TRIAL INTERACTIVE

Checklist for Accurate and Complete Clinical Content Management

KEY TAKEAWAYS

85% of sponsors experience timeline delays due to challenges with the sheer volume and complexity of global regulatory requirements, languages, cultures, and accessibility considerations.[1] Understanding your clinical trial's inherent risks, especially in relation to the content and documents they will generate, is one way to protect your timelines, compliance, quality, and your budget.

This checklist reviews the various content types involved in clinical trials, from study initiation to closeout, and ways to mitigate the inherent risks.

Navigate through the various stages of your clinical trial to learn more about their content types and risk mitigation tips:

Trial Initiation

Training Management

Trial Conduct

Trial Oversight

Closeout

Chart Key

Risk Classification: Some documents are more prone to inaccuracies, mistakes, or oversight

- ▲ Indicates highest risk
- ● Indicates medium risk
- ▼ Indicates low risk

[1] *https://www.mesm.com/blog/tips-to-help-you-avoid-costly-clinical-research-delays*

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TRIAL INITIATION

Clinical trials start to generate large volumes of content early on, beginning with Study Start-Up. Incorrect or missing documentation increases the risk of ethics and regulatory violations, and can impact study initiation, timelines, and budgets, and above all, can harm participant safety.

Activity	Content Type
Site Identification	▲ Regulatory compliance and ethics history ● Confidentiality agreement ● Feasibility questionnaire ● Site Audit Findings ▼ Capability assessments ▼ MSA/Site Contract ▼ Participant recruitment and advertising strategy
Site Qualification	▲ Qualification documentation
Study Start-Up	▲ Clinical trial protocol signature page (PSP) ▲ Form FDA 1572 (and alternate forms that meet local requirements for global trials) ▲ IRB/EC approvals on informed consent forms ▲ Regulatory submission and approval documents ● Site specific documentation ● Training records ▼ Essential documentation package

Trial Initiation Risk Mitigation Checklist

- [ ] **Verify Information:** When a feasibility questionnaire is returned, it's important to verify the information through a monitoring visit and document the findings. Do not take information at face value.

  Scenario: If not done properly, sponsors end up identifying unqualified sites due to errors in the feasibility questionnaires or capability assessments. This could mean that they select a site that cannot recruit enough participants, or the right participant mix to meet their study's diversity considerations.

- [ ] **Do Your Research:** Research sites on regulatory authority websites to look at any previous audit findings (if any) to ensure you understand the full picture of the potential site. Look into training records to ensure site personnel have the appropriate expertise.

  Scenario: Sponsors may overlook critical site issues or site personnel qualifications. This can impact resourcing and budgeting if CRAs have to spend more time on site and more time on calls supporting the site personnel.

- [ ] **Track of Potential Sites in a Central Location:** Keep track of the sites you want to use to avoid duplicate efforts or site withdrawal. Collaborative "rooms," and an eISF can support this, as well as increasing data visibility in a CTMS.

  Scenario: If multiple members of your team are reaching out to a site due to miscommunication, this could cause sites to pull out of the clinical trial.

- [ ] **Understand Country Intelligence:** Know ahead of time when country- and region-specific regulatory agencies meet to review your trial initiation documents as listed above.

  Scenario: Sponsors do not have the proper country intelligence for when agencies meet to approve and face lengthy delays in Study Start Up.

- [ ] **Enter Site Information Contemporaneously:** As you get each piece of useful information, including documents listed on page 3, verify that it goes into the proper eClinical system. This means filing your documents as soon as they are received, instead of putting them aside for later. This ensures real-time access to the most updated information in a single source of truth.

  Scenario: Sponsors could mismanage regulatory submission and approval documents, delaying study close-out and preventing a regulatory green light.

TRAINING MANAGEMENT

Preparing your sites and study teams for a clinical trial requires precise and accurate training materials, records, and documentation. Without these, sponsors risk misinformed teams and noncompliance with regulatory requirements.

Activity	Content Type
Site Training	▲ GCP certification documents ▲ Protocol-specific training materials ▲ Serious Adverse Event (SAE) Training ● Training records ▼ Diversity plan for participants
Study Training	▲ Staff training documentation ▼ Ongoing training amendments ▼ Study-specific training modules and assessments
Corporate Training	▼ Corporate SOP documentation

Training Management Risk Mitigation Checklist

- ☐ **Ensure Your Site and Study Teams Complete Ongoing Training:** Don't leave your training until the day before it's due and spend all day in the LMS. Leverage modern LMS features like oversight dashboards and automated training reminders to ensure training is ongoing and documented in real-time.

- ☐ **Complete a Trend Analysis:** Retroactively examine past mistakes made by your site teams. Look at training records and the completion dates of them to determine whether your teams complete training on time.

  Scenario: New safety considerations arise during the course of trial conduct, but your team does not complete training on the new safety concerns. This compromises both the study's integrity and participant safety.

- ☐ **Provide Supplemental Learning Materials:** Include quick-reference materials like FAQs, inclusion/exclusion sheets, mini-protocol packets, etc. to support continuous learning and compliance.

- ☐ **Implement a Centralized Training Platform:** Use a learning management system (LMS) that integrates with your other eClinical systems to better track and verify training document dissemination and comprehension across sites.

- ☐ **Update Training Materials:** Ensure all training documents from protocol training to SAE training are up-to-date and compliant with the latest regulatory standards.

  Scenario: Protocol-specific training materials are outdated, which causes protocol deviations and delays.

TRIAL CONDUCT

There is a lot of data and documents involved in conducting clinical trials. Keeping track of them in an efficient manner is a challenge for sponsors. Improper indexing of the Trial Master File (TMF) or missed fields in your clinical trial management system (CTMS), can jeopardize the inspection readiness and overall timeline of your study.

All of the regulations in clinical trials can be tied to ALCOA principles. Content should be Attributable, Legible, Contemporaneous, Original, Accurate, Complete, Consistent, Enduring, and Available. When adhered to, these principles ensure eClinical systems function effectively, and are key to regulatory compliance.

Activity	Content Type
TMF Management	Refer to the TMF Reference Model for the full list of required documents. Here are just a few examples of content types that are prone to risk: ▲ Contemporaneous TMF documentation ▲ Document filing and retrieval logs ● TMF index ● Inspection readiness reports ▼ Audit trail documentation
Clinical Trial Management	Refer to the Ultimate Clinical Trial Checklist for a full list of required and expected documents. Here are just a few examples that are prone to risk: ▲ Protocol deviations ▲ Site data ▲ Subjects, Subject Visits, Procedures ● Dashboards and reports ● Principal investigator (PI) ● Site activities ● Sponsor data ▼ Milestones ▼ Site contacts ▼ Team contacts

Trial Conduct Risk Mitigation Checklist

- ☐ **Spot Checks and Data Review:** Don't just look at the data right before you need it. You should be familiar with what is being collected and what information is already in your systems at all times. Data entry and data review should be live and contemporaneous.

  Scenario: If you don't know what documents are in your TMF contemporaneously, you won't know what inspectors can find.

- ☐ **Don't Upload Your TMF Documents the Day Before an Audit:** Auditors take notice if you upload your documents the day before or even the week before an audit. This can result in increased scrutiny and additional audit findings.

- ☐ **Use KPI Dashboards:** Know what kind of metrics are being used and analyze your data so you can prevent big mistakes before they happen. Without reporting the right data, it's difficult to get what you want out of the system.

- ☐ **Customize Your Dashboards:** Ask yourself if the tools are providing the information you need. If you have a dashboard but it's not giving you the most effective views or leveraging automations, talk to your vendor about updating configurations.

- ☐ **Digitize Your Records:** Don't leave various documentation pertaining to sites and studies in a box or a binder. Use eClinical systems like the eTMF and CTMS. Though regulators will accept a paper TMF, it introduces new risks such as storage security and exposure to the elements. A paper TMF also creates more challenges in centralization of documents, i.e. physical documentation for one trial spread across individual sites, countries, etc. Having documents in multiple places can limit the efficacy of TMF oversight and makes it more difficult to achieve contemporaneousness.

  Scenario: Regulators expect the TMF to be complete when they complete an inspection. If they cannot find the documents, due to them being in a binder at a different site, they will stop the inspection. This could lead to timely delays.

Checklist continues on next page

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Trial Conduct Risk Mitigation Checklist

- ☐ **Use and Document Your Data Entry Conventions:** Having TMF and CTMS SOPs for data entry can strengthen document control, version management, and quality. When processes are well documented, it's easier to stay on the same page and teams are less likely to misfile documents or data.

  In the event of an inspection, regulators will want to see written processes and quality systems. Sometimes TMF SOPs can be overlooked.

  Scenario: *Site activities are not well documented. For example, if an investigational product was shipped, but not communicated where it was shipped or when it was returned, then there is no documentation of that activity and you cannot assure compliance.*

- ☐ **Define Quality Mile Markers:** Sponsors should implement risk-based quality checks to ensure the TMF is being maintained, kept up-to-date and that all essential documents are appropriately filed within. Documents should be reviewed and approved as final before moving to the next step.

  Scenario: *TMF document upload errors lead to a poor quality TMF and time-consuming remediation. If the documents remain misfiled or have metadata errors, then you risk inspection findings and further delays.*

- ☐ **Shift Your Approach to TMF Management:** Start filing documents sooner and keep your TMF contemporaneous.

  Scenario: *Every stakeholder must understand your TMF's value, not just those primarily responsible for it. Without setting expectations, stakeholders might not submit documents on time.*

TRIAL OVERSIGHT

All of your documentation should prove oversight of your clinical trial. Monitoring clinical trial sites and studies generates many reports and activity logs. Effective management of monitoring documents is essential to ensure accurate data collection, regulatory compliance, and timely progression of your studies.

Activity	Content Type
Site Monitoring	▲ Compliance audit findings ▲ Investigational Product (IP) / Non-Investigational Product accountability logs ▲ Monitoring visit documentation (letters, reports, etc) ▲ Protocol deviations ● Insurance documentation ● Query resolution ▼ Medical device specific documents ▼ Site performance metrics **For medical device studies, contact info@trialinteractive.com to discuss your documents and their inherent risks.*
Vendor Management	▲ Clinical laboratory improvement amendments (CLIA) ▲ CRO oversight documentation ▲ Lab documentation (manuals, certifications, normal ranges) ▲ Qualification documentation ● Contracts ● IP / device management ● TORO (transfer of regulatory obligations) ▼ Confidentiality agreements ▼ CVs

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Activity	Content Type
Study Monitoring	▲ Centralized monitoring reports ▲ IRB/EC ▲ Medical monitoring oversight ▲ Ongoing regulatory progress reports ▲ Overall study performance reviews ● Investigator Brochures and ICFs at the study monitoring level ● Protocol amendments ● Protocol deviations ● Shipping documents (import/export licenses) ● Study monitoring SAEs ▼ Data and Safety Monitoring Board (DSMB) or a Data Safety Monitoring Committee (DSMC) ▼ Data management ▼ Data trends and analysis reports ▼ Interim analysis ▼ KPI analytics ▼ Quality plans ▼ Recruitment advertising materials ▼ Risk management updates ▼ Study team training management

Trial Oversight Risk Mitigation Checklist

- ☐ **Ensure You Collect All of the Documents Above:** Have awareness about the documents you need to collect and verify that you're documenting the right information. Make sure site and study oversight activities happen and are well documented.

  Scenario: *Delays or inaccuracies in study monitoring reports and logs can obscure your understanding of study-wide issues, leading to ineffective strategic response, inflating costs and prolonging trial timelines.*

- ☐ **Keep Track of Protocol Deviations:** Monitoring is one of the key mechanisms that assures the Sponsor that your trial conduct is in compliance with regulatory requirements, and the trial protocol and procedures.

  Scenario: *Sites have too many protocol deviations and risk getting shut down.*

- ☐ **Create an Agenda for Touchpoints and Take Minutes:** Ensure you meet with everybody you're working with and share an agenda ahead of time to keep the meetings productive. During the meeting, document all the decisions that are made and the issues that arose. Be sure to share the minutes with key stakeholders.

- ☐ **Read Your Minutes:** Throughout the clinical trial, there are meetings. Read the minutes from these meetings for better oversight.

- ☐ **Request Reports From Third Parties:** Get regular status updates from the third parties you work with. Have status updates on the activities. You can also leverage our Vendor Oversight Checklist for evaluating your level of visibility to improve monitoring.

  Scenario: *When contracting out, you need to make sure your vendors are keeping you apprised of their progress. For example, if you are working with laboratories for your studies, make sure they are sharing status updates and alerting you of any inconsistencies.*

Checklist continues on next page

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Trial Oversight Risk Mitigation Checklist

- ☐ **Create a Decision Log:** You can do this in a system like the CTMS. Every time a decision is made, you document it, categorize it, and keep it in a central location. Then you can hold people accountable for the decision.

- ☐ **Perform Regular Quality Checks and Reviews:** Quality is important. Ensure your documents are correct, complete, and live in the right places.

  Scenario: *New regulatory changes happen during the study. You need to monitor these to ensure that you're complying with the latest regulations. This all ties back to ensuring patient safety in your clinical trial.*

CLOSEOUT

At the end of the clinical trial, sponsors must address all necessary aspects of study closeout and archival. Inadequate procedures can delay your timelines, which could be detrimental if you are trying to meet submission deadlines to get it on the market.

Activity	Content Type
Study Closeout	▲ *Clinical study report* ▲ *Closeout notifications to IRB/EC* ▲ *eCTD (global)* ▲ *Final site visit reports* ● *Study closeout letters* ▼ *Final financial statements* ▼ *Final data management*
eTMF Archive	▲ *Access and retrieval procedures* ● *Archival logs and indexes* ● *Archived study documents* ▼ *Archive Plan / Archive Timeline*

Closeout Risk Mitigation Checklist

- ☐ **Create a Closeout Checklist / or Checklists:** Create a checklist that details each step to be completed as study closeout. This can be done in CTMS or you can create events in an eTMF. By using eClinical systems, you can trigger closeout status in CTMS so closeout milestones and activities show up automatically. Make your checklists as detailed as possible.

- ☐ **Set Dependencies Between Tasks:** Create 'quality gates' so you don't close out a site before those steps are complete. After defining your quality mile markers, make sure everyone is aligned.

  Scenario: A sponsor closes a site after database lock, and a database re-lock may result in additional queries being created for a site.

- ☐ **Verify Final Reports:** Confirm that all expected records are present, marked as final, and all quality issues resolved.

  Scenario: Inaccuracies or delays in final site visit reports can result in overlooked issues, compromising study integrity and risking regulatory discrepancies for sponsors.

- ☐ **Run a Listing of All Protocol Deviations:** If you're relying on system outputs for your submissions, you need to run a listing of all protocol deviations. This includes identifying, documenting, and reviewing any instances where the trial's procedures were not followed as planned.

- ☐ **Document Your Access and Retrieval Processes:** The sponsor must designate specific individuals within the organization to manage archives, ensuring access is limited to these appointed individuals. The selection and training of these individuals should be properly documented.

  Scenario: Inadequate procedures risk unauthorized access or retrieval issues, affecting regulatory compliance for sponsors. Poorly managed archives also risk data loss, impacting the study's historical integrity for sponsors.

ABOUT TRIAL INTERACTIVE

TransPerfect's Trial Interactive is an industry leader in practical, global eClinical innovation that simplifies and automates clinical processes for sponsors, CROs, and sites around the world. The 21 CFR part 11 compliant unified platform delivers an author-to-archive collaboration experience with solutions for clinical document management, site selection, site activation, e-learning, compliance training, quality, and more with seamless solution interoperability and indexing to the eTMF. Trial Interactive is consistently selected by clinical professionals for providing the most comprehensive yet intuitive experience with the most complete offering of technology and expert TMF services. Trial Interactive helps study teams streamline their operations by cutting unnecessary expenses, expediting timelines, reducing compliance risks, and improving operational excellence.