association for **clinical data management**

Audit Trail Review: An Exploration of Risk Scenarios and Use Cases

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Building on the insights shared in the White Paper 'Getting started with Audit Trail Review in Clinical Trial Data: An Essential Guide', the ACDM ATR Data Management Expert Group (DMEG) has compiled a comprehensive list of risk case scenarios and use cases where audit trail review (ATR) can be used to help identify potential issues.

The ATR DMEG recommends integrating ATR into existing processes, particularly during the risk assessment phase at study start-up. By implementing prospective ATR and conducting regular reviews of audit trail metadata, organizations can proactively address challenges related to data integrity, quality, and processes.

Each root cause for a scenario has a priority score, KRI and visualization advice, as well as potential corrective and preventive actions and considerations to help users connect the dots between finding anomalies and solving them.

The information presented draws upon the combined understanding and knowledge of the Association of Clinical Data Management (ACDM) Audit Trail Review (ATR) Data Management Expert Group (DMEG) on this topic and is provided as an aid to understanding the risk scenarios and use cases related to audit trail review in clinical research. The information presented is the opinion of the authors and does not necessarily reflect the position of individual companies. Readers should assess the content considering their own knowledge, organisational needs and experience as well as interpretation of relevant guidance and regulations.

A living document for evolving needs

The risk scenarios are a living document, and will be updated over time as new insights, use cases, and risk scenarios emerge. We encourage readers to contribute their experiences and feedback to enhance its relevance and utility. For comments, questions, or suggestions for additional use cases and risk scenarios, please reach out to Jennifer Logue Nielsen, ATR DMEG Chair, at jnni@lundbeck.com.

ATR Risk Scenario Column Descriptions

Reference / Source	Risk Area	Risk Scenario/Use Case (observed anomaly)	ATR	eCOA	ePRO	EDC	Possible Root Cause Issue(s)	Impact (1-25)[1]	Likelihood (1-10)	Sensitivity [2]	Address-ability[3]	Priority Score	KRI & visualization advice	Corrective actions and follow-up	Preventive actions and/or additional considerations
Defines the origin of the risk case scenario. e.g. ACDM members, CluePoints, Sponsor Findings, SCDM ATR Paper, etc.	Risk Area, for example: data quality, regulatory, site performance, patient safety, protocol compliance, regulatory compliance.	Description of the finding from the ATR which could be a risk to the integrity of the data.	Location of the source data used to identify the risk.				Defines the potential cause of the risk scenario finding. Each possible root cause is detailed in a separate cell and Is allocated Impact, Likelihood, Sensitivity, Addressability and Prioity Scores.	Impact = relative severity of impact to patient safety and/ or reliability of trial results.	Likelihood = how likely it is that this is the root cause of the anomaly.	% Sensitivity => the likelihood that the given root cause would be manifested by the observed anomaly.	% Addressable => Likelihood that the given root cause can be effectively confirmed and/or remediated.	Calculated by Multiplying the Impact, Likelihood, Sensitivity and Addressability scores together.	Describes what is expected and how to define/identify when risk criteria has been met. Includes tips for how to visualize data.	Defines possible actions to be taken if scenario occurs.	Considerations around preventive actions or additional information and advice on the risk scenario/use case.

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eCF-SCDM ATR Paper: Appendix 3, 3.4	Data Quality, Protocol Compliance	Average duration to conduct eCOAs or ePROs is very unusual (short or long) at a site. Example: Low confidence in the accuracy/robustness of site entered data. Example: eCOA data captured at one site was captured in a matter of minutes versus the typical 20-minute duration of sites within the wider trial.	Y	Y	Y	N	Site not using eCOA device to conduct assessment directly, but transcribing from a separate source document.	6	2	50%	60%	3.6	KRI: Duration of eCOA/ePRO assessment. Threshold example: variability that is more or less than two standard deviations from the overall mean. Or, determine the risk level by comparing the assessment duration in minutes to the mean for the site/trial.	More visualization, more review of data via central monitoring or CRA, Site Inspection, or retraining as needed.	1. Seek advice from license holder about how long the assessment is expected to take. They may be able to advise on a KRI. For example: CSSRS: 5 min; Source: University of pennsylvania, https://www.med.upenn.edu/cbti/assets/user-content/documents/Columbia-Suicide%20Severity%20Rating%20Scales%20(C-SSRS).pdf SF-36: 7-8 min; https://heartbeat-med.com/resources/short-form-36-sf-36/ 2. Consider the COA/PRO length and frequency of completion. e.g. a one question 'impression of change' assessment could be completed in seconds. A 5 question scale completed weekly could be completed in less than 30 seconds 3. Consider creating internal metrics for durations of assessments based on previous trials. 4. BYOD--might take longer if people get distracted. Know the log-off rules and times. 5. Short responses may be easier to detect. 6. Considerations related to pediatric trials-- the parent/caregiver completing the assessment should be consistent over time.
							Site fabricating participant data	25	1	90%	60%	13.5	Same as above	Involve QA, in addition to the above	If the root cause is determined to be fraud, this is a significant compliance and data integrity concern. Consider consulting QA around documentation and resolution.
							Site staff/raters not properly trained/skilled in conducting assessments	8	3	70%	60%	10.1	Same as above	Ensure any re-training, if required.	Considerations for using a potential wrong version of an assessment
							Site is transcribing into a paper version from the internet	7	3	50%	60%	6.3	Same as above	Ensure any re-training, if required.	Continue to monitor duration of entry
							Participants improperly trained on ePRO completion	7	4	70%	80%	15.7	Same as above	Ensure any re-training, if required.	Continue to monitor duration of entry
							Non-Issue - just part of natural variability in site/rater behavior or user got distracted	1	4	50%	0%	0.0	Same as above	None	

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eCF-SCDM ATR Paper: Appendix 3, 3.4	Data Quality, Protocol Compliance	Unusual variability (high or low) of assessment durations for eCOAs and ePROs within/between participants at the site	Y	Y	Y	N	Site staff/raters not properly trained/skilled in conducting assessments	8	3	70%	60%	10.1	KRI: Time to complete Clinical Outcome Assessments or Patient Reported Outcomes. Threshold example: Consider closer inspection of assessments that have a completion time of 2 or more standard deviations away from the mean completion time.	More visualization, more review of data via central monitoring or CRA, Site Inspection, or retraining as needed.	Preventative actions and additional considerations are similar to the previous risk scenario.
							Some of the assessments fabricated	20	1	70%	60%	8.4	Same as above	Involve QA if this is confirmed.	If the root cause is determined to be fraud, this is a significant compliance and data integrity concern. Consider consulting QA around documentation and resolution.
							For some assessments, the site is not using eCOA/ tablet device to conduct assessment directly, but transcribing from separate source document.	6	2	50%	60%	3.6	Same as above	Ensure any re-training, if required.	In general, sites should be discouraged from creating paper backups for eSource solutions like eCOA--it could affect data quality or compliance, and may also be against licensing requirements for a particular tool. Web-based back-up systems should be used instead.
							Participants improperly trained by site on ePRO completion	7	4	70%	80%	15.7	Same as above	Ensure any re-training, if required.	Continue to monitor variability of duration
							Non-Issue - just part of natural variability or user was distracted	1	4	50%	10%	0.2	Same as above	None	Continue to monitor duration of entry

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Sponsor FindingA74	Data Quality, Site Performance	High data variability due to ClinRO rater change across visits.	Y	Y	N	N	Inadequate training at site on the need for rater consistency across visits. Or too many raters at the site.	9	5	80%	50%	18.0	Determine variability by looking at the standard deviation around the mean ClinRO score, if looking at one measure. Consider other methods like the coefficient of variation if looking at mutiple measures.	Follow up via monitor, consider re-training or decreasing the number of raters	Higher variability in general means higher risks to data integrity.
							Non-issue: Rater has left the site, or potential for high inter-participant variability	3	5	60%	30%	2.7	Same as above.	None	More subjective assessments (for example, schizophrenia symptoms, tend to have higher variability in general.

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eCF-SCDM ATR Paper: Appendix 3, 3.2, 3.3A81	Data Quality, Protocol Compliance	High rate of eCOA assessments being conducted at unexpected times:	Y	Y	N	N	Site not using eCOA/ tablet device to conduct assessment directly, but transcribing from a separate source document (at off-hours).	6	2	50%	60%	3.6	KRI: Assessments done outside of normal business hours, local time. Threshold example: Could be a percentage of the assessments at that site. Alternatively, flag any COAs performed outside the timeframe of 06:00 - 21:00, or whatever timeframe is relevant for the trial.	More visualization, more review of data via central monitoring or CRA, Site Inspection	This scenario applies to assessments done as eSource and performed on a device physically located at the site, such as a tablet or phone. The scenarios are less feasible if assessments completed on a web-based back-up.
							Site is fabricating eCOA data	25	1	90%	60%	13.5	Same as above	Involve QA if this is confirmed.	If the root cause is determined to be fraud, this is a significant compliance and data integrity concern. Consider consulting QA around documentation and resolution.
							Site is meeting with participants outside of normal business hours.	3	2	60%	50%	1.8	Same as above	Would need to be investigated further, but could be a non-issue	
							EDC visit dates reported incorrectly	5	3	40%	90%	5.4	Same as above	Issue any needed queries in EDC to resolve	
							Non-Issue - internet connectivity or device issues, site needed to record data elsewhere first	1	5	60%	20%	0.6	Same as above	Repeated issues relating to connectivity should be investigated. You would also not expect to continue seeing assessments at odd hours once any connectivity issues are resolved.	In general, sites should be discouraged from creating paper backups for eSouce solutions like eCOA--it could affect data quality or compliance, and may also be against licensing requirements for a particular tool. Web-based back-up systems should be used instead.
							Non-issue - Participant visits span multiple days, site location, normal practice for the site, clinical trial with overnight stays	1	5	80%	0%	0.0	Same as above	None	Take into account the overall trial design when visualizing this use case--what might be normal practice in a Phase 1 trial with overnight stays could be quite different than normal practice in a Phase 3 trial.

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Various	Data Quality, Protocol Compliance	Unusually high correlation in daily ePRO entry times between participants at a site (entry times in close proximity each day)	Y	N	Y	Y	Site fabricating ePRO data (If ePRO data is entered into the eCRF)	25	1	90%	60%	13.5	KRI: Consistency of ePRO entries. Look at the frequency and distribution of entry times. Significant deviations from the expected distribution should be investigated.	More visualization, more review of data via central monitoring or CRA, Site Inspection. If confirmed, involve QA.	Consider the phase 1 unit scheduling--for example, participants are always assessed in a particular order e.g. participant 1 always 1st. If the root cause is determined to be fraud, this is a significant compliance and data integrity concern. Consider consulting QA around documentation and resolution.
							Device issue --- the device allows the participant to enter multiple days' worth of data at one time instead of enter data daily, for example.	5	2	70%	30%	2.1	Same as above	May not be adjustable.	Seen in real-life
							Site has passwords to participants ePRO device	23	1	90%	60%	12.4	Same as above	Involve QA if this is confirmed and implement any corrective and preventative actions	Seen in real-life
							Site conducting group sessions with participants each day to guide their ePRO entries	4	1	80%	60%	1.9	Same as above	More investigation required.	Could be an indication that data collection is confusing or otherwise non-optimal. More likely with diary data.
							Site directing participants to complete ePROs at specific time each day, though not required by protocol	3	2	80%	70%	3.4	Same as above	More investigation required	Retrain site if required, but may be a non-issue depending on the trial.
							Non-Issue - just part of natural variability in participant behavior, or the participants must enter data at certain times due to protocol requirement, or participant reacting to app reminders in ePRO device.	1	6	50%	0%	0.0	Not applicable	None	Some trials may send automated reminders to participants to enter ePRO or diary data, or only allow them to enter data at certain times. In which case, high correlation would be expected.

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Sponsor Finding, eCF-SCDM ATR Paper: Appendix 3, 3.6	Data Quality, Site Performance, Protocol Compliance	Missing eCOAs or ePROs for visits that have been performed per EDC, for example.	Y	Y	Y	N	Site error - assessments inactivated in error by the site or not performed in error	8	4	70%	60%	13.4	In general, you would not expect eCOA or ePRO assessments to be missing if there is EDC data for a visit. The percentage of completed ePROs/ eCOAs should be above a certain threshold, such as 80% or 90% , depending on trial requirements.	If appropriate, reactivate missing assessments and complete. Consider documentation if missing assessments will not be completed. Consider any re-training needs the site may have.	Regular monitoring of eCOA and ePRO data by onsite monitors, central monitors, or data management and the site may be the most effective mitigation.
							Participant non-compliance or missed visits	8	3	70%	50%	8.4	Same as above	Continue monitoring that overall compliance meets the expected threshold.	Consider if automated reminders to the participant on the device could be useful. Consider site follow-up with participants that show a certain level of non-compliance.
							System issues: data synchronization issues or platform/ device issues	6	3	60%	70%	7.6	Same as above	Ensure any system issues are resolved.	Consider trending on technical issues reported to the eCOA/ePRO vendor if a certain number of technical issues are reported.

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Sponsor Finding	Data Quality, Protocol Compliance, Regulatory	ePRO/ Diary Data collected after the last protocol defined visit/assessment (or before the signature date of the informed consent).	Y	N	Y	Y	ePRO Diary not inactivated by site, so the participant kept filling out the diary, even though they had completed the trial.	8	7	90%	90%	45.4	Any data that is entered into the eDiary after the participant's date of last visit or assessment should be inspected. Data may come from mutiple systems.	Retrain sites on inactivation procedure via monitor	Data collected after the last protocol defined visit/assessment would typically be deleted as it is not in the protocol defined timeframe
							Site set-up the participant in ePRO Diary system, then the user downloaded the app and got started on diary entries before the informed consent was signed.	8	3	90%	90%	19.4	Any data that is entered into the eDiary before the participant's date of informed consent should be inspected. Data may come from mutiple systems.	Retrain sites on activation procedure via monitor	Data collected before the informed consent is signed would typically be deleted as it is not in the protocol defined timeframe.

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eCF-SCDM ATR Paper: Appendix 3, 1.2	Data Quality, Site Performance, Regulatory	System access (entry/ edit rights) granted without sufficient training	Y	Y	Y	Y	Process issues related to system access, for example, inadequate access control or misconfigured user roles	6	2	90%	90%	9.7	KRI: Unauthorized system access events. Repeated incidents over a certain threshold, for example, x/year or x/month, should trigger additional investigation. May be found during periodic review of accesses or via review of the audit trail.	Update any incorrect accesses immediately. Determine the impact of insufficient training on the data entered or edited by the end user. and act accordingly.	Some assessments might need particular training or experience (e.g. Columbia Suicide Severity Rating Scale [C-SSRS]). Sponsors should ensure the COA provider has a robust process around training, access, and periodic review (if not paper). Consider the frequency of review if incidents increase.
							User error: Wrong access requested	8	5	90%	100%	36.0	Same as above	Update incorrect accesses immediately. Determine the impact of the incorrect access on the data, if any, and act accordingly.	Depending on the system, the access requester could be the end user themself, or a site monitor, for example. Investigate the access request process and retrain or update access request process as needed.
							User error: Wrong access assigned by system administrator	8	2	90%	100%	14.4	Same as above	Update incorrect accesses immediately. Determine the impact of the incorrect access on the data, and act accordingly.	Consider if preventative actions are needed to stop recurrence. May indicate a need for process improvement, for example, adding a QC step when accesses are assigned.

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eCF-SCDM ATR Paper: Appendix 3, 1.1	Data Quality, Site Performance, Regulatory, Protocol Compliance	Data entry/updates performed by unauthorized end user	Y	Y	Y	Y	Process issues related to system access, for example, inadequate access control or misconfigured user roles	12	2	90%	90%	19.4	KRI: Unauthorized system access events. Repeated incidents over a certain threshold, for example, x/year or x/month, should trigger additional investigation. May be found during periodic review of accesses, via review of the audit trail, or via monitoring	Update any incorrect accesses immediately. Determine the impact of the unauthorized access on the data entered or edited by the end user. and act accordingly.	Can indicate communication issues around revocation of access. For example, a site user has left site, but the site not communicated the team change to the Monitor/Sponsor. Consider the frequency of review if incidents increase.
							User error: Wrong access requested, for example, ATR identified a site user had updated participant data at another site in the eCRF. Or, data was detected as being entered by a site user rather than a participant on a PRO	12	5	90%	100%	54.0	Same as above	Update incorrect accesses immediately. Determine the impact of the incorrect access on the data, and act accordingly.	Depending on the system, the access requester could be the end user themself, or a site monitor, for example. Investigate the access request process and retrain or update access request process as needed.
							User error: Wrong access assigned by system administrator	12	3	90%	100%	32.4	Same as above	Update incorrect accesses immediately. Determine the impact of the incorrect access on the data, and act accordingly.	Consider if preventative actions are needed to stop recurrence. May indicate a need for process improvement, for example, adding a QC step when accesses are assigned.

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eCF-SCDM ATR Paper: Appendix 3, 2.2, 2.4	Data Quality, Patient Safety, Site Performance	High rate of data updates, especially for critical data	Y	Y	Y	Y	Site manipulating baseline data (e.g., I/E criteria, endpoint measurements) - to ensure participant eligibility	25	2	90%	60%	27.0	KRI: Frequency of updates to critical data. Consider further investigation if a critical datapoint that has 2 or more changes without query, or non-critical datapoints with 4 or more changes without query. In general, data updates without query are not expected behavior.	Follow-up with monitor, consult with QA and/or perform a site audit.	Monitoring updates to critical data helps ensure the data integrity of related endpoints.
							Site is sloppy in eCRF entry process (e.g., too busy/ rushed, inattentive, etc.)	7	4	50%	50%	7.0	Same as above	Follow-up with monitor, ensure SDV is occurring as planned, and perhaps increase SDV for the site, if 100% SDV is not being performed.	Could also indicate poor form/CRF design and the need for potential update of the data collection tool.
							Site staff are not effectively trained on EDC tool and/ or eCRF entry requirements	5	3	70%	70%	7.4	Same as above	Re-train as needed, or update training on EDC tool. Update eCRF guidelines, if appropriate.	Poor eCRF completion guidelines may impact the rate of data updates.
							Site source documentation is poorly managed, resulting in high rate of discrepant or incomplete entries	7	3	70%	50%	7.4	Same as above	Follow-up via monitor, the expectation is that the site should have suitable source documentation before the trial begins	As source documentation is crucial for ensuring the reliability of clinical trial data, any deficiencies in source documentation may require a Corrective Action Plan , as well as further training and guidance.
							Non-issue: site error or confusion, or a datapoint that is typically updated in a trial (for example, the ongoing field for an AE being removed when the AE end).	1	3	50%	0%	0.0	Same as above	None	Consider if changes to some datapoints should be excluded from counts/ review due to the fact they are updated frequently.

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Sponsor Finding	Patient Safety, Data Quality	Use case: ensuring that key safety and efficacy variables that are updated over the course of the trial, for example, the question I wish I was dead from yes to no, are verified and properly documented/reponse mismatches between similar PRO and COA questions	Y	Y	Y	Y	Data entry error by site staff	12	3	90%	90%	29.2	This is a use case for ATR. Consider visualizing response changes for key safety and efficacy variables in the trial, such as suicide ideation questions, to more easily identify changes and anomalies. You could also visualize by looking at the mean number of changes to key safety and efficacy variables by site and comparing them.	Ensure unusual responses are queried and/or verified per normal trial processes.	Also consider if any differences between patient reported responses and clinician reported responses should be visualized and/or inspected, if a possibility. Also consider SDV strategy for key safety variables when performing the risk-assessment for the trial during the start-up phase.
							Mismatch between scores for similar questions in PRO and COA, for example, questions around suicidal thoughts	15	3	90%	50%	20.3	Same as above	Potential mismatches in related questions answered by the participant and Investigator should be investigated and addressed.	Consider how mismatches will be documted in the trial documentation. Consider future data collection strategies and alignment of data.
							Non-issue: data updated properly	2	4	80%	0%	0.0	Same as above	If the update is correct and verified against the source, no further action is required.	None

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eCF-SCDM ATR Paper: Appendix 3, 2.1	Data Quality, Site Performance	High rate of deleted (or de-activated) data records	Y	Y	Y	Y	System malfunction - auto-deleting records	20	2	90%	80%	28.8	KRI: Deletions across sites. Threshold: look at outliers to the mean and/or investigate peaks in the deletion timeline. Impact will depend on the criticality of the data.	Investigate and resolve any system issues, and ensure re-entry and verification as appropriate	Ensure preventative actions to prevent recurrence, if required.
							Valid data improperly deleted by end user	8	4	70%	70%	15.7	Same as above	Ensure that any data deleted is re-entered via monitoring/source data verification. Consider additional training for end user, if required.	Consider any retraining needs
							Non-issue: Data initially entered (by site) under wrong participant ID, required deletion (normal activity)	2	4	50%	0%	0.0	Same as above	If the deleted records were due to data entry error, no action required.	None

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eCF-SCDM ATR Paper: Appendix 3, 2.3	Data Quality, Site Performance	Unexpected updates to critical data following a key milestone (e.g., interim freeze/lock)	Y	Y	Y	Y	Data fabrication/ manipulation	25	1	90%	80%	18.0	KRI: Post-(interim) lock data updates.	Ensure that any updated critical data has a rationale and is verifiable in the source via monitoring and freeze/lock as corrective action. If fabrication or manipulation is confirmed, consult QA.	In general, updates to critical data after milestones like interim lock or final database lock would not be expected and data updates should be thoroughly documented, including rationale for change.
							System malfunction or other system issue	15	3	80%	80%	28.8	Same as above	Investigate and resolve any system issues, and ensure re-entry and verification as appropriate	Ensure preventative actions to prevent recurrence, if required. If due to system limitations, consider mitigations to prevent update of critical data after key milestones like interim lock.
							Process issues: Data not frozen or locked before interim DBL, poor monitoring	12	6	70%	80%	40.3	Same as above	Ensure that processes are in place to freeze/ lock data at key milestones so critical data cannot be updated and retrain as appropriate.	Ensure that any updated critical data has a rationale and is verifiable in the source via monitoring.

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Sponsor Finding,eCF-SCDM ATR Paper: Appendix 3, 2.5	Data Quality, Site Performance	Datapoint amended long time (example: 6 months) after initial entry	Y	Y	Y	Y	Site performance - long response time to queries	8	3	100%	70%	16.8	Consider determining the rate of updates based your on definition of late updates, then develop applicable thresholds.	Follow-up via monitoring if cycle times for query response are too high.	Consider the criticality of the data when visualizing or looking into changed datapoints
							Monitoring Performance: long delay between data entry and source data verification.	8	3	90%	70%	15.1	Same as above	Ensure monitoring is up to date and continue to check the audit trail for any late updates to data.	Consider if additional monitoring visits may be needed.
							Sytem Issues or incorrect access causing entry delays	8	2	90%	90%	13.0	Same as above	Ensure any access issues or system issues are resolved, and continue to check the audit trail for any late updates to data.	You would expect to see a decrease in late updates to data if the root cause at a site was related to system or access issues.
							Non-issue: Sponsor review or other review resulted in a change, or data update was correct (though untimely), protocol ammendment, eCRF update	1	2	90%	0%	0.0	Same as above	None	Consider follow-up via monitor or potential retraining if late updates to data are over an acceptable threshold at a site, even if the updates are correct.

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Sponsor Finding	Data Quality	High volume (by time) of EDC Data entry - overall and by eCRF form/domain	Y	N	N	Y	Data fabrication/ manipulation	25	1	90%	70%	15.8	KRI: EDC Data Entry Volume. Can be visualized by timeline where a user could look at data entry overall and filtering by form or visit.	If confirmed, consult QA	If the root cause is determined to be fraud, this is a significant compliance and data integrity concern. Consider consulting QA around documentation and resolution.
							Site Performance: Rushed entry, shared passwords, etc.	10	3	80%	60%	14.4	Same as above	Follow-up via monitor. Consider if a site audit may be needed.	Continue to monitor the volume over time.
							Normal behavior - milestones like interim lock or final database lock approaching, or the site has additional staff	1	7	80%	0%	0.0	Same as above	None	You will normally see peaks of data entry activity in most trials. Consider looking into the reasons behind unexpected peaks of activity.

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Sponsor Finding,eCF-SCDM ATR Paper: Appendix 3, 3.2	Data Quality	Entry of participant eCRF data for a visit prior to actual visit date (other than visit planning information)	Y	N	N	Y	Data fabrication/ manipulation	25	1	90%	80%	18.0	KRI: CRFs with future dates. Should be zero.	Follow-up via monitor or consult QA (consider site audit). Consider any retraining needs.	Consider automated fallout if any data entry times are before the actual visit date.
							Planned visit date entered ahead of actual visit date	2	3	90%	50%	2.7	Same as above	Might be OK, or consider re-training if the site if not allowed.	In general, you would not expect to see any data, even a visit date, entered in advance of the visit date as this could change.
							Non-issue: Data entry error, data entered for incorrect participant	1	6	90%	90%	4.9	Same as above	None	Review of the audit trail will show any visits entered before the actual date occurred.

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eCF-SCDM ATR Paper: Appendix 3, 2.3	Data Quality, Site Performance	High rate of eCRF forms being unlocked (or unfrozen)	Y	N	N	Y	Data fabrication/ manipulation	25	1	90%	80%	18.0	KRI: eCRF unfreeze/ unlock frequency. For example, >15% of forms for a participant or site have been unlocked or unfrozen.	Follow-up via monitor or consult QA	Unfreezing or unlocking does not necessarily mean that data has been updated. If this risk scenario is triggered, consider what data was actually updated.
							Process issues: Poor oversight by site, forms being frozen or locked too early by the monitor/DM	8	5	70%	80%	22.4	Same as above	Determine root cause amd adjust process as needed to resolve issue(s)--for example, do not freeze or lock until all SDV and queries, including reconciliation for lab data, is complete.	Inefficiencies in the data review and locking process should be resolved as they have an impact on the overall workload of the monitor/DM.
							Non-issue: Forms unfrozen and/or unlocked in error	8	4	0.9	100%	28.8	Same as above	Freeze and lock forms as required and consider any re-training required.	Continue to monitor

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eCF-SCDM ATR Paper: Appendix 3, 1.3	Patient Safety, Site Performance	Long cycle time from participant visits until data entered into EDC	Y	N	N	Y	Site is delayed in EDC entry (under-staffed, high workload inattentive, etc.)	4	4	90%	60%	8.6	KRI: eCRF data entry timeliness. Data entry turn-around times vary by organization, these are usually 3-5 days from the visit date. The KRI could be triggered if a certain percentage of data entry at the site takes 10 business days or more. Alternatively, the mean across sites can be compared.	Ask monitors to follow-up with the site and continue to monitor site performance.	As data-entry timeliness impacts downstream data cleaning and data review, delays should be addressed to minimize any impact on overall study timelines.
							System malfunction or other system issue	8	2	80%	80%	10.2	Same as above	Investigate and resolve any system issues, and ensure entry and verification as appropriate.	Ensure any preventative actions to prevent recurrence, if required.
							Poor CRF design or overly complex protocols	8	2	70%	70%	7.8	Same as above	Make any needed CRF and/or protocol updates, then ensure entry and verification as appropriate.	Seeing long cycle times on a particular CRF as opposed to across the board could indicate a CRF design issue.
							Poor communication to sites around data entry timelines	8	2	70%	90%	10.1	Same as above	Ensure data entry timelines are communicated to sites, and the CRO, if applicable, and documented in trial documentation appropriately	Data entry timelines around any interim lock or final lock should be communicated in advance.

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eCF-SCDM ATR Paper: Appendix 3, 1.3	Site Performance	Long cycle time for sites to answer EDC queries	Y	N	N	Y	Site is delayed in EDC query response (under-staffed, high workload, inattentive, etc.)	4	4	90%	60%	8.6	KRI: Query response timeliness. Flag sites if the average response time is more than 10 days (or whatever your requirement may be.)	Follow-up via monitor, make sure turnaround time expectations are clear via the eCRF completion guidelines, trial newsletters, etc.	KRI could be dependent on visit frequency, e.g. Phase 4 study with visits a year apart would have a longer average response time for this KRI.
							Site doesn't understand queries (poorly written queries, unclear, incorrectly programmed)	8	3	80%	80%	15.4	Same as above	Correct any confusing wording or incorrectly programmed queries, and continue to monitor cycle times.	Continue to monitor cycle times after updates are made to any queries that the site did not understand, and check for improvement in cycle times.
							Poor communication to sites around query response timelines	8	3	70%	90%	15.1	Same as above	Ensure data entry timelines are communicated to sites, and the CRO, if applicable, and documented in trial documentation appropriately	Query response timelines around any interim lock or final lock should be communicated well in advance.

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CluePoints	Data Quality, Site Performance	High rate of EDC auto-queries generated at site	Y	N	N	Y	Site source documentation is poorly managed, resulting in high rate of discrepant or incomplete entries, or Site is sloppy in eCRF entry process (e.g., too busy/rushed, inattentive, etc.)	7	2	70%	50%	4.9	KRI: Query frequency. Threshold: Consider further inspection of data at sites more than 2 standard deviations from the mean number of queries per site. Consider the criticality and impact of the data on the forms with high query rates when deciding what to monitor.	Ensure source documentation is appropriate and re-train as appropriate.	After the root cause is determined and updated, continue to monitor query rate and ensure that it declines over time.
							eCRF completion guidelines not appropriate to the data being collected	4	3	70%	90%	7.6	Same as above	Update eCRF completion guidelines as needed	
							Poor CRF design	8	3	70%	70%	11.8	Same as above	Consider eCRF updates to improve design and reduce autoqueries	Consider if any updates are needed to your CRF library/ standards
							Queries are incorrectly programmed or not thoroughly tested.	4	4	70%	70%	7.8	Same as above	Correct the query programming	Consider if any updates are needed to your edit check library, if applicable.
							Site staff are not effectively trained on EDC tool and/or eCRF entry requirements	4	4	50%	70%	5.6	Same as above	Ensure (re)training as needed	Ensure any retraining is documented.
							Data fabrication/ manipulation	25	1	90%	50%	11.3	Same as above	Follow-up via monitor or consult QA (consider site audit)	

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ACDM	Patient Safety, Data Quality, Protocol Compliance, Site Performance, Regulatory	Long cycle time from AE start date (or next participant visit date) to AE entry date	Y	N	N	Y	Site is delayed in EDC entry (too busy, under-staffed, inattentive, etc.)	12	5	90%	70%	37.8	KRIs: AE entry timeliness. Different thresholds will be needed based on AE/ SAE/AESI and the visit schedule of the trial	Monitor to remind site of data entry expectations, determine if site audit is necessary	Continue to monitor cycle times for AE entry and adjust strategy as required.
							Site not aware of AE's due to participant non-reporting	12	5	50%	60%	18.0	Same as above	Ensure site staff educate participants with clear instructions on the importance of AE reporting in relation to the safety and efficacy of the treatment.	Continue to monitor cycle times. Consider if more follow-up calls with participants from the site may be needed to check overall participant status, including any AEs.
ACDM, eCF-SCDM ATR Paper: Appendix 3, 1.3	Protocol Compliance, Site Performance, Regulatory	Timeliness of eCRF signatures by PI - Lag time from visit date to eCRF signature is too high or the Investigator has not logged in to EDC for a period of time.	Y	N	N	Y	PI not properly engaged in study oversight	10	5	70%	60%	21.0	KRI: Signature timeliness. Thresholds will depend on your requirement for data review and signature. The requirement might be time-based, for example, monthly or quarterly. It may also be requested at particular intervals in the trial, for example at particular visits, or at Interim database lock, etc.	Follow-up with sites via Monitoring if the KRI is triggered.	Continue to monitor site performance over time to ensure expectations are met.
							Process issue- PI has had instruction that signature is not required until EOS or is not aware of signature expectations	6	5	60%	80%	14.4	Same as above	Ensure that expectations for Investigator review and signature of data are clear in trial documentation and that the CRO is aware of signature requirements, if applicable.	Continue to monitor cycle times and ensure expectations are met. Doing signature once at the end is only appropriate in very short trials. For most, ongoing review of data and signature will be needed.
ACDM	Data Quality	Timeliness of SDV/ SDR relative to data entry (or from data generation; i.e., participant visit date)	Y	N	N	Y	Monitoring performance - Monitor delayed in scheduling site visits, site not cooperating/ accommodating, etc.	6	5	70%	70%	14.7	This KRI would be linked to the monitoring plan and the schedule of visits to the site, as well as the overall monitoring strategy. Here is one KRI example: Percentage of SDV completed on time. Consider follow-up if below a certain threshold, such as below 80% for a site.	Follow up with Monitors to ensure KRIs for SDR/SDV are being met.	There is great variability in monitoring strategies. Some studies might perform 100% SDV, others might have targeted SDV and/or use remote or centralized monitoring. Consult with Monitoring/Clinical operations to determine the best KRI for a particular trial.
							More onsite or remote monitoring visits are needed for the trial	6	5	60%	80%	14.4	Same as above	Ensure the monitoring plan is updated if monitoring visits are added	If the percentage of SDV/SDR being completed on time is too low, consider if the overall monitoring strategy needs update.

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Sponsor Finding	Other	High numbers of cancelled queries in EDC	Y	N	N	Y	Checks not programmed correctly/lack of testing of edit checks	6	6	80%	90%	25.9	Consider inspecting logic and testing for any edit checks that have high numbers of cancelled queries. This could be a particular number, or the mean and standard deviations could be used.	Ensure any incorrectly programmed checks are updated and tested appropriately or inactivated.	This scenario points to process issues around programming and testing of edit checks, rather than data issues. It could also point to the need for potential eCRF updates.
							Non-issue: issue resolved through other means, for example, forthcoming CRF update, or data is correct.	2	4	80%	0%	0.0	Same as above	None	
Sponsor Finding	Data Quality, Protocol Compliance, Site Performance	Missing mandatory forms in EDC for participants that screen fail.	Y	N	N	Y	Inactivated in error by the site or DM	8	5	90%	90%	32.4	Not related to a KRI, was found during review of audit trail over the course of the trial.	Reactivate the forms and ask the site to enter the missing data.	Can also be detected by other means, such as a missing pages report. This scenario could be system dependent.
							Data not collected or not entered by the site	7	5	50%	50%	8.8	Same as above	Ensure all data available is entered, and conduct any retraining on entry requirements as required.	Ensure requirements for data entry related to screen failures is captured in trial documentation like the eCRF Completion Guidelines.
Sponsor Finding	Data Quality, Regulatory Compliance	Additional lines in the audit trail after DBL	Y	Y	Y	Y	Process issues: Access not revoked or CRFs not frozen or locked.	10	3	90%	80%	21.6	Investigate any entries in the audit trail after the date and time of database lock, as this is unexpected behavior.	Ensure that processes are in place to freeze/lock data at key milestones, and to revoke accesses after database lock. Update any processes as needed based on the investigation.	Considering documenting any lines appearing in the audit trail after database lock and why they appear, and document the impact and future mitigations to prevent this.
							Non-Issue: Background processes in the system that do not impact clinical trial data	3	3	90%	40%	3.2	Same as above	Investigate any unexpected rows in the audit trail and assess the impact on clinical trial data, if any.	The system may run background process that appear in the audit trail of the trial but do not have an impact on clinical trial data. If so, consider if any other preventive actions are needed to stop recurrence.
							Non-Issue: Database was unlocked	2	4	100%	0%	0.0	Same as above	Rows in the audit trail should correlate with documentation describing any database unlock and re-lock	Consider trending on any unlocks to determine if any process improvements are needed for future trials.

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Sponsor Finding	Other	System error generating duplicates identified via inspection of the audit trail.	Y	Y	Y	Y	System issue - could be related to a bug, user error, or synchronization issues for example.	6	10	80%	80%	38.4	This finding was not related to a specific KRI. It was found via ongoing review of the audit trail over the course of the trial.	After determining the root cause, ensure it is resolved and that any duplicates are removed. Corrective actions could be contacting the vendor for support, retraining end-users, or resolving synch issues.	Determine the applicability of the issue to other sites/users and proceed accordingly.

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Sponsor Finding	Data Quality, Regulatory Compliance	Dates of SDV were found in the audit trail that did not correlate with a site visit or monitoring report.	y	N	N	y	Fraud: The clinical trial had on-site monitoring, with 100% source data verification (SDV).	20	1	90%	80%	14.4	Found during inspection of the audit trail. Consider visualizing verification events as a timeline, if you expect verification to occur in certain timeframes in a trial.	If the root cause is determined to be fraud, this is a significant compliance and data integrity concern. Consider consulting QA around documentation and resolution. Ensure any affected data is re-verified at the next visit. Consider if monitoring reports should be updated to reflect what SDV did happen.	Consider any retraining needs, and continue to monitor the audit trail over the course of the trial. This type of comparison is complicated by the fact that the data is most likely in different systems.
							System issue or incorrect access	8	3	80%	90%	17.3	Same as above	Ensure the system issue and or access issue is resolved, then ensure that SDV is performed and marked in the system as expected.	
							Process and/or training issue	8	3	70%	70%	11.8	Same as above	Ensure any retraining or process updates as needed. For example, SDV fields should not be completed pre-visit.	
							Non-issue: monitoring performed remotely	1	3	100%	0%	0.0	Same as above	None	

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