

How to Start Risk Management in Clinical Trials

A Checklist of Critical Processes and Records

I. Introduction

Clinical trials are complex and challenging projects that involve many uncertainties and risks. To ensure the safety and quality of clinical trials, it is essential to identify, assess, monitor, and mitigate the potential risks that may affect the clinical trial outcomes, the patients, the sponsors, and the regulators.

The starting point for risk management in clinical trials is to maintain and document all the **critical processes and records** that demonstrate **patient safety, clinical trial data reliability, and profound sponsor decision-making**.

These processes and records provide evidence of the clinical trial design, conduct, analysis, and reporting, and they

are subject to inspection and audit by the regulatory authorities.

But what are the critical processes and records for a clinical trial?

How can you ensure that you have all the necessary records to support your risk management strategy?

In this document, I will provide you with a comprehensive checklist of the critical processes and records for a clinical trial, based on the assessment of the CQAG Group (Clinical Quality Assurance Group) and QA (quality assurance) experts (auditors or compliance functions) with long-term experience in the practical handling of Trial Master Files (TMFs).

This checklist will help you to:

- Identify the critical processes and records that are essential for the quality and integrity of your clinical trial
- Verify that you have all the required records and data for each process and record
- Organize and store your records and data in a systematic and traceable manner
- Prepare for inspection and audit by the regulatory authorities

The Author

Jessica Cordes studied Molecular Life Science in Luebeck and started her business career for 2 years at the Central Lab MDS Pharma Services as a project manager.

She moved to GlaxoSmithKline in 2009 where she worked as country project leader for 4 years.

In 2013, she started at MorphoSys, working in an international role as a clinical trial leader overseeing clinical trials with antibodies and starting with line management responsibilities.

She then moved in 2017 to Medigene as clinical trial manager, planning and implementing a cell therapy clinical trial, where she took over the leadership for Clinical Operations in 2018 while building the group.

In 2021, she joined Immatics being responsible for building a global cohesive Clinical Operations department and leading the operational strategy for the global conduct of all clinical trials.

Since 2023, she has been working as a Senior Consultant and Trainer in her own company Clinical Excellence. She supports small companies in setting up and developing their internal clinical development organization by structuring the department and defining GCP processes as well as providing training. She also supports them in planning and implementing their clinical trials.



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II. Critical Records Checklist

The following list summarizes the critical records for a clinical trial.

For each critical process, you get a list of corresponding critical records that are required.

1. Critical Process: Approval by Authorities

- Critical Record: IRB/IEC Submission
Ensure any (Conditional) Approval, Decision, or Rejection by IRB/IEC
- Critical Record: IRB/IEC Decision
Ensure any (Conditional) Approval, Decision, or Rejection by IRB/IEC
- Critical Record: IRB/IEC Composition
Ensure IRB/IEC Composition is available
- Critical Record: IRB/IEC Documentation of Non-Voting Status
Ensure IRB/IEC Documentation of Non-Voting Status
- Critical Record: IRB/IEC Compliance Documentation
Ensure IRB/IEC Compliance Documentation
- Critical Record: Approvals by other Committees
Ensure Approvals by other Committees (i.e. for GMO, ERA, Radiation Protection, etc)
- Critical Record: Regulatory Authority Decision
Ensure filing of any (conditional) approval, the list of content being approved, and any regulatory authority decisions

2. Critical Process: Auditing

- Critical Record: List of Audit
Ensure a List of all Audits applicable
- Critical Record: Audit Certificates
Ensure filing of all Audit Certificates

3. Critical Process: Clinical Monitoring

- **Critical Record: Site Contact Details**
Ensure Site Contact Details
- **Critical Record: Site Initiation Visit Report**
Ensure Site Initiation Visit Report (incl. confirmation letter, follow-up letter)
- **Critical Record: Source Data Verification**
Ensure Source Data Specification and Agreement, Source Data Verification, Source Document Maps
- **Critical Record: Subject Eligibility Verification Forms and Worksheets**
Ensure Subject Eligibility Verification Forms and Worksheets
- **Critical Record: Subject Identification Log**
Ensure Subject Identification Log
- **Critical Record: Subject Log**
Ensure Subject Log, Consenting Tracker, Enrollment Log, Screening Log, Subject Visit Log
- **Critical Record: Monitoring Visit Report**
Ensure Monitoring Visit Report (incl. confirmation letter, follow-up letter)
- **Critical Record: Site Close-Out Visit Report**
Ensure Site Close-Out Visit Report (incl. confirmation letter, follow-up letter, and open actions)
- **Critical Record: Coordinating Investigator Documentation**
Ensure for the Coordinating Investigator the Clinical Trial Agreement, Confidentiality Agreement, CV, Financial Disclosure, GCP Training, Medical License, Personal Data Consent
- **Critical Record: Form FDA 1572**
Ensure Form FDA 1572 collection
- **Critical Record: Investigator Regulatory Agreement**
Ensure Clinical Trial Site Information Form, Investigator Regulatory Agreement, Qualified Investigator Undertaking Form

4. Critical Process: Clinical Project Management

- **Critical Record: Project Plan**
Ensure specifications on how to perform Clinical Project Management
- **Critical Record: SOP List**
Ensure a comprehensive SOP List (incl. SOPs from the sponsor and any service providers)
- **Critical Record: Training Attendance**
Ensure adequate documentation of training attendance
- **Critical Record: Training Certificate**
Ensure filing of Training Certificate (covering an effectiveness check; i.e. quiz, examen, etc)
- **Critical Record: Communication Plan**
Ensure specifications on how to manage the communication (if not included in the project plan)
- **Critical Record: GCP and Protocol Deviations**
Ensure GCP and Protocol Deviations (incl. deviation log, review)
- **Critical Record: Financial Documentation**
Ensure Financial Documentation (incl. financial summary tracker, invoices payment receipts)
- **Critical Record: Handover**
Ensure documentation if responsibilities have been transitioned
- **Critical Record: Clinical Trial Agreement**
Ensure Clinical Trial Agreement (incl. any other site-related contracts)
- **Critical Record: Clinical Trial Insurance**
Ensure adequate coverage for Clinical Trial Insurance (i.e. policy, certificate, terms & conditions)
- **Critical Record: Clinical Trial Team Log**
Ensure specifications of who is a clinical trial team member (incl. function, start- and stop date, signature)
- **Critical Record: Roles and Responsibility Matrix**
Ensure a comprehensive List of defined Roles and responsibilities (incl. sponsor and any service providers)
- **Critical Record: Risk Log**
Ensure risk management is documented (e.g. RACT)

- **Critical Record: Risk Management Plan**
Ensure specifications on how to perform Risk Management

If you are interested in getting a deeper understanding of the risk-based approach mandated by the Good Clinical Practice Guideline ICH E6(R3), please enroll in my digital training course:



Good Clinical Practice - Refresher

A Refresher Course based on ICH E6
(Revision 3)

[Enroll via the Clinical Excellence Training Academy](#)

5. Critical Process: Clinical Trial Design

- **Critical Record: Clinical Trial Protocol**
Ensure specifications related to the clinical trial design (incl. review, approval, summary of changes, justification for non-substantial amendments)
- **Critical Record: Protocol Signature Page**
Ensure Protocol Signature Page(s) (incl. amendments)
- **Critical Record: Clinical Trial Synopsis**
Ensure a high-level summary of the clinical trial design

6. Critical Process: Clinical Trial Documents

- **Critical Record: Trial Master File Plan**
Ensure specifications on how to manage the Trial Master File

7. Critical Process: Clinical Trial Reporting

- **Critical Record: Clinical Study Report**
Ensure Reporting of Clinical Trials (incl. report, Synopsis, lay summary, and any interim reports)

1. Critical Process: Data Acquisition

- **Critical Record: Final Subject Data**
Ensure Final Subject Data Site, Receipt of Final Subject Data
- **Critical Record: Data Entry**
Data entry must be performed within 10 business days after each visit
- **Critical Record: CRF Development**
Only once a final eCRF has been developed and validated, the first subject can be enrolled
- **Critical Record: Endpoints**
Ensure data reliability for endpoint-related data points

2. Critical Process: Data Analysis

- **Critical Record: Bioanalytical Report**
Ensure Reporting of any Bioanalytical Analysis (incl. pharmacokinetic and pharmacodynamics analysis)
- **Critical Record: Laboratory Results**
Ensure Biochemical Testing, Imaging Uploads, Independent Rater Data, Laboratory Results Documentation
- **Critical Record: Interim Analysis**
Ensure data reliability for all data related to interim analysis
- **Critical Record: Interim Statistical Report(s)**
Ensure Interim Statistical Report(s)
- **Critical Record: Statistical Report**
Ensure Statistical Report

3. Data Management

- Critical Record: Data Management Plan
Ensure Data Management Plan
- Critical Record: Dictionary Coding
Ensure Dictionary Coding, Medical Coding Approval, Medical Coding Consistency Report, and Medical Coding Guidelines
- Critical Record: Data Review Documentation
Ensure Data Review Documentation, Data Review Plan, Data Validation Plan, DB Audit Specification, Third Party Vendor Reconciliation Report

4. Critical Process: Equipment

- Critical Record: Equipment Maintenance Logs
Ensure Calibration Certificate, Calibration Log, Maintenance Logs

5. Critical Process: Independent Data Monitoring Committee

- Critical Record: Independent Data Monitoring Committee
Ensure IDMC Contract

6. Critical Process: Informed Consenting

- Critical Record: Informed Consent Form
Ensure adequate information for patient (incl. checklist, summary of changes, review, approval)

7. Critical Process: Investigational Medicinal Product

- Critical Record: Certificate of Analysis
Ensure Batch Records, Certificate of Analysis, Certificate of Conformance
- Critical Record: Drug Accountability
Maintain adequate drug accountability
- Critical Record: IMP Certificate of Destruction
Ensure IMP Certificate of Destruction, IMP Destruction Documentation
- Critical Record: IMP Quality Complaint Form
Ensure IMP Quality Complaint Form

- **Critical Record: IMP Recall Documentation**
Ensure Evidence of Recall, IMP Recall Documentation, IMP Recall Plan, Notification of IMP Recall
- **Critical Record: IMP Regulatory Release Documentation**
Ensure IMP Regulatory Release Documentation
- **Critical Record: IMP Retest and Expiry Documentation**
Ensure Expiry Extension, IMP Retest and Expiry Documentation, Stability Confirmation
- **Critical Record: IMP Return Documentation**
Ensure Acknowledgement of Return, IMP Return Documentation, IMP Return Form
- **Critical Record: IMP Supply Plan**
Ensure IMP Supply Plan, Placebo Justification Statement
- **Critical Record: IMP Treatment Allocation Documentation**
Ensure IMP Treatment Allocation Documentation, Drug Unit List, Randomization Envelopes, Randomization List
- **Critical Record: IMP Treatment Decoding Documentation**
Ensure Emergency Decoding Authorization Document, IMP Treatment Decoding Documentation, Treatment Decoding Form
- **Critical Record: IMP Verification Statements**
Ensure Controlled IMP Storage, DEA 223, GMP Certificate, GMP Manufacturer's License, GMP Statement, IMP Verification Statements, Manufacturing Authorization, Manufacturer's Certificate of Compliance, TSE Certificate
- **Critical Record: IMP Accountability Documentation**
Ensure Evidence of IMP Transfer, IMP Transfer Documentation, IMP Transfer Plan, and Notification of IMP Transfer
- **Critical Record: IMP Re-labeling Documentation**
Ensure Evidence of IMP Relabeling, IMP Relabeling Documentation, IMP Relabeling Plan, Notification of IMP Relabeling
- **Critical Record: IMP Site Release Documentation**
Ensure IMP Site Release Checklist, IMP Site Release Documentation, Site Greenlight
- **Critical Record: IMP Storage Condition Documentation**
Ensure IMP Storage Condition Documentation Temperature Logs

- **Critical Record: IMP Storage Condition Excursion Documentation**
Ensure Approval For Use (following temp excursion), IMP Storage Condition Excursion Documentation, TempTale Documentation, Temperature Excursion Form
- **Critical Record: Import or Export Documentation**
Ensure any Import and/or Export License(s)
- **Critical Record: Investigator's Brochure**
Ensure specifications related to the Investigational Medicinal Product (incl. review, and approval)
- **Critical Record: QP (Qualified Person) Certification**
Ensure QP (Qualified Person) Certification
- **Critical Record: Marketed Product Material**
Ensure Package Insert, Summary of Product Characteristics

8. Critical Process: Medical Monitoring

- **Critical Record: Medical Monitoring Communications**
Ensure documentation of communication and decisions related to Medical Monitoring
- **Critical Record: Medical Monitoring Plan**
Ensure specifications on how to perform Medical Monitoring

9. Critical Process: Patient Population

- **Critical Record: Eligibility**
Enrolled subjects have to meet all inclusion criteria and do not have to meet any exclusion criteria

10. Critical Process: Quality

- **Critical Record: Quality Plan**
Ensure specification to define Quality (i.e. KPIs, QTLs)

11. Critical Process: Regulatory Affairs

- **Critical Record: Transfer of Regulatory Obligations**
Ensure specifications to whom regulatory obligations are transferred, if applicable

12. Critical Process: Safety Reporting

- **Critical Record: Expedited Safety Report**
Ensure Expedited Safety Report
- **Critical Record: Notification of Safety or Clinical Trial Information**
Ensure Evidence of Distribution of Safety Information and Distribution of Clinical Trial Information, Notification of Safety Information, and Clinical Trial Information
- **Critical Record: Notification to IRB/IEC of Safety Information**
Ensure for Safety Information the Acknowledgement of Receipt, Evidence of Distribution to IRB/IEC
- **Critical Record: Notification to Investigators of Safety Information**
Ensure Safety Information Evidence of Distribution, Notification to Investigators
- **Critical Record: Pregnancy Report**
Ensure Pregnancy Report
- **Critical Record: SAE Reconciliation**
Ensure SAE Reconciliation, SAE Reconciliation Approval, and SAE Reconciliation Report
- **Critical Record: SAE Report**
Ensure SAE Report
- **Critical Record: Safety Management Plan**
Ensure Reference Safety Information Approval Form, Safety Management Plan, Safety Reporting Plan, Safety Reporting Templates
- **Critical Record: Special Events of Interest**
Ensure Special Events of Interest

13. Critical Process: Service Provider Oversight

- **Critical Record: Ongoing Third-Party Oversight**
Ensure Ongoing Third-Party Oversight
- **Critical Record: Third-Party Contractual Agreement**
Ensure Authorization To Proceed, Budget, Contract, Change Order, Data Privacy Agreements, Indemnification
- **Critical Record: Third-Party Selection**
Ensure Third-Party Evaluation, Third-Party Decision

- **Critical Record: Vendor Management Plan**
Ensure specifications on how to oversee service providers

14. Critical Process: Unblinding

- **Critical Record: End of Trial or Interim Unblinding**
Ensure Administrative Interim Unblinding Request Form, End of Trial or Interim Unblinding, Results Release Authorization Memorandum

III. Conclusion

This document has provided you with a checklist of the critical processes and records for a clinical trial that serves as the basis for risk management in clinical trials.

By following this checklist, you can ensure that you have all the necessary documents to support patient safety, reliability of your clinical trial data, and sponsor decision-making.

Do you want to discuss with industry peers how to implement Risk Management in Clinical Trials?

Join our next Clinical Operations Roundtable

and raise all your questions, discuss your challenges, and get best practices from other Clinical Operations professionals.



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