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Outsourcing Audit Trail Review (ATR) in Clinical Trials

A Stage-Based, Practical Guide for Sponsors and CROs

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Introduction

The decision to outsource Audit Trail Review (ATR) needs to be an informed one. There are multiple reasons why a Sponsor may choose to outsource this GxP task to a qualified CRO, and these must be weighed against the benefits of keeping ATR in-house—where an established ATR process exists. In some cases, a Sponsor may not yet have a formalized ATR process. In these cases, outsourcing can serve not only as operational support but also to ensure compliance while internal processes are being developed or matured.

This guide has been created to support decision making and provide guidance to both Sponsors and CROs on how ATR fits into existing processes and systems. Each stage of a project presents different considerations for a Sponsor when determining whether outsourcing is an appropriate option for ATR. These considerations also help CROs understand the Sponsor's specific requirements, including situations where the Sponsor may rely entirely on the CRO's established ATR framework, but must still retain oversight of the process.

Accordingly, this guide is organized into sections aligned with the stages of interventional clinical trials in which ATR is to be implemented. Each section outlines objectives, key considerations, and the benefits and risks associated with outsourcing ATR—whether the Sponsor already has an ATR process in place or is looking to leverage the CRO's expertise to perform this task.

Regardless of which ATR process is used, regulators emphasize risk proportionate review, traceability, and continued sponsor accountability and oversight.

Stage 1 — Decision and Strategy

In this stage, the Sponsor should consider their reasons and goals for outsourcing, determine systems in scope for ATR/metadata review via risk-assessment, and determine whose process will be used for ATR, the Sponsor's or the CRO's. The process choice will have downstream effects on validation responsibilities, training, which tools are used, eTMF placement, and the oversight model.

Determining objectives, goals, risks and scope of ATR outsourcing

1. Clarify internal needs and objectives for outsourcing ATR. Examples could be:
   a. Access to specialized expertise and better technical capabilities, for example, visualization dashboard tools, metadata interrogation tools
   b. Potential for better integration into overall trial-level RBQM processes, ensuring that review efforts focus on critical data and high-risk processes.
   c. Organizational flexibility and scalability, allowing sponsors to adapt resources across projects and trial phases without the burden of hiring and training additional staff.
   d. Timeline adherence
   e. Alignment with overall trial outsourcing strategy (ATR may represent one component of a broader outsourcing model)
   f. Level of Sponsor expertise with ATR/process maturity with ATR

2. Consider outsourcing goals and risks
   a. Consider measurable success criteria for your ATR outsourcing objectives
   b. Consider a risk-benefit analysis. Use a matrix to weigh high/low risk against high/low benefit. Benefits often come from scalability and standardization, whereas risks cluster around compliance, data security, and loss of organizational knowledge. Low benefit areas include non-changeable device/app data or data related to exploratory endpoints where change risk is minimal.

3. Define ATR scope via system risk assessments. This typically includes EDC, eCOA/ePRO, IRT; potentially CTMS, safety, or others based on individual trial endpoints and critical processes. A risk assessment should address the following:

   a. Data collected and GxP criticality. Consider relevant trial metadata as well as audit trails.
   b. Ability of end-users to modify or delete data
   c. Identification of user roles that can modify data
   d. Identification of existing processes that cover review of relevant audit trials –avoid duplication. For example, user access reviews performed by system owners already as a part of system processes. The Sponsor should distinguish trial-level vs system-level ATR to avoid any duplication of reviews.
   e. Rationale for ATR for the GxP system (or not)
   f. Frequency of review
   g. Ability of the system to support review of audit trails
   h. How the review process will be documented

Determining if the Sponsor or CRO process will be used

After determining the objectives, goals, risks and scope with ATR outsourcing, the Sponsor will need to determine whose process for ATR will be used. This section contains overall considerations on the ATR process, and specific considerations for using a Sponsor process or a CRO process. For general information on starting and developing an ATR process, consult the ACDM papers, Getting started with Audit Trail Review in Clinical Trial data-An Essential Guide and Audit Trail Review Hot Topic Questions Answered. Key factors for process choice are summarized below.

Key Factors for choosing Sponsor or CRO ATR Process

Decision Factor	Use Sponsor ATR process when...	Use CRO ATR process when...
Sponsor ATR Maturity	Sponsor has mature SOPs, templates, tools, and experienced SMEs already in place	Sponsor has low internal ATR maturity or experience
CRO Capability & Tooling	CRO tools and dashboards inconsistent, immature or not validated	CRO has validated, inspection tested ATR tools and dashboards
Systems Landscape	Sponsor owns or hosts core GxP systems (e.g., EDC, eCOA)	CRO owns or hosts core systems enabling integrated execution
Inspection and Oversight Strategy	Portfolio-wide consistency and standardized oversight needed	CRO demonstrates inspection-ready documentation and workflows
Resourcing Model	Sponsor prioritizes control and internal consistency across multiple trials or CROs	Sponsor prioritizes scalability and reduced internal resource burden
Study Risk & Complexity	High-risk, pivotal, or adaptive trials	Low-risk or early-phase trials
eTMF Strategy	Standardized sponsor filing across portfolio is needed	CRO maintains robust, inspection-ready eTMF structures
Cost & Efficiency	Existing sponsor infrastructure supports ATR efficiently	Cost efficiency, speed, and scalability are key drivers

Regardless of process ownership, Sponsors retain ultimate responsibility for data integrity and oversight in accordance with ICH E6 R3.

Overall ATR process considerations and best practice

1. Integrate ATR with trial-level RBQM processes: link ATR risks to endpoints and RACT, KRIs, acceptable ranges, thresholds, and ongoing surveillance as applicable; determine how ATR findings feed back into risk management for the trial.
2. The sponsor should maintain a baseline understanding of relevant metadata and audit trail structures sufficient to interpret ATR outputs and make informed, risk based decisions.
3. Right-size the ATR process for Sponsor maturity and size. For smaller organizations, prioritize critical data and high-risk processes, and set pragmatic review cadences.
4. Blinding & access control: ensure blinded reviewers cannot access unblinded data via audit trail review of visualizations, exports, reports and documentation, regardless of process used.
5. Documentation strategy: determine eTMF locations for ATR artifacts (plans, logs, reports, issue follow-ups) and standardize to ensure inspection readiness.

6. Determine how final audit trails for systems in scope will be archived, for example, in a data lake or clinical data repository.
7. Determine how ATR findings are classified and/or reported, monitored, followed up on, and closed.
8. If both organizations have a process, both organizations should perform a gap analysis to identify areas where their processes differ, which could impact staff expectations and actions and may need to be addressed via training.

Considerations if using the Sponsor's ATR process

1. If using Sponsor SOPs/WIs, these will govern methodology, frequency, templates, and eTMF placement. The sponsor will need to determine the level of CRO maturity with the ATR process overall and determine the correct level of training needed by the CRO, and the Sponsor resources needed for that training.
2. There will be a higher training and onboarding effort for CRO staff when using the Sponsor process; however, consistency across studies may ultimately be greater if using the Sponsor process. This is particularly true if a Sponsor is using multiple CROs.
3. As the Sponsor will control the tools and dashboards, CRO access needs and requirements should be considered.
4. Another possibility could be that the CRO uses the Sponsor process with CRO tools, that is replicating the Sponsor process.
5. The sponsor should have an idea on what use cases and risk scenarios for ATR may be applicable to a trial or have a library of standard checks and/or visualizations that can be selected based on trial needs. For examples of potential use cases, consult the ACDM paper, Audit Trail Review: An Exploration of Risk Scenarios and Use Cases.

Considerations if using the CRO's ATR process

1. Determine CRO maturity with ATR processes and tools, by performing a CRO capability assessment, or conducting an audit of the CRO process to ensure due diligence. Look for true risk-based thinking, validated tools, QC/QA as applicable, etc. ATR execution should demonstrate meaningful risk assessment rather than pure procedural completion.
2. A Sponsor with minimal ATR experience could find themselves engaging with a CRO who is perfectly positioned to provide mature functions such as Data Management but is still immature at ATR services. Two pathways forward might be viable, the first being that the CRO engages a vendor to supplement the CRO's existing oversight capabilities to fill the gap, the second that the Sponsor might choose to independently place ATR services with a separate vendor, perhaps as part of an independent data oversight strategy.
3. Verify the overall CRO RBQM process. Sponsors should ensure that CROs implement risk-based ATR methodologies that are aligned with the study's Risk Management Plan. CROs performing audit trail review should have some level of agility with ATR and the ability to adjust the review process based on findings encountered during the trial.
4. Identify which CRO roles will perform ATR for which systems, and how findings will integrate into the Risk-Based Quality Management (RBQM) framework.
5. Determine how factors such as trial phase, endpoints and the location thereof, SDV or tSDV strategies, and blinded status impact the overall ATR process for the trial.

6. Verify visualization and analytics capabilities, including dashboards for trend detection and KRI reporting, as these can be critical for proactive oversight. Assess transparency and access. The goal is to enable timely intervention when risk signals emerge.
7. Assess CRO maturity across external data sources like eCOA or IRT; ensure secure ingest/export of audit trails
8. Identify escalation procedures
9. Assess possibilities for independent review or secondary QC/QA checks, if applicable

In summary, we recommend that a Sponsor use their own ATR process when they are mature, well-resourced, and require consistency and control across a portfolio of trials.

We recommend outsourcing ATR to CROs when the CRO shows higher maturity, better tooling, validated processes, and can deliver efficient, risk-based ATR aligned with trial needs.

Both approaches are acceptable—but the right choice depends on systems, trial risks, people, processes, regulatory expectations, and the maturity of both organizations. Should an assessment conclude the experience and capability are low on both sides, then it may be possible for a CRO to close the gap by engaging with a 3rd party, or the Sponsor to engage with a 3rd party provider directly.

Checklist: Stage 1 – Decision and Strategy

- ✓ **Objectives/success criteria defined; Selection of Sponsor or CRO ATR process**
- ✓ **System risk assessment(s) completed; trial- vs system-level ATR clarified.**
- ✓ **RBQM linkages set (RACT risk, KRIs, thresholds, surveillance).**
- ✓ **Access control and blinding constraints considered.**

Stage 2 — Contractual and Sourcing Alignment

At this stage, the Sponsor should have a general idea about whose process will be used. If the Sponsor process is to be used, the Sponsor should provide requirements and expectations around ATR in the RFP/WO and ask relevant questions during bid defense meetings. Training, access provisioning, QC/QA expectations, and reporting formats should be discussed to the extent possible in this stage. Regardless of which process will be used, early alignment with the CRO will mitigate potential misunderstandings that could lead to issues or delays down the road.

Relevant considerations for CROs if using the Sponsor's ATR process

1. If applicable, determine if a SOP gap analysis should be performed prior to finalizing contract (or after).
2. Determine who will provide and document training on the SOP/process
3. Asses how updates to the SOP/process will be communicated, and how any additional training will be carried out.
4. Assess Quality Issue Management both for ATR findings and ATR performance issues
5. Determine sponsor requirements for use of standard templates and reports.
6. Confirm scope of ATR for the trial with the sponsor.
7. Consider FSP resource models when Sponsor systems are used with CRO staff on a program of trials.

Relevant considerations for Sponsors if using the CRO process

1. If not a part of a previous capability assessment or audit and if possible, request applicable SOPs, de-identified sample plans and reports, relevant KRIs/KPIs, escalation criteria, and an eTMF filing map to assess quality. Determine if KPIs/KRIs applicable to the trial are available from the CRO, or if these should be created by the Sponsor.
2. Ensure CRO ATR documentation meets Sponsor requirements, if not previously assessed.
3. Agree upon the method used to provide Sponsor Oversight of ATR in the trial.
4. Determine the forum for discussion of any findings. For example, this might be a part of regular risk-review meetings or part of data cleaning meetings or separate meetings. Discuss any requirements around the use of standard reports or templates.
5. Assess use of external data systems in the trial such as eCOA/IRT/devices and align on implications for overall ATR process. Discuss access and control requirements for these systems as applicable.
6. Challenge any "100% review" notions—seek risk-proportionate plans.

Checklist: Stage 2 - Contractual and Sourcing Alignment

- ✓ **RFP/WO spells out the process to be used, scope, systems, reporting, metrics, escalation, and eTMF filing**
- ✓ **Bid defense should discuss tools, sample outputs, risk rationale, and oversight dashboards**
- ✓ **Due diligence on security, validation, and inspection history completed**

Stage 3 — Operationalization and Controls

In this stage, the setup and implementation of the trial ATR/metadata review process begins. The 'ATR Plan' is created and the tools to perform the review of audit trails are set up. A risk-based approach focusing on critical-to-quality factors (CTQ) is recommended.

Core activities and controls, regardless of process

1. Finalize the use cases and risk scenarios that are in scope for the trial.
2. Set a risk-based frequency for ATR per study with a documented rationale based on protocol phase, complexity, endpoints, SDV/tSDV strategy, site mix, etc.
3. Identify assigned staff and confirm their qualifications to perform ATR. Also confirm that resourcing is adequate.
4. Finalize training needs, perform training, document training, and identify any compliance expectations.
5. Confirm reviewer roles and access to data sources in scope and mitigate any potential conflicts of interest; consider independent or secondary review, as needed. Determine roles that will provide output to the reviewers as well.
6. Confirm that visualizations and/or audit trail extracts cannot unblind any reviewer roles that are blinded.
7. Consider requirements for user access controls such as read-only access for tools and dashboards.
8. Determine if any personal data from trial participants may be available in the audit trails, and how it can be redacted or removed from outputs to ensure data privacy.
9. Ensure applicable templates meet expectations; adjust as needed
10. Ensure ATR tools support interrogation, trend detection, and traceability of the audit trail risks identified for the trial through validation and Sponsor UAT, if desired.
11. Align and finalize expectations for escalations and quality management. In accordance with ICH E6(R3) §3.6.6, sponsors must be able to identify, evaluate, escalate, and address quality issues in a timely, documented manner, which has direct implications for how audit trail review outputs are generated, reviewed, and retained.

If using the Sponsor's ATR process

1. After the ATR plan is finalized, the Sponsor configures reports/dashboards/KRIs as applicable and grants CRO reviewers' access, after relevant documented training.
2. When using the Sponsor process, plan for the training and change-management load on the CRO team, as well as the training burden on Sponsor roles responsible for training.

If using the CRO's ATR process

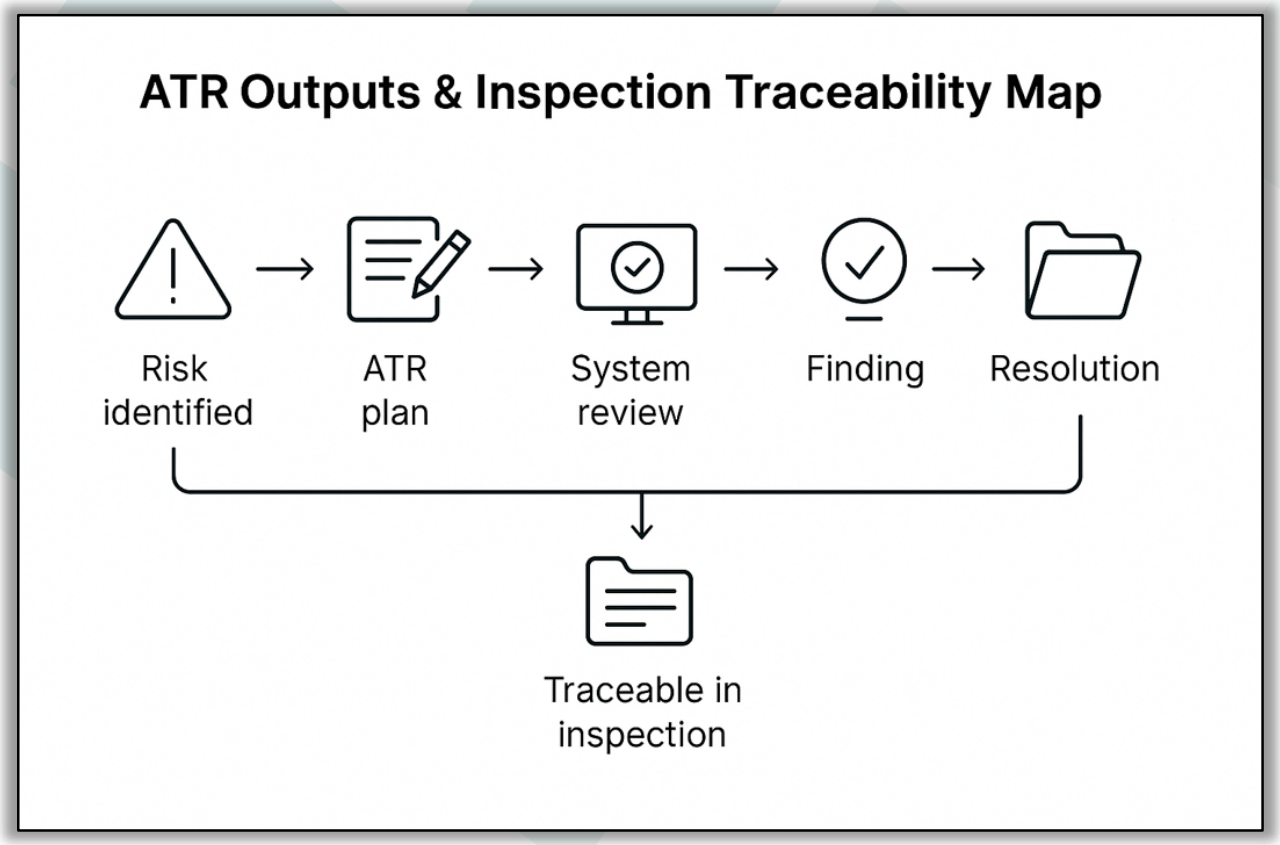
1. The ATR plan is created in the agreed template by the CRO, and the Sponsor reviews and approves the plan and confirms coverage of all systems/data sources in scope.
2. Finalize the process for Sponsor Oversight and how it will be maintained. Define the key touch points and agree how much input into CRO documentation by the Sponsor is required (e.g. will it be necessary for a separate KOM for the ATR process, or will it be included in RBQM setup? Will the Sponsor review each iteration of ATR or only the final report? Can the CRO sign off on ATR documentation, or does sponsor need to approve? etc.)

Checklist: Stage 3 - Operationalization

- ✓ 'ATR Plan' approved; reports and dashboards implemented
- ✓ Training performed and documented
- ✓ Expectations for quality management and escalations finalized

Stage 4 — Execution and adaptation

During this stage, risk-proportionate ATR/metadata review (preferably with adaptive frequency informed by KRIs and review findings), will be performed. Escalation paths and decision trees for potential misconduct, data anomalies, or process and configuration issues should be in place. In line with the sponsor accountability principles established earlier, oversight of ATR execution should be demonstrable throughout trial conduct.



Core activities and controls, regardless of process

1. Execute ATR per plan, document findings, corrective and preventive actions, and verification of resolution.
2. Ensure timely eTMF filing of plans, reports and metadata so inspections can trace risk → review → finding → action → closure.
3. Perform sample-based QC of reviews and underlying reports to verify accuracy, if desired.
4. Adjust review frequency for specific triggers (e.g., high-risk findings, protocol amendments, onboarding of inexperienced sites); maintain real-time oversight via reports and/or dashboards.
5. Ensure continued compliance with the blinding and access controls defined during study setup, including newly added data sources.
6. Ensure contingency plans (for example, temporary inhouse review or backup CRO) and maintain secure access and any decision logs related to the ATR process.

If using the Sponsor's ATR process

1. Finalize frequency for report/dashboard reviews and trend reviews. Set clear expectations for the meetings with the CROs and determine which roles from the CRO and Sponsor are relevant to the meeting.
2. Sponsor initiates escalation and re-risking when applicable KRIs are surpassed

If using the CRO's ATR process

1. CRO leads execution and proposes frequency adjustments; Sponsor verifies logic, challenges thresholds, and ensures findings integrate with RBQM.
2. Verify that ATR execution aligns with the agreed methodology through review of reports, trends, and sponsor oversight activities.

Checklist: Stage 4 - Execution and Adaptation

- ✓ **Reviews performed per plan; findings/action items closed; documentation filed**
- ✓ **KRIs/KPIs monitored; frequency adapted to risk; escalations timely**
- ✓ **Independent sampling/QC performed as needed; blinding remains intact**
- ✓ **Contingency plan options ready**

Stage 5 — Closure and learning

In the closeout stage, ensure all ATR findings/issues are resolved and documented, all documentation is filed, and learnings harvested. This ensures process improvement and informs outsourcing strategies for future trials.

Core activities and controls, regardless of process

1. Close all actions arising from ATR; reconcile reports and logs to ensure nothing is open.Consider producing a summary of overall audit trail findings for the trial, particularly if documentation is maintained in multiple documents.
2. Ensure retention and filing of ATR documentation and audit trails, as applicable. Audit trails should be human-readable per section 6.2 of the EMA Guideline on computerised systems and electronic data in clinical trials.
3. Feed lessons into SOPs/WIs, training, and a library of standardized risk-based checks, as appropriate.
4. Explore automation/AI with human oversight to enhance anomaly detection, as the organization gains maturity with the process. Any automation or AI model used should be fit for purpose and inspection ready. Version 7.0 (Dec. 2025) of the MHRA GCP inspection dossier template asks the following questions in relation to artificial intelligence and machine learning for inspections within the UK:
   a. Names of the systems or tools used
   b. What these systems/tools are used for
   c. How long these systems have been used for
   d. Whether these systems/tools were developed by your own organization or purchased from service providers
   e. How systems are trained and/or validated by your organization
   f. The documented processes that are in place relating to the management of systems/tools including (re)validation, user training and operational use (including human oversight

Having this type of information on hand and easily accessible for any inspection is recommended. Ensure AI-enabled capabilities (yours or the CROs) continually align with emerging regulatory expectations including the FDA Draft Guidance on Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products (2025), the EMA Reflection Paper on AI in the Medicinal Product Lifecycle (2024), FDA/EMA Guiding Principles of Good AI Practice (2025), and applicable principles within ICH E6(R3) Good Clinical Practice.

If using the Sponsor's ATR process

1. Sponsor compiles any end-of-study summary and updates internal libraries, SOPs, and templates based on cross-program trends (portfolio-level consistency may be easier to ensure using the Sponsor's process, as stated previously).

If using the CRO's ATR process

1. Request a lessons-learned meeting (trends, KRIs hit, mitigations) and align on how outputs from the current trial will influence the process in future trials.
2. Check eTMF completeness against the agreed filing plan.

Checklist: Stage 5 - Closure and Learning

- ✓ **All ATR issues closed; final reports and evidence filed**
- ✓ **End-of-study summary completed; lessons learned integrated into process**
- ✓ **Reusable risk-based checks refined for future studies/CROs**

Conclusion

Outsourcing Audit Trail Review is becoming a practical necessity for many clinical trial teams, but it's not a one-size-fits-all decision. As this guide shows, choosing whether to use the Sponsor's or the CRO's ATR process isn't just about preference, it's about understanding your systems, your level of maturity, and what each study truly needs.

Across every stage of the trial, one message stays the same: even when ATR is outsourced, the Sponsor still carries the responsibility for data integrity. That means keeping enough in-house knowledge to interpret audit trail outputs, ask the right questions, and ensure the work being done genuinely supports patient safety and data quality—not just compliance.

CRO-led ATR can offer useful efficiencies, advanced tools, and scalability, while Sponsor-led ATR provides consistency and strong control across a portfolio of trials. Neither choice is "better" on its own—the right decision depends on risks, resources, and the systems involved. What matters most is clear communication, agreed-upon expectations, and a shared commitment to risk-based thinking.

If organizations stay grounded in those principles, ATR outsourcing becomes far less about navigating complexity and far more about enabling smarter, more reliable trial execution. With the right structure and oversight, Sponsors and CROs can work together to build an ATR approach that is efficient, transparent, and fully inspection-ready.

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