical Study Specific Training Portal
- Job Aid Sponsor Staff Study-Specific Training Process

2.6 System Access

A study is likely to use many different systems. Managing access to these systems is essential to ensure no one is accessing study data when they are not working on the study. Some good practices are discussed in this chapter.

Granting access

After a new person joins the study, access is requested based on their role. Generally:

- CTM (may be delegated to GCTA) arranges access for global and local study team
- LTM arranges access for site staff

For IDM trials, the IDMM (may be delegated to UGCTA) arranges unblinded access for unblinded global and local study team members. IDM arranges unblinded access for unblinded site staff. Note: since unblinded study team members have no access to CTMS, the IDM/IDMM/UGCTA need to reach out to blinded study team members (e.g. CTM/GCTA) to have the required unblinded staff included correctly in CTMS.

For specific vendor systems, the CTM/IDMM (or (U)GCTA) may arrange access for site staff as well. In that case, it is recommended to create a guide that shows who is responsible for which accesses for the study. An example is shown below:

ALL2005_Quick Reference Card_Syst

In some cases, system access for site staff is granted automatically after entry in CTMS (e.g., DrugDev or SafetyPortal). In other cases, access can be granted when the user enters the request directly in a vendor portal (e.g., StudyWorks). For vendors who require MaSCoT (Master Site Contact Tool) reports to create system access for site staff, it is important that site details in CTMS are accurate so that they reflect correctly in the MaSCoT reports.

Revoking access

When site staff and/or study team members leave a study, their system access must be revoked. It is recommended to do this ***within 10 business days***. The CTM/IDMM (or (U)GCTA) is responsible for ensuring that former study team members no longer have access to study systems. Likewise, the LTM/IDM is responsible for ensuring that former site staff no longer have access to study systems. For some systems, access is automatically revoked when an end-date is entered in CTMS, (e.g., DrugDev). It is recommended that the vendor access guide includes guidance for revoking system access, and which roles are responsible for performing this task.

System Access Reviews

A review on access to all study systems must be performed for global and local teams and site staff according to the frequency specified in the SOP for the system/ vendor. Some system access reviews such as for RAVE* is quarterly; however, others are semi-annually. Documentation of review should be filed according to the V-TMF Content map. Most systems allow you to run a user report. If a report is not available, then request it from the system/vendor Helpdesk or project manager.

- CTM/IDMM (or (U)GCTA) to review global and local team access and ensure access is being revoked where needed using the TCL.
- LTM/IDM to review site staff access and ensures that access is being revoked where needed.

*During review of RAVE study user reports, the study team may discover that a principal investigator's name is missing on the report. This means the investigator is not linked to the site number, and this can impact the completeness of data management reports. If an investigator's name is not linked to the respective site in RAVE, then the CTM should follow the Stefanini Mapping Flow Process attached below to request the investigator be linked to the respective site.

Adobe Acrobat Document

Stefanini Mapping Flow Process

It is suggested to include a slide quarterly in the SMT meeting to notify the team that it is time to perform the review. The latest user reports can be included in the slide.

Real life example:

EXAMPLE%20-%20RAVE%20Access%20Q

2.7 CTM, IDMM and (U)GCTA Handovers

Through the life of the study there will be changes to study team members which require proper handover/transition. When a new member joins the study and who will take over your role, you will need to follow the below steps to ensure you have a successful handover.

- Schedule a series of handover meetings. It is recommended to have at least two (initial and final); however, depending on the study complexity, it is advised to have interim meetings.
- Request access to systems, SUMMIT, protocol specific trainings, and updates to the Trial Contact List. When the transition is finalized, access can be removed from the CTM/IDMM/(U)GCTA transitioning off the trial. The Trial Contact List should be updated with an end date so the CTM/IDMM/(U)GCTA leaving the trial does not get assigned to any SUMMIT trainings going forward.
- Forward study-specific meeting invitations to the new CTM/IDMM/(U)GCTA, and request that the new member takes over invitations for certain meeting invitations (e.g., SMT, IDMT, Country Calls).
- The handover document must be used to perform the transition, and the fully executed document should be filed in V-TMF.

Please access the appropriate SOPs & forms for instructions:

- For CTM Handovers:
  - TV-SOP-12920: Study Plans and Systems During the Study Set Up and Conduct
  - Study Handover Form for Global Clinical Development Operations (GCDO) Trial Leader and/or Clinical Trial Manager -TV-FRM-07286
- For IDMM Handovers:
  - TV-eFRM-14877: Study Handover Form for Independent Drug Monitoring Manager
- Study Handover Form for (unblinded) Global Clinical Trial Associate (GCTA) – please contact your Functional Manager to obtain the latest version.

2.8 Notes-to-File / Memo-to-File & Inspection Narratives

During inspections, inspectors will reconstruct the trial by looking at trial documentation located in TMF, review entries in systems, and by interviewing study personnel (site and sponsor reps). Inspections can occur any time, sometimes even years after the trial has ended. Therefore, Good Documentation Practices are critical as teams during inspections might need to explain what happened, when it happened, what the impact was, which actions were taken, and the associated corrective and preventive actions. Therefore, to follow the ALCOA+ principles, where ALCOA stands for documentation to be Attributable, Legible, Contemporaneous, Original, Accurate, and Complete, and ALCOA+ recommends data to also be Complete, Consistent, Enduring and Available.

The issue management process is documented in TV-SOP-04282 including references on how to further escalate minor/major/significant issues. Depending on the severity of the issue, a TrackWise record is to be created.

There are however situations that might require a clarification for which one can consider to document by means of a Note-To-File (NTF)/Memo-to-File (MTF) or Inspection Narrative (IN).

Caution: Whereas there is no FDA/EMA Regulatory requirement for use of NTFs/MTFs, warning letters were issued by the FDA and other inspectorates for the misuse of NTFs/MTFs. For example: 2009 J&J Warning Letter: "*NTF was used to override the decision made to select an investigator site with a previous history of non-compliance*."

2.8.1 Note-to-File (NTFs) / Memo-to-File (MTFs)

When NOT to use an NTF/MTF

Do not use NTFs/MTF to capture findings that should be documented and escalated per TV-SOP-04282 and related documents. For those issues refer to the below systems and processes in place:

- OneCTMS
- Monitoring Visit Reports and follow-up letters/other letters to sites
- Issues Tracking tools
- Official internal meeting minutes, e.g., CFTT, SMT, IDMT etc.
- For systemic issues with potential impact on subject safety and / or data integrity/trial conduct, escalate and/or document as a Self-Identified Issue (SII); refer to:
    - TV-SOP-04282: Identification and Management of Clinical Trial Issues and Protocol Deviations
    - TV-WI-07697: Nonconformance and CAPA Management Process for GCP/GLP Health Authority Inspection Observations, Internal Audit Observations, Supplier Audit Observations, and Self-Identified Issues in TrackWise Event.
    - Job Aid: Initiate/update/close a Self-Identified Issue (SII) in TrackWise (TW) with the support of the GD-Central TrackWise Entry team
    - Job Aid: Assessment of Self-Identified Issues - connection between TV-SOP-04282 and TV-WI-07697
    - Self-Identified Issue (SII) Support Sharepoint page, including the Self-Identified Issue Decision-Making Tool

Following above guidance will ensure the issue is captured in our Quality Management System and can be easily retrieved during inspections.

Reminder: The NTF/MTF does not replace the need to file an actual procedural document!

Then when to consider use of a NTF/MTF?

A NTF/MTF can be considered in the following instances (if in doubt, contact the CRM representative on your trial):

- Clarify or add information regarding site-specific regulatory file requirements.
- Clarify or add information regarding source document standards.
- Document and address any issue that is protocol- and/or site-specific and that cannot be resolved without a change from previous procedures.
- To document the reason for missing, delayed, or erroneous documents in the clinical trial master file or in the site master file.
- To document those certain sections of the files are not applicable.

Source

- NTFs/MTF use, abuse and misuse: "Perspect Clin Res. 2011 Jan-Mar; 2(1): 38–40". Link to article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3088955/

How to write a NTF/MTF?

The purpose of documentation in clinical trials is to tell a complete story, and a NTF/MTF should contribute to that completeness by explaining any gaps. Make sure you include these items:

- Study protocol title and if needed, site nr, PI name and country
- Date(s) related to the event
- Clear description of the non-compliance addressed
- Impact of the non-compliance on e.g., process, patient safety, data integrity. However, if that is the case, refer to the issue management processes described under 2.8.1.
- Provide root cause of the non-compliance
- Corrective and preventative actions (include when these were implemented and completed)
- Ensure supporting documentation can be retrieved (e.g., if referring to meeting minutes, include type of meeting, date and V-TMF ref #)
- Follow the ALCOA-C principles (documentation should be Attributable, Legible, Contemporaneous, Original, Accurate, and Complete)
- Ensure that the NTF is finalized after all actions are closed; do not include pending actions.
- Signature(s) and date(s) from individuals involved in creating the NTF/MTF

Example of a NTF/MTF template:

NTF_memo_template .docx

Note: Avoid filing a stack of NTFs with the same date, which were created and filed all at once in preparation for an inspection or as a corrective action from a monitoring visit, can create red flags for Inspectors.

2.8.2 Inspection Narratives

An Inspection Narrative (IN; previously known as Storyboard) can be used to summarize and gather information describing a systemic and/or significant event that has occurred. These can be central findings for which a mCTMS entry was made and the IN to then capture additional supporting documentation regarding it. An IN can be used for both central and site issues.

The IN can prevent the loss of background/history of events, especially if an inspection is conducted years after First Patient In (FPI) and study team members might have transferred off the trial or left the company. The IN can help to provide a consistent and coordinated answer/response in case an issue is brought up during an inspection or audit. The expectation is to have the IN function as a summary/oversight document, rather than duplicating/replacing official sources used. For instance: include VTMF numbers for relevant supporting documents instead of downloading from VTMF and inserting them in the IN.

Each study team member holds responsibility to create a Study/Country/Site level IN. If needed, the GTL can request a study team member to complete an IN. The decision to create an IN is based on the impact an event has/had on patient safety, data integrity, and patient's rights

It is highly recommended to create at least a IN for significant quality issues, as these issues are most likely challenged during (mock-)sponsor, site inspections and audits.

Consider the following elements when creating the IN (see also templates below under "Two types of Inspection Narratives"):

- What was the issue about?
- Who identified the issue?
- When was the issue identified?
- Where did the issue occur?
- When did the study team became aware of the issue and how?
- What was the extent/scope of the issue? Number of subjects, sites, countries impacted (consider Serious Breach reporting (TV-SOP-18636: Evaluation and Reporting of Serious Breaches) requirements for certain countries cross-Trial/Compound/TA, systemic issue)?
- Impact of the issue on subjects' safety, data integrity, patient rights, trial execution etc.
- Root cause of issue, if known?
- Was a TrackWise (TW) record(s) created? If so, add TW number(s).
- Was the issue escalated via the *REACT system? If so, add REACT number(s)
- CAPA (if applicable):

  - Open/closed
  - When was the CAPA finalized/closed out or due date (*Timely CAPA is expected*)?
  - Preventative actions (i.e., If the issue has a cross-trial, TA impact, what actions were taken, if any needed?)
  - Who was impacted by the CAPA, and how was this communicated/was training provided after the event (as applicable)?
  - Was the issue or will the issue be included in the Clinical Study Report (CSR) (if applicable)?
  - Any sensitivity analysis performed/to be performed? Exclusion of data?
  - Residual risk after CAPA?
- Was this issue reported to ethics committees or Regulatory Authorities?
- Have any sites been put on temporary hold? If so, state the reason why and indicate when the hold was lifted.
- Have any sites been closed due to the issue?
- If requested by the inspector, who are the best individuals/roles to be interviewed for the event captured in the IN and what supporting documentation can be provided (upon request).

* REACT is a module within TrackWise used to escalate potential significant issue to Sr. Mngt. The process is documented in TV-WI-10623 (ETS - Processing REACT Escalation Records in the Event Tracking System for Pharmaceuticals). This WI is intended to be used in conjunction with TV-SOP-25014 (Escalation of Janssen Quality and Compliance Issues).

Two Types of Inspection Narratives **(INTERNAL DOCUMENTS)**

- Central level: used to capture significant central systemic issues/problems that occurred during the trial.
  EXAMPLE of a Central Level Inspection Narrative (*right click – presentation object – edit*):

  Central Inspection Narrative template.pp

- Site level: the selected sites of interest by the team have a high probability of being inspected. The expectations of content are the same as for central level inspection narratives.
  EXAMPLE of a Site Level Inspection Narrative (right click – presentation object – edit):

  Site Inspection Narrative template.pp

Notes:

Inspection Narratives **(INTERNAL DOCUMENTS)**:

i) should not be provided to inspectors or auditors
ii) is intended for internal use only and **should NOT** be filed in the essential part of the V-TMF. Instead, it can be filed in the "Non-Essential" filing location in V-TMF since this folder is not visible to inspectors.
iii) avoid filing it in a regulatory trial file
iv) do not refer to the IN in trial documents/presentations filed in V-TMF
v) **should not** replace opening a (Significant-) Quality Investigation in TrackWise/REACT. Rather, it should include reference to the TrackWise/REACT number instead.

2.9 Vendor Oversight

Vendor oversight is a 'hot topic' that HA inspectors focus on a lot. Even though we delegate tasks to our vendors, J&J Innovative Medicine as the sponsor should be able to show oversight on vendor outsourced activities. Maintenance of the External Service Provider (ESP) plan is one crucial step supporting that.

The vendor(s) involved in a study are to be captured in the **External Service Provider Oversight Summary** (**TV-FRM-09678**) created by the GTL with input from the Responsible Functional Department members, who are responsible for their vendors. Refer to the to 'Instructions Sheet' within the ESP overview, on how to complete the ESP.

From a Sponsor perspective, we must be able to provide documentation on vendor oversight. For example, meeting minutes must be taken and filed in the V-TMF per the Meeting Plan (**TV-FRM-03346**). TMF Quality Review Oversight for TMF content managed by the vendor is also part of the annual requirements (as per TV-SOP-12844 – and the relevant section in Job Aid: Quality Review).

Vendor issues should be escalated as appropriate, and proof of follow-up actions taken should be documented.

J&J Innovative Medicine Policy TV-POL-00535 Vendor R&D Supplier Selection and Management requires that a list of vendor procedures be maintained in the V-TMF for vendors providing services. Evidence of vendor training as required by TV-POL-00535 should be substantiated via training attendance list, training log/record, or meeting minutes of a designated training session or Kick of Meeting. Vendor Key Performance Indicator (KPI) metrics should be reviewed in the weekly/biweekly status meetings and review captured in meeting minutes.

Ensure access to the vendor systems is checked and maintained regularly. Refer to the Strategic Partnership SharePoint for more information about vendor oversight and management:

Note: the ESP Oversight Plan is to be reviewed annually by the GTL.

2.10 Country Oversight

There are many sections in this document that will help demonstrate country oversight, and there are many reports which can be run to ensure oversight of countries participating in a study. Please refer to the VIPER home page for the useful reports. In **Chapter 3** of this document, we have listed some examples of VIPER reports that may be used for country oversight.

Some suggested VIPER guidance for country oversight:

- Viper dashboard support tools
- Viper guidance document for CTMs and GCTAs

These above resources provide guidance regarding which VIPER reports which may be run to maintain study and country oversight. It is important that running these reports is documented, for instance, by including them in the Study Management Team (SMT) and Independent Drug Management Team (IDMT) meeting slides/meeting minutes or meeting minutes from country calls (if applicable). Additionally, it is important that you follow-up on issues, and ensure CAPA's, mitigations, and effectiveness checks are put in place.

ATLAS is a useful place for reports and metrics, both for studies that implemented or not implemented Dynamic Site Monitoring.

All SMT and IDMT meeting proceedings should be filed in V-TMF. Guidelines have been developed for SMT Meetings, and you can find all of the information here: SMT Example Slide Deck and Instructions.

Even though it is not required, meeting minutes from the country calls between LTM and CTM and between IDM and IDMM may also be filed in V-TMF (non-essential space) to document country oversight. It is important to track and resolve actions and decisions.

Tip sheet for the conduct of the LTM & CTM conversations:

Consideration Document Country (

Templates have also been created for IDMT meetings and IDM country call meetings. These can be found on the IDMM Knowledge Hub SharePoint page (only accessible for IDMMs and UGCTAs).

Requests for deviations to Monitoring Visit schedules

Some studies are in scope of dynamic site monitoring which uses a data driven, flexible study and site-specific model for scheduling monitoring visits.

For studies that are not in scope of dynamic site monitoring e.g., ED & CP and IDM studies there is no uniform process for documenting requests from Site Managers/Independent Drug Monitors for deviations from the Monitoring Visit (MV) schedule. Study visits are outlined in the Monitoring Guidelines (MG) or in the Operational Management Plan (OMP) for ED&CP studies. Any deviation to the MG/OMP such as visits scheduled out of window or additional visits requires central team approval. Specific instructions relating to which visits need approval may be given in the MG/OMP. CTMs/(U)GCTAs/IDMMs should track these requests/approvals to best document this information. The CMM/ARBM SME group has created the Monitoring Visit Deviation Tracker to document On-Site MV deviation requests from Site Managers. IDM visit deviations are visible through the V-TMF dashboard metrics reports.

2.11 Informed Consent

Master informed consent forms (ICFs) are developed by the central team.

Always reference the most recent version of **TV-SOP-04047: Development of the Informed Consent Form Documents**, and the associated ICF templates, Forms, and Job Aids. If your trial is using electronic ICFs, also refer to **TV-SOP-13518: Electronic Informed Consent Form (eICF) for J&J Innovative Medicine Sponsored Clinical Studies.**

An Informed Consent (ICF) & eConsent SharePoint site is available to help users and ICF authors navigate the ICF and eConsent process.

TV-FRM-10628: Master ICF Review & Approval Form

For all ICFs, **TV-FRM-10628: Master ICF Review & Approval Form** is used to document review and approval of the Master ICF. For ICF Amendments it is also used to record reconsenting instructions for patients, and is required to be completed, signed, and filed for all ICFs and amendments.

ICF Amendments require the Study Responsible Physician (SRP)/Study Responsible Scientist (SRS) to confirm if reconsenting is required. If reconsenting is required, the "Reconsenting Instructions" elements at the bottom of the Form tab of the TV-FRM-10628: Master ICF Review & Approval Form need to be provided to record how and when the new information needs to be communicated to patients. The CTMs then disseminate the following information to the LTMs:

1. Reconsenting Instructions
2. The final ICF Addendum(s)/ Amendment(s)
3. The tracked change version of the updated ICF documents

TV-FRM-11186: Master ICF Tracking Template

The ICF versions developed for a study should be tracked using **TV-FRM-11186: Master ICF Tracking Template** and uploaded to V-TMF.

TV-FRM-11186 can be used in the following ways:

- TV-FRM-11186 contains worksheets for tracking the master, country, and site ICFs. It is acceptable to maintain three separate files for each section for ease of implementation by the applicable study team members.
- Local teams are also able to create their own local ICF trackers and would need to provide the study teams with the V-TMF number (location) of their local ICF tracker.
- Local team trackers can be included in the Master ICF Tracking Template.

The Master ICF Tracking Template can be found in TruVault, and it tracks the following:

- Which types of consent/assents are used in the study?
- Different versions of consent/assent forms
- Version dates
- What has changed in each version?
- Country and site-specific consent/assent forms, IRB/IEC approval dates and dates sent to site.

Always keep an updated version of the ICF tracker in V-TMF for study, country, and site level.

2.12 Protocol Deviations & Major Issues Management and Reporting

The process for managing protocol deviations, issues and if and how to escalate is described in **TV-SOP-04282: Identification and Management of Clinical Trial Issues and Protocol Deviations**. It is imperative to ensure the study team provides oversight as outlined in this SOP, and all appropriate deviations and issues are properly reviewed, documented, and timely closed.

The (potential) Major Protocol Deviations and Major Issues are discussed during the Deviation and Issue Escalation Review meeting. Major PDs and Major issues from the unblinded team, should be discussed in a blinded way, not sharing any potential unblinding information. As of version 8 (31-Jan-2022) of TV-SOP-04282, the CTM/IDMM is tasked to filter out Major Issues that don't need input from the study team before the Deviation and Issue Escalation Review meeting. The currently effective SOP version also now lists Findings that require immediate reporting.

It is of importance that issues are closed within 90 days per company policy., Ensure the reason for the delay in issue closure is properly documented in OneCTMS.

For studies with an Independent Drug Monitor (IDM) component, if a blinded Study-Specific Issue System is not available, a secure (unblinded) tracker separated from the study dedicated system/central tracker (TV-FRM-04433: Deviation and Issue Tracking Log) is used for documenting and managing secure Protocol Deviations and Issues. Access to this secure (unblinded) tracker is restricted and maintained by the IDM and IDMM in restricted V-TMF. If issues and PDs are not closed within 90 days, the reason should be included in the Deviation and Issue tracking log. Off-line discussions can take place in between Deviation and Issue Review meetings, however they must be documented and discussed with the study team as necessary.

For trials with an IDM component, IDMM will ensure the secure (unblinded) Major Protocol Deviations are managed by the Secure Data Supplier until release at study unblinding.

For finalization and reporting of Major Protocol Deviations (i.e., Clinical Study Report) at the end of the study, the GDM reviews the listing of protocol deviations to ensure correct classification. All major protocol deviations (PD) need to be finalized for reporting before the database hard lock. For studies with an IDM component, at trial unblinding, GDM is to receive the final list of secure (unblinded) Major Protocol Deviations from the Secure Data Supplier, if applicable. At the end of the study, the Major Protocol Deviation report needs to be circulated to the study team (SRP, SRS, GTL, CTM, IDMM) for review, signed by SRP, and filed in the V-TMF.

Here are useful resources on the Protocol Deviations and Major Issues process:

- Issues and Deviations – Reports to Use
- TV-SOP-04282: Identification and Management of Clinical Trial Issues and Protocol Deviations
- Job Aids in Blackbird + Summit training Course (in Blackbird)
- OneCTMS CTM Manual (can be found within OneCTMS)
- Quality SME Office Hours slides and Q&A document

2.12.1 Self-identified issues and CAPA

In November 2021, a new Job Aid was released on “Assessment of Self-Identified Issues”. The Job Aid is related to TV-SOP-04282 and TV-WI-07697 (Nonconformance and CAPA Management Process for GCP/GLP Health Authority Inspection Observations). This Job Aid provides guidance on how to assess Self-Identified Issues and whether they meet the nonconformance criterion for a Quality Investigation and entry into TrackWise.

A training on this process can be found here: Self-Identified Issues Awareness Session.

If a Self-Identified Issue is identified for your study, they are assigned as follows: all global CAPAs are assigned to the GTL. All country / site CAPAs are assigned to the CTM / LTM / IDMM, and either role would be responsible depending on the issue.

More resources on Self-Identified issues:

- Self-Identified Issue Decision-Making tool
- FAQ: covers key questions & answers provided
- Chapter 2.8 of this guidance document

2.12.2 Privacy incidents and data processing

- The General Data Protection Regulation (GDPR) portal contains a training that provides information on fair and responsible handling of personal data. Any organization targeting the EU market must comply with the GDPR for its personal data processing, relating to its EU operations or business.
- Refer to the Job Aid "Privacy Incident Management" for how to define Privacy Incidents (i.e. minor/major), and how to document, report and remediate the incident. Note: if a privacy incident is identified, inform the GTL, and report the privacy incident to the Johnson & Johnson Global Service Desk using the IRIS Self-Service Portal (via call, chat or submitting an Incident Ticket).

2.13 Financial Information in V-TMF

Study **financial information should NOT** be filed in V-TMF and should NOT be part of the Trial Master File.

- Contracts must all be redacted, removing the financial information therein. To prepare for inspections, the Contract & Compliance Services (CCS) Compliance team can assist in the redaction of Supplier and Clinical Trial Agreements supported by the J&J Innovative Medicine R&D Procurement (JRP) and Contract & Compliance Services (CCS) functions. If a study is identified for a Regulatory Authority GCP Inspection or Government Submission for drug registration applications, CCS can be approached for support by e-mailing JRP CCS QRF Requests *(RA-JANUS-JRPCCSQRFRe@ITS.JNJ.com)*
- Meeting minutes from SMT and/or Country 1:1 Calls should never include study-specific financial information. If the minutes are being filed in V-TMF, financial information must be removed prior to filing.
- It is acceptable to share and file financial reminders with meeting minutes (example: Reminder for Continuous Forecasting) since this does not contain any financial detail of budgets and payments.
- Ensure any study/country specific financial details are not included in the formal meeting minutes that are filed in the TMF and that the sharing of financial information is restricted to those that are involved with the process.

- For blinded studies, be conscious that some financial investigational product site contract arrangements can cause unblinding.
- All financial documentation should be managed in its respective source system (e.g., eMarketplace, ICD, etc.) and a placeholder should be in place in V-TMF. However, in situations where there is supplemental financial information (such as an emailed quote or a team-created budget tracker), the Non Essential's "J&J Financial Confidential" classification can be used for the filing of non-redacted financial documents. The "J&J Financial Confidential" classification in the NE filing space is viewable by JNJ employees and augmented staff with WWIDs (i.e., flex-LTMs, SMs, team members). This classification should be used ONLY if it is acceptable for the content to be seen by all JNJ internal users.

2.14 Outsourced Studies

For outsourced studies that are managed by alliance CROs, teams should refer to the Project Outsourcing Manual (POM) which is available on the Sourcing Portal. The POM section 2.2.C 'Regulatory Inspections' provides guidance on inspection management in partnership with the CRO. The Task Ownership Matrix (TOM) provides information on the CRO responsibilities.

Guidance regarding TMF Quality can be obtained from the appropriate TMF Operations Manual which are available in the TMF Portal here:

- TMF operations manual for alliance CROs - IQVIA
- TMF operations manual for alliance CROs - PAREXEL
- J&J Innovative Medicine-ICON/PRA TMF Strategy Plan -

Regular meetings and quality checks are needed to ensure quality of the study and the CRO's work is compliant. More guidance can be found in the "CTM Guide for Outsourced Studies" located in the JJCO Playbook. Inspection readiness preparation is even more paramount for non-alliance CROs since there is no standard guidance. It is critical to set expectations ahead. (The CTM guide for Outsourced Studies is a great starting point).

Some other great resources are:

- Outsourcing Toolkit
- CTM/GTL Role-Clarity Tool for Outsourced Studies
- For the IDMM role, the RCT for Outsourced Studies is available on the IDMM knowledge hub restricted page.
- MV Review tracker template for reviewing CRO's Monitoring Visit Reports (highly recommended activity). For IDMMs, a similar template called Outsourced Oversight tracker is available on the IDMM knowledge hub restricted page.

2.15 Guidance on Electronic Signatures by CROs and Sites

Both CROs and Sites can sign using electronic signatures. While not all electronic signatures would need to be compliant with 21 CFR part 11, there are certain signatures that are required under predicate rules / regulation, and hence, if applied electronically, would need to be compliant with Part 11. For sites specifically, signatures on documents such as Protocol Acknowledgement page, Protocol Amendment Acknowledgement, Signed Form FDA 1572 (IND studies), Financial Disclosure Form(s) and Informed Consent, if applied electronically, will need to be compliant with Part 11.

If the site is applying electronic signatures to these document types, we should expect them to use systems that have been validated and compliant with Part 11 e-signature requirements.

Resources

- Data Management Standard (TV-QPS-00010) contains expectations for electronic signatures applied by CROs or Sites.
- Electronic Signatures Training in SUMMIT on 3rd party or vendor signatures.

Chapter 3: V-TMF, VIPER Reporting & Tools

There are many reports that can be used to maintain oversight on trial activities in the study. Please refer to the VIPER home page and TMF portal for the useful reports. In this chapter are some suggested reports that are useful; however, the list is not all inclusive. V-TMF dashboards can also be used by IDMM to visualize the IDM visit report & IDM FU Letter metrics. P VIPER dashboards provide good insight in your studies. However, they cannot be used in case of inspections. Always refer to the source to support the quality of your study.

There are several trainings developed for how to use the VIPER dashboards and run TMF reports:

- On the VIPER dashboard catalogue here.
- Several CTM/GCTA's trainings are found on the OBT SharePoint, here.
- CTM VIPER Resources here

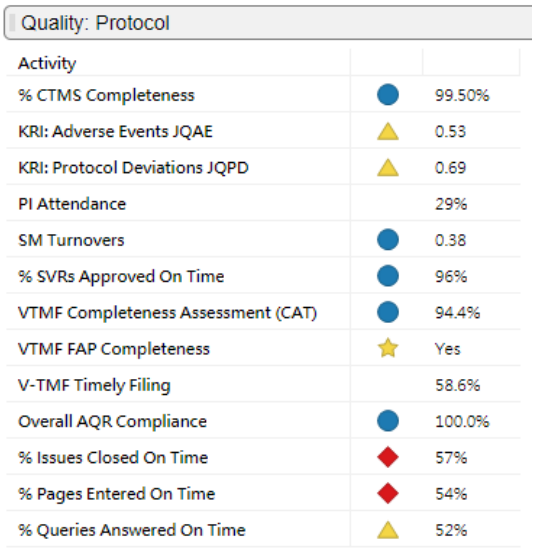
For further information, training, and useful tools, please visit the V-TMF Portal.

3.1 VIPER 'GTL/GTM/CTM Executive Summary' Dashboard

The purpose of the 'GTL/GTM/CTM Executive Summary' Dashboard in VIPER is to visualize the operational metrics and milestones at a Protocol, Country, and Site level.

The Summary pulls data from various dashboards such as, oneCTMS data entry compliance dashboard, site quality AE and entry time dashboard, and the TMF Quality and Metrics Dashboard.

This dashboard gives you a first glance of the status of the study and an indication on what you need to pay more attention to.



Quality: Protocol		
Activity		
% CTMS Completeness	●	99.50%
KRI: Adverse Events JQAE	▲	0.53
KRI: Protocol Deviations JQPD	▲	0.69
PI Attendance		29%
SM Turnovers	●	0.38
% SVRs Approved On Time	●	96%
VTMF Completeness Assessment (CAT)	●	94.4%
VTMF FAP Completeness	★	Yes
V-TMF Timely Filing		58.6%
Overall AQR Compliance	●	100.0%
% Issues Closed On Time	◆	57%
% Pages Entered On Time	◆	54%
% Queries Answered On Time	▲	52%

3.2 Trial Master File

The VIPER V-TMF Dashboard has very useful reports for checking the status of filing activities, which will be discussed in sections separately:

- EDL Assessment Tool Report (EAT)
- AQR Compliance Report
- Timely Filing
- FAP Compliance is an assessment of Filing and Archiving Plan (FAP) Completion and Timeliness. As per TV-SOP-12844: Management of the Trial Master File (TMF), a FAP is required for all Global Development managed studies and must be completed and approved in V-TMF within 90 days of study start. Study start is based on First global Site Opened Actual Date (FSOA) +90 Days.

The VIPER reports are intended as a tool and should be used as a starting point to assess the various areas, however users shouldn't rely solely on the reports, as additional analysis and checks may be needed.

The VIPER reports are an internal tool only. They aren't available to Inspectors and should not be shared or offered. If an inspector does inquire about metrics or reports, you should contact the TMF CoE via the TMF CoE Inspection mailbox: RA-RNDUS-TMF-CoE-Ins@ITS.JNJ.com.

The VIPER V-TMF Dashboard can be accessed from the VIPER homepage.

The TMF Portal contains useful Quick Reference Cards and Instructional Videos that provide instructions on how to operate the VIPER dashboard.

3.2.1 EDL Assessment Tool Report (EAT)

The EAT Report is a tool to aid in assessing the health of the TMF. It can be used to verify Expected Document List (EDL) settings, view what TMF content has been filed in V-TMF, and helps in identifying what may be missing or filed incorrectly. Metrics are based on V-TMF EDL, Milestone, and Documents filed (or referenced to an external system in V-TMF).

Note: The EAT Report does not provide the full picture of completeness. For example,

- The metric only requires the filing of a single document to satisfy the metric for that classification (i.e., it only indicates if a single document has been filed and does NOT account for a requirement of multiple documents to be filed within a classification, such as CVs).
- Also, it is possible that a document is filed incorrectly, whether in an incorrect classification or filing level.

These instances may create potential findings during Inspections. The Detailed Report section of the EAT report can aid in identifying these. However, the Overall % metrics don't account for these scenarios.

Resources

- EAT Report Quick Reference Guide
- EAT Definition File

3.2.2 AQR Compliance

To confirm that V-TMF review is completed for each Functional Area, at protocol-, country-, and site level, an Annual Quality Review (AQR) Confirmation Form **(TV-eFRM-02260)** and evidence of the review must be filed in V-TMF. To keep track of which AQR Confirmation Forms have been filed and which ones are still pending, the **AQR Compliance Report** can be used. This report will help to quickly identify any compliance risks/issues with regards to TMF Annual Quality Review for a study.

Note: the threshold for AQR compliance changed from 70% to 80%, effective as of 18Mar2022.

Resources

- To decide whether AQR is required based on site status in CTMS
- V-TMF Job Aid in Blackbird
- AQR Compliance Report Quick Reference Card
- Video: How to use/interpret the AQR Compliance report in VIPER- Last and Passed views
- Video: How to use/interpret the AQR Compliance report in VIPER - future views

3.2.3 Timely Filing

With inspectors being able to request access to V-TMF, and as we need to be always inspection ready, it is important that study documents are filed in V-TMF timely.

The Timely Filing dashboard allows you to see the study's performance. It can help identify which Functional Areas or countries need to improve on their filing timelines. It is very common for Inspectors to request timely filing reports to assess whether documents are being filed in a timely manner or being uploaded only upon Inspection Notification.

Timely filing follows the industry standard of 30 calendar days to ensure documents are available in the final repository (V-TMF). Please note that only certain document classifications are in scope for the

30-calendar day filing metric, refer to Timely Filing Inclusion Exclusion List for more details. Note: the timely filing % threshold changed from 70% to 80%, effective as of August 2022.

The 80% threshold will be applicable for new trials from trial start. For "older and ongoing trials", the expectation is that 80% timely filing is expected from 01 August 2022 onwards.

Resources

- Timely Filing Report Quick Reference Card
- Timely Filing Tip Sheet

3.2.4 Document Status Dashboard

The Document Status dashboard in V-TMF allows to identify issues such as:

- Missing descriptions
- Documents still in Draft > 30 calendar days
- Document date errors
- Original Paper TMF reconciliation
- Open Workflows/Tasks
- QR'd files requiring action

Refer to the Quick Reference Card for instructions on how to use this dashboard along with this Link to the report: https://jnj.sharepoint.com/teams/TMFPortal/Training/Learning%20Toolkit%20QRCs/V-TMF%20Document%20Status%20Dashboard.pdf

Document Status Dashboard Instructional Video can be located here: https://web.microsoftstream.com/video/c271382b-debf-43df-8e56-0535c44dc493?list=studio

3.2.5 Duplicate Document Report

This report is accessible through V-TMF and can show if there are any duplicate study documents. Refer to the Quick Reference Card for instructions on how to use this report

The **Duplicate Document Report** can be found in the Reports>all reports drop-down or via the below links.

- Product/Study Level: https://V-TMF.veevavault.com/ui/#reporting/viewer/0RP000000003I05
- Country/Site Level: https://V-TMF.veevavault.com/ui/#reporting/viewer/0RP000000003I04

3.2.6 Study Document Finder and Essential Document Tracker

The **Study Document Finder** has been created by study teams to list essential study documents in the study mainly to support the local teams to find important study documents quickly (e.g., documents needed for submissions and SIVs such as protocols and amendments, ICF, training documents, etc.). This document is not mandatory to use; however, it could be a helpful tool for the study and local teams to find these documents quickly, either in their normal day-to-day work or during inspections. It is especially helpful to list out the site training materials that are included in the Learning Management System (LMS). The SMs can easily find the V-TMF numbers for all the current training materials.

Tips:

- Make sure the Study Document Finder only lists the most critical documents for the local teams. Otherwise, it will become too cluttered.
- To make sure the central/local teams are aware of the Study Document Finder and are using it - add a slide to the CFTT or SMT meeting slides with the location.

The **Essential Document Tracker** has been created by study teams to keep track of the essential documents in your study to support any questions you may get during an inspection. It lists the essential documents and their versions, as well as why the document was updated and when it was released. This document is also not mandatory but helps give a history of the trial documents that can be useful.

Templates/examples:

3.3 ATLAS

ATLAS contains many compliance metrics. For Issues and Protocol deviations, ATLAS metrics are available in the Non-Dynamic Site Monitoring (DSM) dashboard, Study Management. In addition, “Issue and Protocol Deviation Details” is now available in the PANORAMA dashboard in VIPER.

3.3.1 Quality oversight with ATLAS

ATLAS is an action-based platform and quality oversight tool that pulls in data from multiple sources such as CTMS, V-TMF, EDC, and CRO data feeds (where applicable), to identify trends and systemic

issues across subjects, sites, countries, and trials. It has the potential to support our study teams by identifying potential issues or data trends that may indicate a systemic issue. Key Performance Indicators (KPIs) and Key Risk Indicators (KRIs) provide visuals for teams to direct their focus to the right areas at the right time. The reports have the potential to highlight 'outliers', such as sites that are different from the norm.

- Outliers can signify a potential risk; however, all potential risk signals require further investigation.

ATLAS is a crucial tool in monitoring the quality and compliance of the study at different levels and detail (trial, country, and site level).

For the latest information on 'Which Studies are In or Out of Scope' please refer to the ATLAS SharePoint site.

3.3.2 What metrics can I find in ATLAS?

The number of metrics in ATLAS can be overwhelming. Fortunately, there are many resources available to help you use the platform, like the CTM-GTL ATLAS Guide. This guide provides operational guidance for the DSM (Dynamic Site Monitoring) and Non-DSM dashboards and shows what metrics you can find in ATLAS, what they mean, how you can breakdown per study, region, country and site and the relevant metrics to be used during SMT/CFTT presentations to analyze trial level risk/data or during the Country 1-on-1 meetings to discuss mitigation plans as applicable.

Resources

- Training and resources: https://jnj.sharepoint.com/teams/ATLAS
- CTM-GTL ATLAS training
- Where and how to get started with ATLAS
- KRI Definitions Site and Country Level
- QRM3 to ATLAS mapping

3.4 VIPER 'Site Visit Report Metrics' Dashboard

VIPER has a dashboard entirely dedicated to Monitoring Visit Compliance– it's called the 'Site Visit Report Metrics' Dashboard.

3.4.1 'Site Visit Report Metrics' Dashboard

This 'Site Visit Report Metrics' Dashboard can be accessed via the VIPER homepage and provides an overview of the following:

- submission and approval details for all report types as well as follow up letters
- information on visit report rejection, site visit cycle times, and Remote vs. On-site visit distribution
- details for reports that are still pending approval as well as highlighting potential data quality issues with visit reports and follow-up letters

For CTM/IDMM/(U)GCTA, the two most useful reports for inspection readiness are:

1. Site Visit Report metrics, detailing the below metrics:
    - % Submitted on Time
    - % Approved on Time
    - % Submitted on Time over Time (trending)
    - % Approved on Time over Time (trending)
    - On Time Metric Details
    - % Submitted on Time by Submitter
    - % Approved on Time by Approver

2. Follow-up Letter metrics, detailing the below metrics:
    - % FULs filed within 15 Days
    - % Expected FULs
    - % FULs filed within 15 Days over Time
    - % Expected FULs over Time
    - Follow-up Letter Metric Details
    - % Submitted on Time
    - % Approved on Time
    - % Submitted on Time over Time (trending)
    - % Approved on Time over Time (trending)
    - On Time Metric Details
    - % Submitted on Time by Submitter
    - % Approved on Time by Approver
    - % FULs filed within 15 Days
    - % Expected FULs
    - % FULs filed within 15 Days over Time
    - % Expected FULs over Time
    - Follow-up Letter Metric Details

Resources

Instructions on how to operate the VIPER 'Site Visit Compliance Metrics' Dashboard are found in this Training.

3.5 VIPER Signature History and Compliance Dashboard

The Signature history and compliance dashboard facilitates tracking of the collection of investigator case book signatures for RAVE EDC study milestones while providing assessment of compliance with requirement for maintaining evidence of regular periodic investigator review and approval of eCRF content. It provides a comprehensive list of investigator signatures and dates for each mapped trial milestone in addition to those applied to fulfill requirement for periodic, time-based review. Compliance with this requirement is assessed per Subject, and it is met provided the gap between investigator signatures for a Subject is no greater than 184 days.

The dashboard reports may be filtered by Study, Subject Status, current compliance, Country, Site, Therapeutic Area along with other standard VIPER filters. Users may apply date filters to evaluate compliance for specific periods.

The dashboard can be accessed via the VIPER homepage, is refreshed daily and has the following two report tabs:

- Cross-Study Signature Compliance
- Site Compliance

3.6 Training

3.6.1 Global & Local Team Training

In each study, the sponsor global and local teams will have to complete study/protocol-specific trainings through SUMMIT. It is important to be able to demonstrate that local teams were trained prior to working on the study and prior to creating any materials which may be used to train site staff.

For further information please review **TV-POL-01111: Management of Clinical Study-Specific Training,** and associated Forms and Job Aids.

Which trainings should I upload to SUMMIT?

Clinical Study Specific training (previously known as Protocol-specific training) is any information specifically related to a protocol, program, or therapeutic area. It has the purpose of training the sponsor's global and local teams involved in the study on the specific protocol details.

Examples of training topics:

- Protocol & compound
- Investigator's Brochure
- Study procedures, like performing feasibility, Site Qualification and Site Initiation Visits
- Trial-specific plans/guidelines e.g., Monitoring Guidelines, eCRF Completion Guidelines
- Vendor manuals e.g., LabCorp or RTSM system Manuals
- Study-specific systems
- Patient or site materials
- IP Procedures e.g., the IP Preparation Instructions (IPPI) and Site IP Procedures Manual (SIPPM)
- Blinding Plan (for IDM trials)
- Any topics requiring extra attention or re-training.

Trainings are uploaded to SUMMIT through TruVault. Completion Records may also be uploaded if a live training is delivered in a Study Management Team (SMT) or an IDMT meeting. Attendees will be marked with the training completion in SUMMIT.

When a new version of a protocol, a study manual, or other important update to in trial procedures is available, it is important to consider if a new training module must be created. Also consider if updates to study documents such as the Major Protocol Deviation criteria or eCRF Completion Guidelines should be delivered via the protocol specific training process.

You can find real-world examples of training curricula from different studies here:


ALL2005_Training Tracker.xlsx


CLL3011-Training Tracker.xlsx

Trainings can consist in different formats:

- PowerPoint slides
- Recordings
- Read and acknowledge
- Or a combination of these!

For example, live protocol training is often given for a new protocol. The session can then be recorded, and slides and recordings uploaded to SUMMIT. The protocol document can be included in this training as a read and acknowledge.

Retiring trainings

When a training is no longer needed, it can be retired by the training team. For example, if Monitoring Guidelines v2.0 Training is available, Monitoring Guidelines v1.0 Training can be retired so that new team members don't have to undertake unnecessary training. Before retiring a training, be 100% certain that it is not needed anymore. Also, keep in mind that full training and not only updates may be provided/required. In this case, the initial version of the training needs to be available as well.

It is important to conduct a periodic review of all Sponsor Staff Clinical Study Specific Training content and curricula. This formal review should be documented.

Optional trainings

When a training is only applicable to a small group within a study team, an optional training can be created (e.g., country-specific amendments or processes in which only certain countries are participating). SUMMIT is not flexible enough to push a training to only a few members of a team. Training will always be assigned to the ENTIRE global and/or local team.

In the above scenario, the training team can create an optional training. This training will not be assigned automatically in SUMMIT. Team members will have to register themselves through a link provided by the training team. Always make sure you follow up to assess if the optional training was completed on time, as this will not be shown in any metrics.

Who should be assigned which training?

Protocol Specific Training is assigned based on the information that is included in TV-eFRM-09596: Trial Contact List. Training is assigned depending on an individual's role.

Training is divided between the global, the local and the IDM/IDMM curriculum. The global/central team is assigned the global curriculum, and the local team is assigned the local curriculum. For IDM trials IDM and IDMM roles are applicable and these unblinded roles are assigned to the IDM/IDMM curriculum.

The global team usually consists of:

- GTL
- CTM
- GPL
- Global Data Manager/Data Delivery Lead
- Central Monitoring Manager
- SRP/SRS, SIPS and PIPS

The local team consists of:

- GTL*
- CTM*
- LTM
- SM

The local/global unblinded team consists of:

- IDM
- IDMM

*Of note, any training that is being added to the local curriculum is assigned to the GTL and CTM as well.

When uploading training materials to the Protocol-Specific Training Portal/CTL&D upload location, the decision can be made whether to assign the training to local curriculum only, global curriculum only or both. The only trainings that are usually assigned to both the global + local + IDM/IDMM (if applicable) curriculum are protocol training and training on the Investigator Brochure. The Job Aid Study Specific Training Process has a list of suggested trainings for Global, Local and IDM/IDMM-specific training curricula.

Central/Local Team Training Compliance

Assigning training to team members is only the first step. It is important to assess if the training was completed on time. Some reports and tools are available to use for this purpose.

Reports from SUMMIT

The training team can provide training reports upon request via the CTL&D Study-Specific Training Intake Portal. Below are some examples of the reports that can be requested:

Overall Curriculum Compliance Report

This report will show you training compliance of study team members:

- % Of trainings that were completed on time
- % Of trainings that were completed in general

The report is often missing team members. Also, this report does not show:

- Metrics for team members that left the study
- Exact dates that team members have completed a training
- Whether team members have completed optional trainings

Below is a real-world example of a Curriculum Compliance Report:

54179060CLL3011
Overall curriculum c

Detailed Training Report

This report shows all persons that ever worked on a study and when they completed a training. This also includes optional trainings.

Even though the report contains a lot of information, it is not an easy overview. It does not clearly show team members that are not compliant. For this, we would recommend using a tracker.

Below is a real-world example of a Detailed Training Report:

54767414MMY2036_
26Mar2019.xls

Training Compliance Tracker

Combining information from three sources, you can make a Training Compliance Tracker:

- Trial Contact List
- Overall Curriculum Compliance
- Detailed Training Report

With this tracker, you can quickly review study team compliance. See below real-world example of a Training Compliance Tracker:

MMY2036_Training
Compliance_03Oct2

Resources

- CTL&D Study-Specific Training Intake Portal
- Clinical Trial Learning & Development (CTL&D) Home
- Job Aid Study Specific Training Process
- TV-POL-01111: Management of Clinical Study-Specific Training & associated Job Aids.

3.6.2 Site Staff Training with LMS & GPTP

Refer to TV-POL-01111: Management of Clinical Study-Specific Training & associated Job Aids

The Clinical Trial Learning and Development (CTL&D) group is responsible for the development of the Global Protocol Training Plan (GPTP), which is used for documenting site staff training. The GPTP provides a summary of trainings to be assigned to site staff based on role and delegated tasks. The GPTP is a *living* document that may be updated several times throughout the course of a study. With each update, CTL&D will send a notification e-mail to the study team when the LMS is updated with the revised training content and include the V-TMF number for the updated document.

The study team is ultimately responsible for the content of the GPTP; therefore, the team should be prepared to provide information to the reviewer in the event of audit. The "Summary of Changes" reveals the history of the document and must be updated with each revision. Consequently, the study team should provide input into the Summary of Changes whenever needed.

It is important to demonstrate that all site staff are trained prior to performing any study procedures/assessments and that the Learning Management System (LMS) and Training Logs (TL) accurately reflect training compliance. It is the responsibility of the local team to make sure the GPTP is followed.

Site Managers and IDMs must reference the delegation log (DL) and ensure that training modules are assigned to site staff according to the tasks they will perform. At least one site staff member (for IDM trials at least one blinded and one unblinded site staff member) must be qualified to perform each study-specific task noted on the DL. Training assignments are allocated using the 'Assign Tasks' functionality in the LMS. Note: CTMs do not have access/visibility of this function.

Site contact information should be correct and complete in OneCTMS as the Site Staff information in LMS is integrated with OneCTMS. When site staff leave, it is important to enter end dates in OneCTMS to prevent future training being assigned.

Delegation Log

The study-specific Delegation Log (DL) (TV-eFRM-04980) is utilized. The study-specific DL is filed in the study -level V-TMF: Site Management > Site Set-Up Documentation > Site Signature Sheet. Deployment of site staff training through the LMS is dependent on the accuracy of the task delegations assigned in the system. Therefore, it is critical for the SM/IDM to assign tasks in the LMS ASAP upon receipt of the delegation log from the site. The DL should be reviewed at every on-site and off-site monitoring visit. The SM/IDM is responsible for ensuring delegated tasks are accurately reflected in the LMS, including any revisions that may have occurred since the log was initially completed by the site.

Training Reconciliation

Training reconciliation should be conducted at every monitoring visit. Details regarding training reconciliation must be documented by the SM/IDM in the appropriate visit report and per the On-Site and Off-site Monitoring Visit Report Instructions for Use (IFUs).

For studies utilizing the LMS, training can be completed directly in LMS or outside of the LMS.

Ideally all study-specific training is completed within the LMS, however there may be situations where this is not possible, and training is completed outside the LMS. The SM/IDM must review the Training Log (TL) or other acceptable source documentation to verify training completion and mark the training as complete in the LMS in a timely manner. The Training Log (TL) should be completed appropriately and filed in the Investigator Site File (ISF) as proof of training completion.

While the SM/IDM is responsible for training reconciliation at the site level, the LTM/CTM/GTL/IDMM is responsible for oversight of training reconciliation at the country and study level.

Filing Requirements for Training Documentation

For studies using the LMS, a PDF report of training completion is automatically loaded into the Sponsor TMF at the study level on a weekly basis in a PDF format during the study and at study closure. This report includes training completed directly in LMS as well as trainings that have been completed outside LMS and subsequent training completion verified by the SM/IDM within the LMS. These reports will be viewable during inspections and audits.

Despite the automatic filing of the Training summary report in V-TMF, Site Managers must ensure that Site staff are filing their certificates in the ISF.

How to run a DrugDev Training Report

If the study uses DrugDev as LMS, there is a useful report which can be run within the system. This report shows which site staff members have completed their training and which training modules are still pending. Site staff training is a local responsibility; however, this report may be used to check overall compliance and follow up with local teams.

To run the LMS training report:

1: Log into the study's DrugDev portal.

2: Click on the Training tab.

3: Select "Export Training Detail"

4: Click on the report link and it will open in Excel.

The report contains the following information:

- Site staff details
- Training details
- Completion status (completion date and method of training)

Resources

- TV-POL-01111: Management of Clinical Study-Specific Training & associated Job Aids.
- Job Aid: Investigational Site Staff Training Process for LMS Studies
- Study-Specific Training Process & LMS Handbook – Local Study Team Roles
- Clinical Trial Learning & Development Portal.

3.7 Data management

Data integrity is part of inspection readiness. Sites need to enter the data and resolve queries in a timely manner. There are several dashboards available in VIPER that are useful to review data entry metrics.

- EDC Collection and Cleaning Dashboard
- Site quality and AE and entry time

3.7.1 EDC Collection & Cleaning Dashboard in VIPER

This dashboard provides real time data for many useful metrics, for example:

- Missing pages
- Missing visits
- Pages pending SDV
- Open queries
- Missing Local Lab Ranges

Here is a link to training on how to use the dashboard: training.

Data Cleaning Tracker using VIPER Reports

Real life example of a Data Cleaning Tracker is attached for reference. Please NOTE that this is not mandatory but only an option in case this would help CTMs to have a more efficient country oversight. GCTAs can support the study team by running these VIPER reports for review on a regular basis.

EXAMPLE_ALL2005_
Data%20Cleaning%2

Investigator Names Missing in Data Sets

There have been reported cases of investigator names missing from data sets. Principal Investigator names need to be listed for a clean DM dataset. A Rave Study User Report can be requested in SAM to check for missing PI names. The SAM team provides the data in a spreadsheet in about 2 business days. If any investigators are not on the spreadsheet, then submit a SHARP request (SHARP (stefanini.com) to have the missing PI names "mapped" to the site in EDC by following the Stefanini PI Mapping Process Flow.

3.7.2 Site Quality and AE & Entry

For studies using ARBM and which have a designated Central Monitoring Manager (CMM) working on the study, the CMM will run these reports and provide updates during the Central Monitoring Working Group (CMWG) Meetings. For studies not using ARBM, it is expected that the CTMs run and review these reports. CTMs should follow up with the countries on any issues identified.

Training on the dashboard can be found here: Training.

The Site Quality AE & Entry dashboard can be accessed via the VIPER homepage.

3.7.3 Medidata RAVE EDC Form Inactivation

Sponsor users are not to inactivate any Rave EDC forms with data unless a query was issued prior, and the site has confirmed it is OK to inactivate. The CTM has global responsibility/oversight of our studies and as a result, the quality review responsibility for this process. The CTM, or other delegated role will complete the quarterly quality review by reviewing the EDC Std Rpt - Inactivated Datalist report in Rave (see next topic below for more details). The CTM (or designee) reviews the report by confirming that all data points inactivated by a sponsor user have a query issued, and that the site responded 'ok to inactivate' prior to the form being inactivated. The CTM (or designee) will then file the inactivated datalist report after quality review has been completed in V-TMF.

For more information, see the Job Aid on this process.

3.8 Financial Disclosure

The Financial Disclosure report can be found in the PANORAMA dashboard of VIPER. The report contains 2 sections intended for regulatory submission activity:

- Top section displays all site contacts with a financial disclosure template and financial interests have been disclosed.
- Middle section displays all site contacts with a financial disclosure template and no financial interests have been disclosed.

The source of the report is CTMS. All site contacts linked to a Financial Disclosure Template in the CTMS document management screen are reported at various timepoints during the study (ie; initial, interim, or after 1 year of study closure).

- If a contact discloses financial interest at any timepoint, the report value for the contact will be "Disclosure-Financial Interest to Disclose".
- If a contact does not have financial interest to disclose at any timepoint during the study, the report value for the contact will be "Certification-No Financial Interest to Disclose".

Ensure the report is checked regularly for completeness and any financial interest disclosed.

Resources:

- TV-SOP-06894: Preparing Financial Disclosure to Support US Marketing Applications
- TV-WI-01978: Financial Disclosure

CHAPTER 4: Contingency plan(s) – Major Disruptions

Major disruptions have seemed to occur more frequently in the recent years. Some of the notable events include the COVID-19 pandemic, geopolitical crisis, climate changes, and cyberattacks.

These events have great impact on how we conduct our clinical studies, they highlighted the interconnectedness of our world, and the importance of Business Continuity Plan (BCP). It is also an expectation of the regulators for the sponsor companies to have measures in place to mitigate the risks, protect the subjects' safety and data integrity.

The BCP Quality Framework helps to ensure that we are prepared to respond to disruptions efficiently. This framework is documented in the policy TV-POL- 02184 "Business Continuity Plan Quality Framework".

General guidance

In case of a Major Disruption, the study team is to perform an impact assessment and monitor status on the site(s) / country-ies impacted during CFTT meetings and SMT/IDMT meetings If impact is confirmed, then TV-eFRM-16926 "Protocol Contingency Plan (PCP) for Major Disruptions" is to be created by the GTL/CTM or designee, and the Major Disruption has to be documented in the CFTT, SMT/IDMM meeting minutes. In addition to the impact, the mitigations are to be included for study-specific requirements, as well as referring to supporting documentation filed in VTMF.

In case the impact assessment outcome shows no impact of the major disruption on clinical trial activities, then this decision is to be documented in the CFTT meeting minutes.

The PCP is a living document and after all mitigations were implemented successfully and impact is determined to be negligible, then the PCP is to be finalized and filed in VTMF (refer to the VTMF-content map for filing location).

APPENDIX: GTC Inspection Readiness Checklist

Inspection Readiness Checklist	
Protocol Number	
Protocol Title	
Team member Name	
Role	
Date *(DD-MMM-YYYY)*	

Instructions:

- The GCO IR checklist is not a formal document and can be adapted to the individual needs of each study team.
- The IR checklist cannot be filed in V-TMF; however, it can be filed in the Non-Essential area of V-TMF.
- Only areas of 'high risk' for any inspection have been included on this checklist; therefore, this checklist may not be inclusive of all areas applicable to your study.
- Please check the box when the task has been completed or indicate 'not applicable' (N/A) if this task is not required for your study.
- Recommended timing for using this checklist depends on study design and duration:
    - Annually (or a higher recurrence in case of shorter studies)
    - At the end of the trial
    - After an inspection is announced
    - At a certain % of enrolled patients (e.g., 25-50-75 or 30-60-90%)

For archived studies all required QC/completeness V-TMF checks should have been performed and signed off before V-TMF archiving. Inspection preparation checks will be performed if any archived studies are selected.

Tick box once checked		TASK / ACTIVITY	Comments
Study Team Training / CV / Role			
1.	☐	Confirm with entire study team that their job description (JD) and CV (with current role matching JD) is available and has been filed appropriately in 'My Training Plan' (access via learning at Pharma R&D website). CV and JD Statement Form should be filed for Flex staff instead of full CV and JD.	
2.	☐	Confirm with entire study team that all their training is up to date – including: ☐ Role Specific Training (Core Curriculum) ☐ Protocol/study specific training	
Work with (U)GCTA to ensure all team study-specific training is tracked and documented			
3.	☐	Team training curriculum set up in SUMMIT	
4.	☐	Documentation on Training Compliance has been reviewed and follow up actions taken. Recommendation is to review documentation on a quarterly basis.	
V-TMF Completeness Tasks * In case of an IDMM study: all below mentioned items should be checked and filed in the restricted V-TMF by the IDMM together with the UGCTA. For the IDM team IDMT slides are to be filed in V-TMF instead of SMT slides.			
5.	☐	Run EAT Reports – V-TMF Filing Compliance	
		Work with gCTAs for countries < 95% compliant to send detailed EAT report and follow-up until compliance improves	

6.	☐	Ensure the availability of all study-related documentation according to expected documents list (EDL)	
7.	☐	Work with gCTAs to ensure all versions for key Essential Documents are filed (e.g., IB, ICFs, Protocol, Monitoring Guidelines, Site IP Procedures Manual)	
8.	☐	Confirm Monitoring Guidelines/OMP were finalized prior to First Site Open • If not, prepare storyboard	
9.	☐	Ensure Annual Quality Review for the Filing and Archiving Plan is completed for all functions and the Curation Activity Review is completed • Date of most recent annual Quality Review: _____ • Confirm that both QRC Form and QR evidence have been filed: _____ • Date of FAP: _____ • Next target date for completion: _____	
10.	☐	Ensure all SMT slides/minutes are filed	
11.	☐	Ensure pertinent study correspondence is filed, if not already documented in SMT slides/minutes (consider global/regional crisis-related communications)	
12.	☐	Ensure documentation on country and site selection is filed	
Vendor Oversight			

13.	☐	Ensure Meeting Plan is in place, evidence (e.g., meeting minutes) is available and the plan is being followed	
14.	☐	Documentation present supporting actions described in ESP Oversight Plan/Meeting Plan (i.e., meeting minutes, CRO/vendor oversight reports/trackers filed in V-TMF)	
15.	☐	Ensure a SOP list is available for outsourced trials	
16.	☐	For outsourced studies, confirm emergency cover is operational to provide 24/7 contact information for emergency unblinding and urgent safety questions	
Trial Oversight Activities			
17.	☐	Recommendation: Create a study timeline to capture key dates, milestones, documents, trainings, and central team turnover/changes	
18.	☐	Work with gCTA to ensure Master ICF Tracker is maintained and up to date	
19.	☐	Ensure Issue Tracking is available and filed ☐ Inspection Narratives ensure detailed documentation developed for all key central issues ☐ Work with LTMs / local teams to confirm that all country / site level issues are appropriately documented	
20.	☐	☐ Review list of confirmed Major PDs with clinical on a quarterly basis, maintain list of all confirmed Major PDs	

		☐ Maintain list of all Major PDs downgraded to Minor and rationale for downgrading. Ensure site has been informed and documentation is available and filed. ☐ All Protocol Deviations and Major Issues requiring team input to be reviewed during Centralized Findings meetings and minutes of these meetings filed in V-TMF * In case of an IDM study: the Deviation and issue tracking log (TV-FRM-04433) should be available in V-TMF. Work with the IDMs to confirm all country/site issues and PDs are appropriately documented.	
21.	☐	Review SAE documentation, verify that all SAEs have been reported; in case of late SAE reporting, make sure documentation is on file (escalation to study team, corrective/preventative action taken).	
22.	☐	Ensure the global/regional crisis protocol contingency plan and any TA specific documentation is updated and filed in V-TMF	
23.	☐	Work with CMM to ensure ARBM Plan (if applicable) is in place and is being followed; plus, availability of any required documentation for risk assessments	
24.	☐	Ensure Monitoring Guidelines (MG)/OMP are in place and are being followed. Ensure any deviations from MG/OMP are documented (i.e., out of window MVs tracked, approvals for deviations from monitoring schedule available and filed).	
Metrics and Oversight Reporting *(run metrics reports and follow-up on any risk signals)*			

25.	☐	Check for any compliance issues in the VIPER and ATLAS dashboards and ensure appropriate action has been taken/is planned – ensure discussions are documented and filed in V-TMF, e.g.: ☐ EAT Report ☐ AQR Compliance ☐ Timely Filing ☐ Site Visit Compliance ☐ EDC Collection & Cleaning Dashboard ☐ Site Quality and AE & Entry	
Trial Specific Oversight/Medical review			
26.	☐	Check with CMM, SRP and IDAR for any data compliance/safety concerns and ensure appropriate action has been taken/is planned – ensure discussions are documented and filed in V-TMF	
Trial Contact List			
27.	☐	Work with (U)GCTA to ensure TCL is up to date, including for all trial team members and vendors (especially start and end dates)	
28.	☐	Work with (U)GCTA to ensure handover documentation is filed for any turnover within the study team (CTMs, LTMs, SMs, IDMs, IDMMs)	

Outputs from the checks (e.g., location of VIPER reports or relevant trackers, pending actions/follow up requirements) can be captured in the Comments column within the checklist.

Teams can also decide to implement a separate tracker. An example is provided below that can be adapted to each team's needs/preference.

GTC IR Checklist Tracker.xlsx

Note: For IDM trials, helpful inspection preparation guidance and a checklist (IDM Audit and Inspection Preparation Slide deck template & Checklist) is available on the restricted IDMM knowledge hub page.